
# EFFECT OF RINGER LACTATE PRELOADING ON INDUCTION DOSE REQUIREMENT OF PROPOFOL AND ITS HAEMODYNAMIC STABILITY AT A TERTIARY CENTER

BY

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# EFFECT OF RINGER LACTATE PRELOADING ON INDUCTION DOSE REQUIREMENT OF PROPOFOL AND ITS HAEMODYNAMIC STABILITY AT A TERTIARY CENTER

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# Nepal Health Research Council (NHRC)

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Principal Investigator

National Medical College, Birgunj

**Ref: Approval of thesis proposal**

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Dr. Arushi Jaiswal
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**Ref: Ethical Approval of Research Proposal**

Dear Dr. Arushi Jaiswal,

Thank you for the submission of your research proposal entitled **"Effect of Ringer Lactate Preloading on Induction Dose Requirement of Propofol and its haemodynamic stability at a Tertiary Center. (Ref: PG-NMC/565/079-080)."** to the Institutional Review Committee, National Medical College. The proposal was ethically reviewed by IRC. We are pleased to inform you that the above mentioned research proposal has been approved from ethical point of view by IRC of National Medical College on 30 September 2022.

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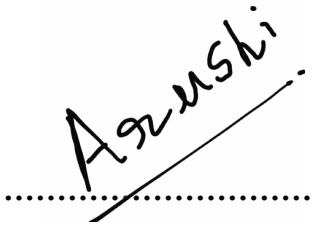

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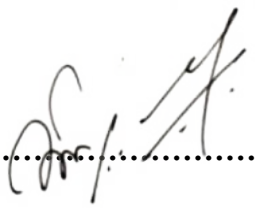

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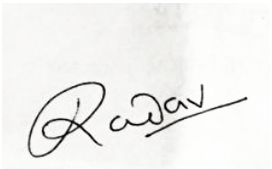

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DATE: 28 January 2025

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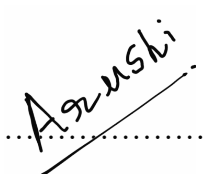

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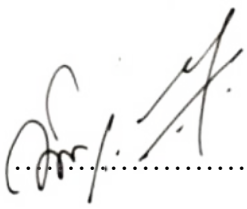

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**Dr. Arushi Jaiswal**

MD Anaesthesiology Resident

# DEDICATION

*This work is dedicated to my parents*

***Mr. Om Prakash Jaiswal*** *and* ***Mrs. Seema Jaiswal****,*

***Mr. Raj Kishor Prasad Shah, Mrs. Asha Devi,***

*My sister* ***Aditi Jaiswal,*** *My brother* ***Utkarsh Jaiswal***

*and my love* ***Dr. Ravi Kumar Shah***

*for their unconditional love, immense support, values and*

*the instillation of authenticity to carry out the work.*

***"Nothing in this world is possible without all of you."***

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# ABBREVIATIONS

| | |
|---|---|
| **ASA** | American Society of Anaesthesiologists |
| **ATP** | Adenosine triphosphate |
| **CI** | Cardiac index |
| **DBP** | Diastolic blood pressure |
| **ECF** | Extracellular fluid |
| **ECG** | Electrocardiogram |
| **EDTA** | Ethylenediaminetetraacetic acid |
| **$ETCO_2$** | End-tidal carbon dioxide |
| **GABA** | Gamma amino butyric acid |
| **HES** | Hydroxy ethyl starch |
| **HR** | Heart rate |
| **IRC** | Institutional review committee |
| **IV** | Intravenous |
| **LDH** | Lactate dehydrogenase |
| **MAP** | Mean arterial pressure |
| **MBP** | Mean blood pressure |
| **min** | Minutes |
| **NIBP** | Noninvasive blood pressure |
| **NS** | Normal saline |

| | |
|---|---|
| **PAP** | Pulmonary artery pressure |
| **pH** | Potential of hydrogen |
| **PVR** | Pulmonary vascular resistance |
| **RL** | Ringer's lactate |
| **SBP** | Systolic blood pressure |
| **sec** | Seconds |
| **SpO2** | Oxygen saturation |
| **SPSS** | Statistical Package for Social Science |
| **SV** | Stroke volume |
| **SVR** | Systemic vascular resistance |
| **Vdss** | Volume of distribution at steady state |

# ABSTRACT


## Background

The induction of anaesthesia is a critical step in the management of patients undergoing surgical procedures. Propofol is a commonly used anaesthetic agent due to its rapid onset and short duration of action, making it ideal for procedures. However, Propofol administration can result in significant hypotension, which can be detrimental to haemodynamic stability. Ringer lactate is a crystalloid solution commonly used for volume replacement in perioperative settings.

## Objective

To evaluate the effect of Ringer lactate preloading on the induction dose requirement of Propofol and its haemodynamic stability at a tertiary center.

## Methodology

This study was a hospital-based comparative study conducted for one year (1st April 2023 to 31st March 2024) after obtaining ethical clearance from the Institutional Review Committee of the National Medical College (PG-NMC/565/079-080), Nepal Health Research Council (519/2022 MT) and also registered at ClinicalTrials.gov (NCT05777135). A total of 60 patients were selected in the study and allocated into two groups of 30 each (Group I and Group II) by ballot method and patient code was given. Group I (n = 30) preloading with Ringer lactate 10 ml/kg over 30 minutes before surgery was done and the Propofol dose requirement for induction of anaesthesia with visualization of loss of eyelash reflex was noted. In Group II (n = 30) no preloading was done and the Propofol dose requirement for induction of anaesthesia with visualization of loss of eyelash reflex was noted. The effect (heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure) was recorded in both groups.

## Results

The mean dose of Propofol required for induction was significantly lower in Group I preloading 1.80 ± 0.18 mg/kg compared to Group II without preloading 2.46 ± 0.44 mg/kg with a P value of < 0.001 which was statistically highly significant. Propofol dose required to achieve the loss of eyelash reflex in Group I (17.17 ± 4.67 seconds) compared to Group II (21.50 ± 5.74 seconds), with a P value of 0.002. Haemodynamic stability, as indicated by heart rate and mean arterial pressure, was better maintained in the preloading group, suggesting that Ringer lactate contributes to improved haemodynamic stability during induction. Although the incidence of coughing and involuntary movements was not statistically significant between groups, the overall reduction in Propofol requirement was notable.

## Conclusion

These findings support the routine use of Ringer lactate preloading to optimize Propofol dosing and maintain haemodynamic stability, potentially improving patient safety and cost-effectiveness in clinical practice. Preloading with Ringer lactate significantly reduces the induction dose of Propofol required to achieve the loss of eyelash reflex and enhances haemodynamic stability during anaesthesia induction. Further studies with larger sample sizes and diverse patient populations are recommended to confirm these results and refine anaesthesia protocols.

## Keywords

Anaesthesia induction, Haemodynamic stability, Preloading, Propofol, Ringer lactate.

# INTRODUCTION

# INTRODUCTION

Anaesthesia is an essential component of surgical procedures, and its main goal is to ensure patient safety and comfort during surgery. The induction of anaesthesia requires careful attention to the patient's haemodynamic status and airway management.

The use of intravenous anaesthetic agents, such as Propofol, is common practice during anaesthesia induction, and understanding the interaction between Ringer lactate and Propofol is crucial for several reasons. Ringer lactate, typically administered as a large volume of fluid, can dilute the concentration of Propofol in the bloodstream. Additionally, Ringer lactate may alter the pharmacokinetics of Propofol, affecting its distribution, metabolism, or elimination, which can result in a decreased required dose. Ringer lactate can influence blood pressure and cardiac output, affecting the uptake, distribution, and clearance of Propofol, ultimately leading to a reduced dose requirement.[1] Moreover, optimizing Propofol dosing based on individual patient characteristics and the concurrent administration of Ringer lactate can improve the efficiency of induction and anaesthesia procedures, enhancing workflow in clinical settings.

Propofol is a short-acting intravenous anaesthetic that provides rapid and smooth induction of anaesthesia and minimal adverse effects compared to other intravenous anaesthetics.[2] However, Propofol induction can result in a rapid decrease in blood pressure, leading to haemodynamic instability.[3] In addition, Propofol-induced hypotension may increase the risk of perioperative myocardial ischaemia, especially in patients with pre-existing coronary artery disease.[4] Hence, strategies to enhance the haemodynamic stability of patients during Propofol induction are warranted.

Preloading with fluids before induction of anaesthesia has been suggested as a method of improving the haemodynamic stability of patients during induction with Propofol.[5] Ringer lactate is one of the commonly used fluids for preloading, which contains lactate as a buffer and electrolytes that are similar to the plasma.[6] Ringer lactate is beneficial in maintaining the pH and electrolyte balance and improving the microcirculation in the tissues.[7]

Several studies have evaluated the effect of Ringer lactate preloading on the haemodynamic stability of patients during anaesthesia induction with propofol. Pradhan et al.[1] conducted a study that demonstrated the beneficial effects of preloading with Ringer lactate, emphasizing its role in stabilizing haemodynamics during the induction phase of anaesthesia. The study suggested that fluid preload with Ringer's lactate helped maintain intravascular volume, thereby reducing the impact of Propofol's vasodilatory effects, which often lead to hypotension. This intervention was found to not only decrease the amount of Propofol needed for effective anaesthesia but also minimize the incidence of hypotension, highlighting its potential as a safe and effective strategy in anaesthetic practice.

Agarwal et al. conducted a study titled “Prevention of Hypotension During Propofol Induction: A Comparison of Preloading with Ringer Lactate and Intravenous Ephedrine”**,** which compared the effectiveness of Ringer lactate preloading and intravenous ephedrine in preventing hypotension during propofol induction. The study concluded that Ringer lactate preloading is a safer and simpler method for maintaining haemodynamic stability during propofol induction, particularly in patients at risk of cardiovascular complications.[8]

Similarly, another study, "Hemodynamic Effects of Propofol: Data from Over 25,000 Patients" by Hug CC et al.[9] provides a comprehensive analysis of the cardiovascular and haemodynamic consequences of propofol administration based on data from over 25,000 patients. The review emphasizes the drug's well-documented effects, such as dose-dependent decreases in blood pressure and heart rate. It highlights the variability in patient response due to factors like age, underlying cardiovascular conditions, and the use of concomitant medications. The study suggests that while propofol generally causes vasodilation and myocardial depression, these effects can be managed with proper dosing and monitoring. Additionally, the literature review underscores the importance of individualized care in optimizing patient safety during the use of propofol in clinical anaesthesia and sedation.

Research by Turner et al.[10] and Al-Ghamdi[11] examined the effectiveness of preloading with crystalloids or colloids in mitigating propofol-induced hypotension, revealing that these interventions were not fully effective in preventing or reducing the occurrence of hypotension. Turner et al. found that although preloading with fluids

could marginally increase intravascular volume and enhance haemodynamic stability, it did not significantly prevent the drop in blood pressure associated with propofol administration. Similarly, Al-Ghamdi's study showed that while colloid and crystalloid solutions are commonly used to counteract the vasodilatory effects of propofol, they failed to offer complete protection against hypotension, particularly in patients with preexisting cardiovascular conditions or advanced age. Both studies suggest that while fluid preloading may be beneficial in certain circumstances, it is not a definitive solution, and additional strategies such as controlled administration of propofol, the use of vasopressors, or individualized patient management are necessary to more effectively mitigate the risks of hypotension during anaesthesia induction. These findings challenge the assumption that preloading alone can reliably prevent haemodynamic instability when using propofol in clinical settings.

The conflicting results of these studies suggest that the effect of Ringer lactate preloading on the induction dose requirement of Propofol and its haemodynamic stability may vary among patients. This study aims to evaluate the effect of Ringer lactate preloading on the induction dose requirement of Propofol and its haemodynamic stability.

# REVIEW OF LITERATURE

# REVIEW OF LITERATURE

## RINGER LACTATE

### Introduction

Ringer's lactate (RL), also known as lactated Ringer's solution (LRS), is a widely used intravenous (IV) fluid solution in medical practice. Its composition closely resembles the electrolyte content of human plasma, making it a preferred choice in situations requiring fluid and electrolyte replacement. Initially developed by Sydney Ringer in the 1880s, this solution was later modified by Alexis Hartmann in the 1930s with the addition of lactate to provide an acid-buffering effect, and hence it is sometimes referred to as Hartmann's solution.[12, 13] Ringer's lactate is often used in surgical settings, trauma care, and burn management due to its favorable physiological properties.

### Composition of Ringer's Lactate

Ringer's lactate solution contains several key electrolytes dissolved in sterile water to maintain isotonicity. A typical composition per liter of Ringer's lactate is:[14]

- Sodium ($Na^+$): 130 mEq/L

- Potassium ($K^+$): 4 mEq/L

- Calcium ($Ca^{++}$): 1.5 mEq/L

- Chloride ($Cl^-$): 109 mEq/L

- Lactate (as sodium lactate): 28 mEq/L

- Water for injection: to make 1 liter

The solution is isotonic, with an osmolarity of approximately 273 mOsm/L[15] and pH of about 6.5,[6] which is comparable to the osmolarity of the plasma.[16] In comparison, normal saline (NS) has an osmolarity of about 286 mOsm/L.[17] The lactate component

in Ringer's lactate serves as a precursor to bicarbonate, which plays a role in buffering metabolic acidosis when metabolized in the liver.

**Physiological Effects of Ringer's Lactate**

**1. Fluid and Electrolyte Repletion**

Ringer's lactate is primarily used for fluid replacement therapy due to its composition, which mimics extracellular fluid (ECF) more closely than other IV fluids like normal saline. Sodium and chloride are present in concentrations similar to those in the ECF, helping to prevent disturbances in electrolyte balance. The potassium and calcium levels are lower than in intracellular fluid, but their presence supports critical physiological functions, including cellular action potentials and muscle contraction.[18] This balanced profile helps avoid the risk of electrolyte disturbances such as hyperchloremic metabolic acidosis, which can occur with the use of 0.9% normal saline.[19]

**2. Acid-Base Balance**

One of the distinguishing features of Ringer's lactate is its role in maintaining acid-base balance. The lactate present in Ringer's lactate acts as a bicarbonate precursor and is metabolized in the liver to generate bicarbonate, thereby contributing to the buffering of metabolic acidosis. This makes Ringer's lactate particularly useful in patients experiencing mild to moderate metabolic acidosis.[20] In contrast to normal saline, which can exacerbate acidosis due to its high chloride content, Ringer's lactate provides an alkalinizing effect that can be beneficial in critically ill patients.

**3. Intravascular Volume Expansion**

Ringer's lactate is effective in expanding intravascular volume, a critical requirement in the management of hypovolemia. The solution is distributed primarily in the extracellular space, with approximately 25% of the infused volume remaining intravascular.[21] This property makes Ringer's lactate particularly useful in cases of acute blood loss, trauma, and surgery, where rapid expansion of plasma volume is necessary to restore haemodynamic stability and ensure adequate tissue perfusion.

## Clinical Applications

### 1. Hypovolemia and Shock

Ringer's lactate is commonly used in the management of hypovolemic shock, where rapid fluid replacement is essential to restore circulating blood volume. In trauma and surgery, patients often lose significant volumes of blood or extracellular fluid. Ringer's lactate electrolyte composition helps restore fluid volume without causing significant electrolyte imbalances, making it a better option than normal saline for large-volume resuscitation.[22] It is particularly useful in haemorrhagic shock, burn patients, and during surgical procedures to prevent dehydration and maintain blood pressure.[23]

### 2. Perioperative Fluid Management

In the perioperative setting, fluid management is vital for maintaining tissue perfusion and electrolyte balance. Ringer's lactate is frequently administered to prevent perioperative hypotension and to replace the fluid loss that occurs during surgery. In cesarean sections and major abdominal surgeries, Ringer's lactate helps to stabilize the patient's haemodynamic status while also correcting mild metabolic acidosis that may develop during prolonged surgery.[24, 25]

### 3. Metabolic Acidosis

Patients with metabolic acidosis, such as those with diabetic ketoacidosis or sepsis, often benefit from the buffering capacity of Ringer's lactate. The conversion of lactate to bicarbonate in the liver helps neutralize excess acid and correct the acid-base imbalance. Ringer's lactate is thus indicated for use in conditions involving mild to moderate metabolic acidosis, though it must be used with caution in patients with severe liver disease or lactic acidosis, where lactate metabolism may be impaired.[26]

### 4. Burn Resuscitation

In the treatment of burn patients, fluid resuscitation is a critical part of the management strategy to prevent shock and organ failure. The Parkland formula, a widely used guideline for calculating fluid requirements in burn patients, recommends

the use of Ringer's lactate as the resuscitation fluid of choice. Ringer's lactate ability to restore intravascular volume while maintaining acid-base balance makes it superior to other fluids for burn patients.[27]

# PROPOFOL

## Introduction

Propofol is the most often used intravenous anaesthetic in contemporary anaesthesia practice.[28, 29] It may be administered as a bolus, an infusion, or in combination. Propofol is prepared in a lipid emulsion which gives it the characteristic milky white appearance and the colloquial name "milk of amnesia." The formula contains soybean oil, glycerol, egg lecithin, and a small amount of the preservative EDTA. A strict aseptic technique must be used when drawing up Propofol as the emulsion can support microbial growth.[30-32] The 2,6-Diisopropylphenol compound was created as a result of early 1970s research on substituted phenol derivatives having hypnotic effects.[33]

Following the elimination of Cremophor, the formulation is composed of 1.2% pure egg phosphatide, 10% soybean oil, 2.25% glycerol, and 1% (weight/volume) Propofol. This formulation is a milky white, slightly viscous material with a pH of 7. Every commercially available formulation is light-insensitive and stable at room temperature.[33]

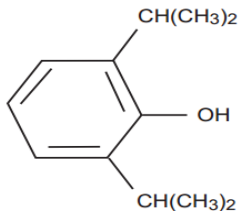



**Figure 1: Chemical structure of Propofol, an alkylphenol derivative.**

## PREPARATION AND PROPERTIES

Since Propofol is an insoluble medication, emulsification requires a lipid carrier.[34] The emulsifying agent in current Propofol formulations is egg lecithin, which is made up of long-chain triglycerides, while the oil phase is soybean oil. This arrangement

promotes the growth of microorganisms and raises the levels of plasma triglycerides. The solution comes in 1% and 2% concentrations and has a milky white color. The pKa is 11. Propofol has an octanol/water partition coefficient of 6761:1 at a pH of 6-8.5.[35]

Propofol is formulated as an emulsion that has a milky white colour and a rather thick texture and has a high solubility in oil (i.e., lipophilic).[36] Propofol is formulated as a macro-emulsion with soybean oil (100 mg/ml), lecithin (12 mg/ml), and glycerol (22.5 mg/ml) that can easily become unstable.[37] Propofol is available in 1% and 2% concentrations in emulsions. Propofol 1% in a vial consists of 200 mg of the drug (10 mg/ml in a volume of 20 ml).[38]

## PHARMACOKINETICS

The two-compartment and three-compartment models have been used to describe pharmacokinetics. Whole-blood Propofol levels in the two-compartment model drop quickly following a single bolus administration due to redistribution and elimination. The initial distribution half-life of Propofol is 2 to 8 minutes. [33]

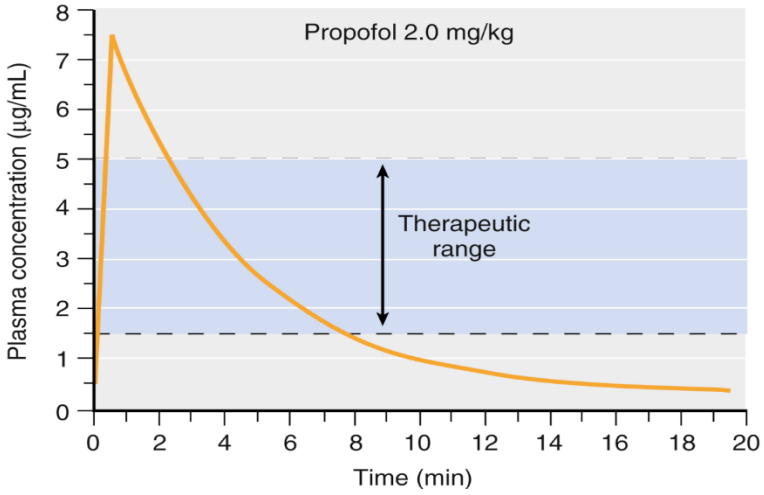



**Figure 2: Simulated time course of whole blood levels of Propofol after an induction dose of 2 mg/kg.**

The elimination half-life in the three-compartment model is 4 to 23.5 hours, while the initial and slow distribution half-lives are 1 to 8 minutes and 30 to 70 minutes, respectively. Propofol returns to the central compartment slowly due to a deep

compartment with limited perfusion, as indicated by the extended elimination half-life. For infusions lasting up to eight hours, Propofol has a context-sensitive half-life of less than forty minutes. Propofol has a clearance of 1.5 to 2.2 L/min, which is greater than the blood flow in the liver and highlights the drug's extrahepatic absorption.[33]

The liver quickly breaks down Propofol into glucuronide and sulfate, which results in water-soluble substances that the kidneys eliminate. In urine, approximately 1% of Propofol is eliminated undigested, while 2% is eliminated in feces. It has been proposed that extrahepatic metabolism or extrarenal elimination is the reason why Propofol clearance outpaces hepatic blood flow. Renal, intestinal, and pulmonary extrahepatic metabolism sites are possible. After a bolus dose, the lungs are in charge of around 30% of the absorption and first-pass elimination. Patients with cirrhosis of the liver do not exhibit any signs of decreased Propofol elimination, even though it is cleared by metabolism quite quickly. During the anhepatic stage of orthotopic liver transplantation, Propofol is eliminated extrahepatically.[33]

Propofol pharmacokinetics are influenced by several variables, including gender, age, weight, underlying medical conditions, concurrent drug use, etc. It may lessen cardiac output and hepatic blood flow, which could compromise its clarity. Propofol has a half-life of 4–7 hours, a volume of distribution ($Vd_{ss}$) of 2–10 L/kg, and a clearance of 20–30 ml/kg/min.[33]

**Table 1: Pharmacokinetic variables of Propofol.**

| | **Adults** | **Children** |
|---|---|---|
| **$Vd_{ss}$ (L/kg)** | 2-10 | 2-24 |
| **Clearance (mL/kg/min)** | 20-30 | 30-40 |
| **Distribution half-life (min)** | 2-8 | 1-6.5 |
| **Elimination half-life (hrs)** | 4-7 | 2.5-12 |
| **Hepatic Extraction Ratio** | > or = 1.0 | > or = 1.0 |

## PHARMACODYNAMICS

### Mechanism of Action

Propofol is thought to work by interacting with GABA receptors to provide sedative-hypnotic effects. Transmembrane chloride channels called GABA receptors bind to GABA, the primary inhibitory neurotransmitter in the central nervous system. The activation of $GABA_A$ receptors leads to an increase in transmembrane chloride conductance, which in turn causes the postsynaptic cell membrane to become hyperpolarized and the postsynaptic neuron to functionally inhibit itself. Propofol primarily mediates its hypnotic activity through binding to the $GABA_A$ receptor β-subunit. By interacting with these particular $GABA_A$ receptor components, Propofol lengthens the time that GABA activates the chloride channel, causing the membranes to become hyperpolarized. It also decreases the pace at which GABA dissociates from the receptor.[39] Additionally, it appears that the α2-adrenoreceptor system contributes indirectly to Propofol's sedative effects.[40] Propofol does not change the excitability of spinal motor neurons, as indicated by the H reflex, indicating that the drug-induced spinal cord depression that occurs during Propofol anaesthesia is not the source of immobility, unlike volatile anaesthetics.

Propofol's pharmacologic action's necessary dose or blood concentrations are lowered by several medications related to anaesthesia. In the absence of any other medication, the Propofol Cp50 (blood concentration required for 50% of participants to not respond to a specified stimulus) ranges from 2.3 to 3.5 µg/ml. The Cp50 of Propofol needed to stop movement on a skin incision is 16 µg/ml; this is significantly decreased when alfentanil or fentanyl concentrations are raised. Usually, awakening happens at concentrations lower than 1.6 µg/ml.[33]

## USES

### Induction and Maintenance of Anaesthesia:

It is the IV induction agent that is most frequently utilized. Dose: 1- 2.5 mg/kg IV dose reduced with increasing age.[33]

To maintain anaesthesia, an IV continuous infusion of 50–150 (100–300) µg/kg/min mixed with either opiate or $N_2O$ is recommended.

In less than 15 seconds, an IV infusion of 1.5 to 2.5 mg/kg Propofol causes unconsciousness in around 30 seconds. [39]

**Sedation:**

In the intensive care unit, Propofol is used to sedate patients undergoing mechanical ventilation as well as during surgical procedures. Regardless of the length of the infusion, continuous Propofol infusion allows for quick recovery after stopping the infusion and titration to the appropriate level of sedation. Half or less of the infusion rates needed for general anaesthesia are needed for sedation to support regional anaesthesia in healthy patients.[33]

Dose: 25-75 µg/kg/min IV

**Table 2: Hypnotic Uses of Propofol.**

| | |
|---|---|
| Induction of general anaestheia | 1-2.5 mg/kg IV dose reduced with increasing age |
| Maintenance of general anaesthesia | 50-150 µg/kg/min IV combined with $N_2O$ or an opiate |
| Sedation | 25-75 µg/kg/min IV |

**ADVANTAGES:**

1. Rapid and smooth induction
2. Depth of anaesthesia can be increased rapidly
3. Suppression of cough reflex and laryngeal reflex
4. Less incidence of postoperative nausea vomiting (PONV)
5. Can be used as a continuous infusion for a long period due to its short context-sensitive half-time
6. Propofol decreases the stress response.

7. Quicker and complete recovery of psychomotor function compared with thiopentone.
8. Amnesic and antioxidant properties
9. Does not cause malignant hyperthermia.
10. Minimal residual effect on the central nervous system.

**DISADVANTAGES**

1. Pain on injection
2. Allergic reactions
3. Myoclonus
4. Apnea
5. Hypotension- most common side effect during induction of anaesthesia
6. Chances of infection if strict asepsis is not taken
7. Rarely, thrombophlebitis of the vein into which Propofol is injected
8. Lactic acidosis –Propofol infusion syndrome
9. Hypertriglyceridemia

**CONTRAINDICATIONS**

1. Propofol is contraindicated in patients with allergies to eggs, egg products, soybeans, or soya products.
2. Obstetrical procedures (Propofol crosses the placenta; and may be associated with neonatal depression).
3. Propofol is not recommended for use in nursing mothers because Propofol has been reported to be excreted in human milk, and the effects of oral absorption of small amounts of Propofol are still not known.
4. Propofol is not recommended for anaesthesia in children below the age of 3 years because safety and effectiveness have not been established yet.

Pradhan et al.[1] conducted a randomized comparative study to evaluate the effectiveness of Ringer lactate preloading versus intravenous ephedrine in preventing hypotension caused by propofol during the induction of general anaesthesia. The study reported that patients in the Ringer lactate preloading group experienced a lower incidence of hypotension, with a mean systolic blood pressure drop of approximately

10-15 mmHg, compared to the ephedrine group**,** which showed a drop of 5-10 mmHg. However, while ephedrine was more effective in minimizing the immediate drop in blood pressure, it was associated with side effects like tachycardia, as the mean heart rate in the ephedrine group increased by 15-20 beats per minute**,** whereas the Ringer lactate group showed no significant change in heart rate. Additionally, the study highlighted that Ringer lactate preloading works by maintaining intravascular volume and cardiac preload, thereby countering the vasodilatory impact of propofol. In contrast, intravenous ephedrine acts as a sympathomimetic agent, increasing vascular tone and heart rate to stabilize blood pressure. While both methods were effective, the study emphasized that Ringer lactate preloading is a safer, cost-effective, and non-pharmacological approach, avoiding the side effects associated with ephedrine, such as tachycardia and hypertension. The findings suggest that fluid preloading with Ringer lactate is a reliable and practical strategy for maintaining haemodynamic stability during propofol induction, particularly in patients at risk of cardiovascular complications.[1]

Agarwal et al.[8] in the study "Prevention of Hypotension During Propofol Induction: A Comparison of Preloading with Ringer Lactate and Intravenous Ephedrine", the authors investigated two strategies for preventing hypotension during propofol induction: Ringer lactate preloading (10 mL/kg) and intravenous ephedrine (6 mg). The study revealed that both interventions effectively reduced the incidence of hypotension, but their mechanisms and outcomes differed. In the Ringer lactate group, the mean systolic blood pressure (SBP) dropped by 12-15 mmHg, and diastolic blood pressure (DBP) by 8-10 mmHg. In contrast, the ephedrine group experienced a smaller decline in SBP of 5-8 mmHg and DBP of 4-6 mmHg, indicating better immediate blood pressure control. However, the ephedrine group showed a significant increase in heart rate, with a rise of 15-20 beats per minute, a potential drawback due to the risk of tachycardia. Conversely, the Ringer lactate group had minimal changes in heart rate, making it a safer option for patients with cardiovascular risks. Overall, while ephedrine provided more immediate haemodynamic stability, Ringer lactate preloading proved to be a simpler, safer, and more physiologically based strategy for maintaining stable blood pressure without the associated tachycardia and hypertensive side effects of ephedrine.[8]

Hug CC et al.[9] conducted the study "Hemodynamic Effects of Propofol: Data from Over 25,000 Patients" which extensively analyzed the haemodynamic consequences of propofol administration in a large cohort of over 25,000 patients across various clinical settings. The study focused on evaluating the impact of propofol on blood pressure and heart rate during induction and maintenance of anaesthesia. It was observed that propofol typically causes a dose-dependent decrease in systolic blood pressure (SBP) and diastolic blood pressure (DBP), with a mean reduction of approximately 20-30% in SBP and 10-20% in DBP. This vasodilatory effect was most pronounced during the induction phase, with a mean drop in SBP of 15-30 mmHg within the first minute of injection. Additionally, heart rate decreased by an average of 5-10 beats per minute after induction, although this was less marked than the decrease in blood pressure. The study also found that the magnitude of hypotension was influenced by factors such as the dose of propofol, the speed of administration, and the presence of preexisting hypovolemia or cardiovascular instability. In patients with low baseline blood pressure or those who were elderly, the hypotensive effect was more pronounced, suggesting that dose adjustments or preemptive interventions might be necessary in these populations. The authors concluded that while propofol provides excellent anaesthetic induction, its haemodynamic effects, particularly the risk of hypotension, need to be carefully managed, especially in high-risk patients.[9]

Vikas et al.[41] studied "Prevention of Hypotension During Induction of Anesthesia with Propofol and Fentanyl: Comparison of Preloading with Crystalloid and Intravenous Ephedrine",[41] the authors aimed to evaluate the effectiveness of crystalloid preloading (Ringer lactate) versus intravenous ephedrine in preventing hypotension during induction with propofol and fentanyl. The study divided patients into three groups: one group received Ringer lactate preloading (10 mL/kg), another received ephedrine (6 mg intravenously), and the third was a control group with no intervention. The study assessed the incidence of hypotension, systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate. The results showed that the ephedrine group experienced the smallest decrease in blood pressure, with a mean SBP drop of 5-8 mmHg and a mean DBP drop of 4-6 mmHg, indicating superior haemodynamic stability. In contrast, the crystalloid preload group had a mean SBP drop of 12-18 mmHg and DBP drop of 6-10 mmHg, which was higher than the ephedrine group, but still significantly reduced compared to the control group. Heart

rate in the ephedrine group increased by 12-15 beats per minute, while the crystalloid preload group experienced a slight increase of 5-7 beats per minute. The study found that while both interventions reduced the incidence of hypotension compared to the control group, the ephedrine group was more effective in preventing the immediate fall in blood pressure, albeit with a potential risk of tachycardia. The authors concluded that intravenous ephedrine provides more immediate stabilization of blood pressure during propofol and fentanyl induction but carries the risk of tachycardia, while crystalloid preloading is a safer and simpler alternative, though less effective in preventing hypotension.[41]

Turner et al.[10] conducted the study "Administration of a Crystalloid Fluid Preload Does Not Prevent the Decrease in Arterial Blood Pressure After Induction of Anaesthesia with Propofol and Fentanyl", the effectiveness of crystalloid fluid preload (10 mL/kg Ringer lactate) in preventing hypotension during propofol and fentanyl induction was evaluated. The results showed that in the crystalloid preload group, the mean systolic blood pressure (SBP) dropped by 20-25 mmHg, and the mean diastolic blood pressure (DBP) decreased by 10-12 mmHg after induction. The control group (no preload) experienced a similar decrease, with SBP dropping by 22-28 mmHg and DBP by 12-15 mmHg. Despite the preload, there was no significant difference in the blood pressure reduction between the groups. The study concluded that crystalloid preload did not prevent the hypotensive effects of propofol and fentanyl, suggesting that other strategies might be required to better manage hypotension during induction.[10]

Al-Ghamdi[11] in the study "Hydroxyethylstarch 6% Preload Does Not Prevent the Hypotension Following Induction with Propofol and Fentanyl", the effectiveness of Hydroxyethylstarch 6% (HES) preload (10 mL/kg) in preventing hypotension during anesthesia induction with propofol and fentanyl was assessed. The results showed that HES preload did not significantly reduce the incidence or severity of hypotension compared to a control group with no preload. Both groups experienced a mean systolic blood pressure (SBP) drop of 18-25 mmHg and a diastolic blood pressure (DBP) decrease of 10-15 mmHg within the first minute of induction. Heart rate increased by 8-12 beats per minute in both groups. The study concluded that despite restoring intravascular volume, HES preload was ineffective in preventing

hypotension caused by the vasodilatory effects of propofol and fentanyl, suggesting the need for alternative strategies.[11]

The safe administration of anaesthesia is the primary goal of an anaesthesiologist. One of the most crucial steps in the administration of general anaesthesia is the induction of anaesthesia since it is typically linked to a variety of haemodynamic changes. Propofol is one of the most often used anaesthetics in practice today. Propofol has a quick start of action and quick recovery. Additionally, it offers good intubating conditions and, at low dosages, has strong anti-emetic properties.[42] In addition to these benefits, it also has some negative effects that limit how often it can be used. Propofol's most notable and significant adverse effect is a drop in arterial blood pressure that occurs during the induction of anaesthesia, regardless of the existence of cardiovascular illness. The reduction in peripheral vascular resistance and the reduction in cardiac output are the main causes of the drop in arterial pressure. Propofol has a hypotensive effect on blood pressure because it reduces systemic vascular resistance,[43, 44] or cardiac output.[45] This is achieved through a combination of decreased myocontractility,[42] altered baroreflex mechanism,[46] and venous and arterial vasodilatations.[45, 47, 48] Therefore, the anaesthetist's job during induction is difficult preserving haemodynamic stability.

# OBJECTIVES

# OBJECTIVES

## GENERAL OBJECTIVE

- To evaluate the effect of Ringer lactate preloading on the induction dose requirement of Propofol and its haemodynamic stability.

## SPECIFIC OBJECTIVES

- To estimate the Propofol requirement for induction dose with respect to the loss of eyelash reflex in Ringer lactate preloaded versus the control group.
- To compare the haemodynamic response of the Ringer lactate preloading group and without preloading group on the induction dose requirement of Propofol.

# HYPOTHESIS

# HYPOTHESIS

**Null hypothesis:**

Preloading of Ringer lactate does not affect the induction dose requirement of Propofol.

**Alternate hypothesis:**

Preloading of Ringer lactate affects the induction dose requirement of Propofol. There is a difference in induction dose requirement with Propofol which is real.

# METHODOLOGY

# METHODOLOGY

## SETTING

This study was a hospital-based comparative study. The study was conducted in the Department of Anaesthesiology at the National Medical College and Teaching Hospital, Birgunj, Nepal. This is a tertiary-level teaching hospital. The proposal of this thesis was submitted and approved by:

a. Institutional Review Committee (National Medical College): PG-NMC/565/079-080
b. Nepal Health Research Council: 519/2022 MT
c. Registered at ClinicalTrials.gov: NCT05777135

## STUDY DURATION

The duration of the study was 12 months which was conducted between (1st April 2023 to 31st March 2024).

## STUDY DESIGN

Comparative study.

## SAMPLING TECHNIQUE

Convenience sampling technique.

## SAMPLE SIZE DISTRIBUTION

A total of 60 patients (30 in each group).

The sample size was determined from the previous similar study[49]

$$n = 2 \times \left[\frac{Z_\alpha + Z_\beta}{\Delta}\right]^2 \times \sigma^2$$

Where n = minimum sample size for each group

$Z_\alpha$ = 1.96 (95% confidence interval)

$Z_\beta$ = 0.84 (80% power)

σ = 2.0 mg/kg (standard deviation of Propofol dose requirement)[49]

Δ = 1.5 mg/kg (expected effect size)[50]

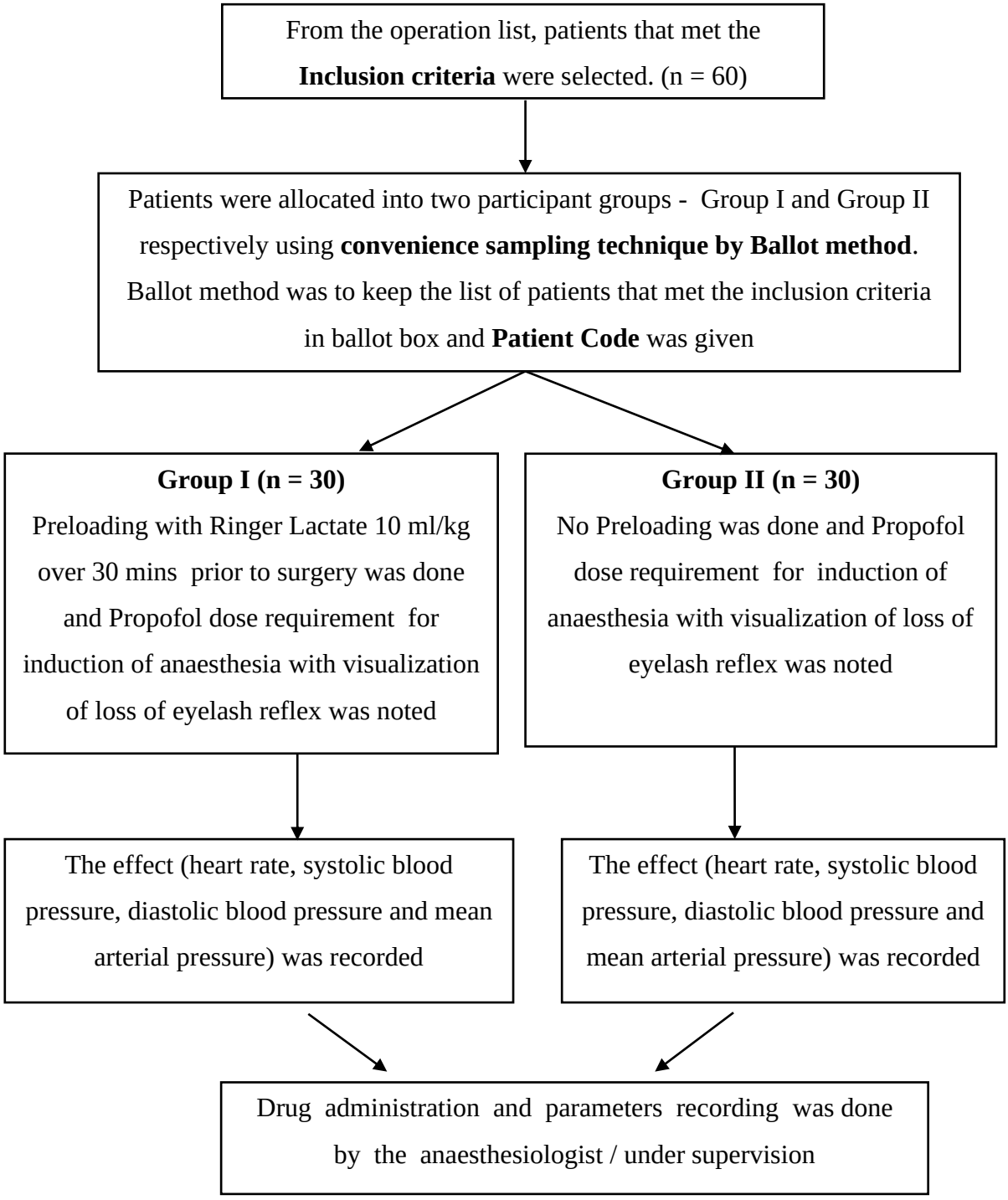
$$n = 2 \times \left[\frac{1.96 + 0.84}{1.5}\right]^2 \times 2^2$$

n = 27.87

The minimum sample size is 27.87 round off to 30.

A total of 60 patients were selected in the study and allocated into two groups of 30 each (Group I and Group II) using a convenience sampling technique by Ballot method and Patient code was given.

## SAMPLING METHOD



# SELECTION CRITERIA

## Inclusion Criteria

1. Patients scheduled for elective surgeries
2. American Society of Anaesthesiologists (ASA) class I patients
3. Age between 18 - 45 years
4. Any surgery under general anaesthesia requiring endotracheal intubation
5. Body mass index (BMI) –18.5 - 24.9 $kg/m^2$

## Exclusion Criteria

1. Emergency surgery
2. Patients with multiple injuries, pregnancy
3. Airway Mallampati grade II, III and IV
4. Allergy to Propofol
5. Haemodynamically unstable patient.

## DATA COLLECTION

1. All patients that met the inclusion criteria were visited the day before surgery for pre-anaesthetic evaluation and were allocated to Groups I and II by ballot method and patient code was given.
2. Patients were advised to have a Tablet of Alprazolam 0.25 mg at night and to keep nil per oral for 8 hours. Injection Ranitidine 150 mg and Injection Metoclopramide 10 mg intravenous were given at 6 am on the morning day of operation.
3. On the day of surgery, after confirming the pre-anaesthetic checkup, patients were mobilized to the operation theatre.
4. Monitors like electrocardiogram (ECG), noninvasive blood pressure (NIBP), pulse oximetry (SpO2), and End-tidal carbon dioxide ($ETCO_2$) were monitored continuously.
5. Intravenous lines were secured and Ringer lactate 10 ml/kg was given 30 mins before the surgery to patients included in the study intervention group (Group I).
6. All drugs given in the operation theatre were given by the supervisor or under supervision.
7. All patients (Groups I and II) were preoxygenated with 100 % oxygen for 3 minutes and premedicated with intravenous Glycopyrrolate 0.2 mg, Midazolam 0.03 mg/kg, and Fentanyl 2 mcg/kg.
8. After 3 minutes, patients were induced with titrated doses of intravenous Propofol following visualization of loss of eyelash reflex which was noted, and the dose requirement of Propofol was documented.
9. Anaesthesia was maintained with 100% Oxygen and Isoflurane.
10. The airway was secured with an appropriate size endotracheal tube following injection of Vecuronium 0.1 mg/kg intravenous and bag and mask ventilation for 3 minutes.
11. Endotracheal tube placement was confirmed and the patient was kept on a ventilator in volume control mode and ventilation was aimed to maintain normocarbia.
12. After the surgery injection of Ondansetron 0.1 mg/kg intravenous was given and residual neuromuscular blockade was reversed with an injection of

Glycopyrrolate 6 mcg/kg intravenous and an injection of Neostigmine 0.05 mg/kg intravenous.

13. Patients were assessed clinically and extubated. Heart rate, Systolic blood pressure, Diastolic blood pressure, and Mean arterial pressure were recorded before preload (baseline), after injecting Propofol, and after intubation 0, 1, 3, 5, and 10 minutes following intubation for statistical analysis.

## DATA ANALYSIS

All the collected data were entered in Microsoft Office Excel Worksheet 2021 and statistical analysis was done using the IBM Statistical Package for Social Science (SPSS) version 27. The mean, standard deviation, number, and percentage (%) were determined as applicable for both groups. Student t-test (two-tailed, independent) was used to find the significance of study parameters on a continuous scale between two groups. The Chi-square and Fisher Exact tests were used to find the significance of study parameters on a categorical scale between the groups. A 95% confidence interval (critical t-value of 1.96 from the t-distribution) was used for the study and a P value of less than 0.05 was considered statistically significant. These findings were then presented in the form of tables. The final results were discussed and then a conclusion was derived.

## ETHICAL CLEARANCE

Ethical approval was obtained from the Institutional Review Committee of the National Medical College, Nepal Health Research Council, and National Clinical Trial before the start of the study. The aim and objectives of the study along with its procedure, risks, benefits, and protocol were explained in an easily understandable local language to the parents or the nearest relative attendants at the time of enrollment of each case. Written informed consent was taken from each patient and assured that the entire information and recording would be kept confidential. The consent was taken during a pre-anaesthetic checkup (one day before the operation schedule). Participation in the study was entirely voluntary, and any participant may withdraw at any time.

# RESULTS

# RESULTS

The present study entitled "Effect of Ringer lactate preloading on induction dose requirement of Propofol and its haemodynamic stability at a tertiary center" was conducted at National Medical College and Teaching Hospital, Birgunj, Nepal from 1st April 2023 to 31st March 2024.

A total of 60 patients were selected in the study and allocated into two groups of 30 each (Group I and Group II) to compare the effect of Ringer lactate preloading on the induction dose requirement of Propofol and its haemodynamic stability. The observations made in the study are submitted below.

**Table 3: Gender distribution among the patients.**

| Gender | Group I (n = 30) | | Group II (n = 30) | | Degree of freedom (df) | Chi-square ($X^2$) | P value |
|---|---|---|---|---|---|---|---|
| | Number | Percentage (%) | Number | Percentage (%) | | | |
| Male | 4 | 13.3 | 8 | 26.7 | | | |
| Female | 26 | 86.7 | 22 | 73.3 | 1 | 1.667 | 0.333* |
| Total | 30 | 100 | 30 | 100 | | | |

*Fisher's Exact Test

In Group I 13.3% of the patients were males and 86.7% were females and in Group II it was 26.7% and 73.3% respectively. Samples were matched with a P value of 0.333 which was statistically not significant as given in Table 3.

**Table 4: Comparison of Height, Weight, and BMI between the groups.**

| | Group I Mean ± SD | Group II Mean ± SD | Degree of freedom (df) | t-test | P value |
|---|---|---|---|---|---|
| Height (m) | 1.6085 ± 0.03 | 1.6004 ± 0.05 | 58 | 0.625 | 0.535 |
| Weight (kg) | 56.57 ± 6.91 | 55.33 ± 7.01 | 58 | 0.686 | 0.496 |
| BMI ($kg/m^2$) | 21.82 ± 2.13 | 21.54 ± 1.82 | 58 | 0.540 | 0.591 |

P value derived using Independent t-test.

Table 4 shows the mean height, mean weight, and mean BMI of the patients in Group I and Group II. The BMI for Group I and Group II was 21.82 ± 2.13 $kg/m^2$ and 21.54 ± 1.82 $kg/m^2$ respectively. Samples for BMI were matched with a P value of 0.591 which was statistically not significant.

**Table 5: Comparison of Propofol dose given between the groups.**

| | Group I Mean ± SD | Group II Mean ± SD | Degree of freedom (df) | t-test | P value |
|---|---|---|---|---|---|
| Propofol dose given (mg/kg) | 1.80 ± 0.18 | 2.46 ± 0.44 | 58 | - 7.51 | < 0.001* |

P value derived using Independent t-test; * – significant.

The Propofol dose given in Group I was 1.80 ± 0.18 mg/kg whereas in Group II was 2.46 ± 0.44 mg/kg which was statistically highly significant with a P value < 0.001 shown in Table 5.

**Table 6: Mean Visualization of Loss of Eyelash Reflex.**

| | Group I Mean ± SD | Group II Mean ± SD | Degree of freedom (df) | t-test | P value |
|---|---|---|---|---|---|
| Mean Visualization of Loss of Eyelash Reflex (seconds) | 17.17 ± 4.67 | 21.50 ± 5.74 | 58 | - 3.204 | 0.002* |

P value derived using Independent t-test; * – significant.

In Group I, the Mean visualization of loss of eyelash reflex was 17.17 ± 4.67 seconds, whereas in comparison to Group II it was 21.50 ± 5.74 seconds which was statistically significant with a P value of 0.002 as given in Table 6.

**Table 7: Comparison of mean Heart rate (beats per minute) in both groups.**

| Heart rate (beats per minute) | Group I Mean ± SD | Group II Mean ± SD | Degree of freedom (df) | t-test | P value |
|---|---|---|---|---|---|
| Baseline | 86.93 ± 13.97 | 87.07 ± 14.98 | 58 | - 0.036 | 0.972 |
| After IV administration of Propofol | 86.73 ± 12.71 | 84.00 ± 14.78 | 58 | 0.768 | 0.446 |
| At intubation (0 minute) | 84.50 ± 14.22 | 85.97 ± 14.58 | 58 | - 0.394 | 0.695 |
| 1 minute after intubation | 85.67 ± 13.93 | 86.40 ± 15.75 | 58 | - 0.191 | 0.849 |
| 3 minutes after intubation | 85.27 ± 12.17 | 87.50 ± 16.51 | 58 | - 0.596 | 0.553 |
| 5 minutes after intubation | 84.13 ± 11.47 | 87.43 ± 12.51 | 58 | - 1.064 | 0.292 |
| 10 minutes after intubation | 84.33 ± 11.11 | 85.80 ± 14.28 | 58 | - 0.444 | 0.659 |

P value derived using Independent t-test.

The haemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure) were compared between Group I and Group II at baseline, after iv administration of Propofol, at intubation (0 minute), 1 minute after intubation, 3 minutes after intubation, 5 minutes after intubation, and 10 minutes after intubation.

The mean percentage change (heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure) was compared with baseline value in both groups. An increase or decrease in Heart rate and Mean arterial pressure by 20% was considered significant in this study. The mean heart rate in Group I, when compared to Group II, was statistically not significant as shown in Table 7.

**Table 8: Mean percentage change in Heart rate (beats per minute) within the groups.**

| Heart rate (beats per minute) | Group I | | Group II | |
|---|---|---|---|---|
| | **Difference from baseline** | **Percentage change (%)** | **Difference from baseline** | **Percentage change (%)** |
| Baseline | - | - | - | - |
| After IV administration of Propofol | 0.2 | 0.23 | 3.07 | 3.589 |
| At intubation (0 minute) | 2.43 | 2.79 | 1.1 | 1.286 |
| 1 minute after intubation | 1.26 | 1.45 | 0.67 | 0.783 |
| 3 minutes after intubation | 1.66 | 1.91 | 0.43 | 0.50 |
| 5 minutes after intubation | 2.8 | 3.22 | 0.36 | 0.42 |
| 10 minutes after intubation | 2.6 | 2.99 | 1.27 | 1.48 |

Table 8 shows the mean percentage change in heart rate from baseline in each group. A rise in heart rate by 20% from baseline was considered significant in this study. On analysis, there was no significant difference in heart rate from the baseline at any point in time in both groups. The maximum increase in heart rate was 3.22% in Group I, whereas in Group II it was 3.589%.

**Table 9: Comparison of mean Systolic blood pressure (mm Hg) in both groups.**

| Systolic BP (mm Hg) | Group I Mean ± SD | Group II Mean ± SD | Degree of freedom (df) | t-test | P value |
|---|---|---|---|---|---|
| Baseline | 117.33 ± 11.08 | 116.77 ± 10.48 | 58 | 0.203 | 0.839 |
| After IV administration of Propofol | 115.40 ± 11.86 | 103.07 ± 10.76 | 58 | 4.216 | < 0.001* |
| At intubation (0 minute) | 112.27 ± 13.91 | 105.50 ± 12.26 | 58 | 1.998 | 0.050* |
| 1 minute after intubation | 114.60 ± 10.25 | 107.37 ± 13.28 | 58 | 2.362 | 0.022* |
| 3 minutes after intubation | 114.27 ± 11.09 | 109.00 ± 13.72 | 58 | 1.634 | 0.108 |
| 5 minutes after intubation | 119.37 ± 13.16 | 110.67 ± 10.45 | 58 | 2.835 | 0.006* |
| 10 minutes after intubation | 117.57 ± 13.61 | 114.43 ± 18.02 | 58 | 0.760 | 0.450 |

P value derived using Independent t-test; * – significant.

Table 9 shows the comparison of mean systolic blood pressure between the groups. In both groups, there was a fall in systolic blood pressure. After IV administration of Propofol, the P value < 0.001 was statistically highly significant. At intubation, 1 minute after intubation, and 5 minutes after intubation, the P value was < 0.05 which was statistically significant.

**Table 10: Mean percentage change in Systolic blood pressure (mm Hg) within the groups.**

| Systolic BP (mm Hg) | Group I | | Group II | |
|---|---|---|---|---|
| | **Difference from baseline** | **Percentage change (%)** | **Difference from baseline** | **Percentage change (%)** |
| Baseline | - | - | - | - |
| After IV administration of Propofol | 1.93 | 1.65 | 13.7 | 12.46 |
| At intubation (0 minute) | 5.06 | 4.34 | 11.27 | 10.25 |
| 1 minute after intubation | 2.73 | 2.34 | 9.4 | 8.55 |
| 3 minutes after intubation | 3.06 | 2.62 | 7.7 | 7.00 |
| 5 minutes after intubation | 2.04 | 1.75 | 6.1 | 5.54 |
| 10 minutes after intubation | 0.24 | 0.20 | 2.34 | 2.12 |

Table 10 shows the mean percentage change in systolic blood pressure from baseline in each group. On analysis, there was no significant difference in systolic blood pressure from the baseline at any point in time in both groups. The maximum increase in systolic blood pressure was 4.34% in Group I, whereas in Group II it was 12.46%.

**Table 11: Comparison of mean Diastolic blood pressure (mm Hg) in both groups.**

| Diastolic BP (mm Hg) | Group I Mean ± SD | Group II Mean ± SD | Degree of freedom (df) | t-test | P value |
|---|---|---|---|---|---|
| Baseline | 75.63 ± 10.40 | 71.27 ± 10.46 | 58 | 1.621 | 0.110 |
| After IV administration of Propofol | 72.13 ± 7.91 | 62.20 ± 9.58 | 58 | 4.378 | < 0.001* |
| At intubation (0 minute) | 69.67 ± 11.61 | 65.70 ± 10.86 | 58 | 1.366 | 0.177 |
| 1 minute after intubation | 72.67 ± 9.52 | 65.10 ± 12.00 | 58 | 2.705 | 0.009* |
| 3 minutes after intubation | 72.30 ± 12.00 | 67.10 ± 12.91 | 58 | 1.615 | 0.112 |
| 5 minutes after intubation | 74.47 ± 10.47 | 69.07 ± 9.27 | 58 | 2.114 | 0.039* |
| 10 minutes after intubation | 72.53 ± 10.67 | 69.50 ± 10.66 | 58 | 1.101 | 0.275 |

P value derived using Independent t-test; * – significant.

Table 11 shows the comparison of mean diastolic blood pressure between the groups. In both groups, there was a fall in diastolic blood pressure. After IV administration of Propofol, the P value was < 0.001 which was statistically highly significant, at 1 minute after intubation the P value was 0.009 which was statistically significant, and at 5 minutes after intubation the P value was 0.039 which was statistically significant.

**Table 12: Mean percentage change in Diastolic blood pressure (mm Hg) within the groups.**

| | Group I | | Group II | |
|---|---|---|---|---|
| **Diastolic BP (mm Hg)** | **Difference from baseline** | **Percentage change (%)** | **Difference from baseline** | **Percentage change (%)** |
| Baseline | - | - | - | - |
| After IV administration of Propofol | 3.5 | 4.73 | 9.07 | 13.59 |
| At intubation (0 minute) | 5.96 | 8.06 | 5.57 | 8.34 |
| 1 minute after intubation | 2.96 | 4.00 | 6.17 | 9.24 |
| 3 minutes after intubation | 3.33 | 4.50 | 4.17 | 6.24 |
| 5 minutes after intubation | 1.16 | 1.57 | 2.2 | 3.29 |
| 10 minutes after intubation | 3.1 | 4.19 | 1.77 | 2.65 |

Table 12 shows the mean percentage change in diastolic blood pressure from baseline in each group. The maximum increase in diastolic blood pressure was 8.06% in Group I, whereas in Group II it was 13.46%.

**Table 13: Comparison of mean arterial pressure (mm Hg) in both groups.**

| Mean arterial pressure (mm Hg) | Group I Mean ± SD | Group II Mean ± SD | Degree of freedom (df) | t-test | P value |
|---|---|---|---|---|---|
| Baseline | 90.27 ± 11.96 | 85.70 ± 11.29 | 58 | 1.520 | 0.134 |
| After IV administration of Propofol | 86.33 ± 8.40 | 75.97 ± 10.43 | 58 | 4.236 | < 0.001* |
| At intubation (0 minute) | 84.20 ± 11.46 | 78.60 ± 12.01 | 58 | 1.847 | 0.070 |
| 1 minute after intubation | 86.03 ± 10.36 | 79.87 ± 11.91 | 58 | 2.139 | 0.037* |
| 3 minutes after intubation | 86.33 ± 12.37 | 80.93 ± 12.82 | 58 | 1.660 | 0.102 |
| 5 minutes after intubation | 87.10 ± 12.54 | 83.43 ± 11.05 | 58 | 1.201 | 0.235 |
| 10 minutes after intubation | 86.70 ± 11.08 | 83.10 ± 11.49 | 58 | 1.235 | 0.222 |

P value derived using Independent t-test; * – significant.

Table 13 shows the comparison of mean arterial pressure between the groups. In both groups, there was a fall in mean arterial pressure. After IV administration of Propofol, the P value < 0.001 was statistically highly significant, and at 1 minute after intubation, the P value was 0.037 which was statistically significant.

**Table 14: Mean percentage change in Mean arterial pressure (mm Hg) within the groups.**

| Mean arterial pressure (mm Hg) | Group I | | Group II | |
|---|---|---|---|---|
| | Difference from baseline | Percentage change (%) | Difference from baseline | Percentage change (%) |
| Baseline | - | - | - | - |
| After IV administration of Propofol | 3.94 | 4.46 | 9.73 | 12.03 |
| At intubation (0 minute) | 6.07 | 6.87 | 7.1 | 8.78 |
| 1 minute after intubation | 4.24 | 4.80 | 5.83 | 7.21 |
| 3 minutes after intubation | 3.94 | 4.46 | 4.77 | 5.90 |
| 5 minutes after intubation | 3.17 | 3.59 | 2.27 | 2.81 |
| 10 minutes after intubation | 3.57 | 4.04 | 2.6 | 3.21 |

Table 14 shows the mean percentage change in mean arterial pressure from baseline in each group. The maximum increase in mean arterial pressure was 6.87% in Group I, whereas in Group II it was 12.03%.

**Table 15: Comparison of complications amongst patients in both groups.**

| Complications | Group I (n = 30) | | Group II (n = 30) | | P value |
|---|---|---|---|---|---|
| | Number | Percentage (%) | Number | Percentage (%) | |
| Apnoea | 1 | 3.3 | 2 | 6.7 | 0.590 |
| Involuntary movement | 1 | 3.3 | - | - | |
| Coughing | 5 | 16.7 | 3 | 10.0 | |
| None | 23 | 76.7 | 25 | 83.3 | |

P value derived using Independent t-test.

In both groups, the majority of patients did not have any complications as shown in Table 15. However, from the various complications, in Group I there was apnoea in 3.3%, involuntary movement in 3.3%, and cough in 16.7% of patients. In Group II there was apnoea in 6.7% and cough in 10% of patients. P value was 0.590 which was statistically not significant.

# DISCUSSION

# DISCUSSION

The study aimed to evaluate the effect of Ringer lactate preloading on the induction dose requirement of propofol and its impact on haemodynamic stability at a tertiary center. The comparative study found that preloading with Ringer lactate significantly reduced the propofol dose required to achieve the loss of eyelash reflex, facilitated faster anaesthesia onset, and enhanced haemodynamic stability by maintaining intravascular volume and blood pressure.

The mean induction dose of Propofol after preloading with Ringer lactate was statistically highly significant in this study (P value < 0.001). The Propofol dose given in Group I was 1.80 ± 0.18 mg/kg whereas in Group II was 2.46 ± 0.44 mg/kg. Analogous research conducted by Manisha and Brahma,[1] Hug CC et al.,[9] Anil et al.,[51] Suganya et al.[49], and Djaiani and Ribes[52] likewise revealed various degrees of reduction in the required induction dose following preload. Group I's induction dose requirement may have been lowered as a result of the preloading effect with Ringer lactate before the induction dose requirement of Propofol.

In the preloading group (Group I), the mean visualization of loss of eyelash reflex was 17.17 ± 4.67 seconds, whereas in comparison to the non-preloading group (Group II), it was 21.50 ± 5.74 seconds which was statistically significant with a P value of 0.002. The statistically significant difference in the mean time to visualization of loss of eyelash reflex between the preloading group (Group I) and the non-preloading group (Group II) suggests that preloading with Ringer lactate has a noticeable impact on the induction process with Propofol. The faster loss of the eyelash reflex in the preloading group indicates a quicker onset of anaesthesia, which can be attributed to several factors such as improved haemodynamic stability, reduced Propofol requirement, and enhanced drug distribution.

The observed results, where the preloaded group (Group I) required a lower dose of propofol (1.80 mg/kg) and demonstrated a faster onset of anaesthesia (mean 17.17 seconds to loss of eyelash reflex) with better haemodynamic stability, can be attributed to the effects of Ringer lactate preloading. Preloading optimizes intravascular volume, enhancing cardiac output and maintaining blood pressure, which prevents the hypotensive effects of propofol. This stable haemodynamic

environment improves perfusion, ensuring more efficient and predictable delivery of propofol to the central nervous system, thereby reducing the required dose. Additionally, better intravascular volume prevents reflexive compensatory mechanisms like vasoconstriction, which could delay drug distribution in non-preloaded patients. The enhanced perfusion and drug distribution in the preloaded group facilitates a quicker onset of anaesthesia, as reflected by the shorter time to loss of eyelash reflex, while simultaneously minimizing the cardiovascular depressant effects of propofol. Together, these factors lead to a more effective, efficient, and safer induction process in the preloaded group.

This study showed that the heart rates of the two groups were similar, with no statistically significant difference seen. A rise in heart rate by 20% from baseline was considered significant in this study. On analysis, there was no significant difference in heart rate from the baseline at any point in time in both groups. This was consistent with research by Bilotta et al.[53] which found that patients induced with a decreased Propofol infusion rate did not have a change in heart rate. Suganya et al.,[49] Pensado et al.,[54] and Cullen et al.[55] had justified quoting it as haemodynamic changes related to dose-dependent.

This study also shows that the rise in the mean percentage change in heart rate following Propofol administration in Group II was comparable to the rise in heart rate seen in research by Anil et al.[51] and Fairfield et al.[56] Propofol may initially lower systemic vascular resistance, which triggers a reflex increase in sympathetic activity mediated by baroreceptors in the aortic arch and carotid sinus, raising heart rate. This could account for some of the increase in heart rate.[56] This study's mean percentage rise in heart rate following Propofol induction contrasts with Kataria et al. (0.74%),[57] Djaiani and Ribes's (8%),[52] and Edomwonyi et al. (8.65%)[58] heart rate reduction following induction.

When comparing the intragroup assessment of heart rate to the baseline, it is observed that Group II's heart rate increased (3.589%) after receiving Propofol, whereas Group I's mean heart rate increased at different intervals, peaking at 3.22% five minutes after intubation. This rise in heart rate following Propofol injection is comparable to findings by Elisabeth Dewhirst et al.,[59] Akintimoye et al.,[60] and Nitin Shah et al.[61]

In both groups, there was a fall in mean systolic blood pressure. After the administration of Propofol injection, the P value < 0.001 was statistically highly significant. At intubation, 1 minute after intubation, and 5 minutes after intubation, the P value was < 0.05 which was statistically significant. On analysis, there was no significant difference in mean percentage change in systolic blood pressure from the baseline at any point in time in both groups. The maximum mean percentage change in systolic blood pressure was 4.34% in Group I, whereas in Group II it was 12.46%. This might have resulted from preloading with Ringer lactate after the total Propofol induction dosage requirement was lowered. This lowered the total Propofol dose required for induction and led to more stable haemodynamic characteristics.

In both groups, there was a fall in diastolic blood pressure. After administration of Propofol injection, the P value was < 0.001 which was statistically highly significant, at 1 minute after intubation the P value was 0.009 which was statistically significant, and at 5 minutes after intubation the P value was 0.039 which was statistically significant. The maximum mean percentage change in diastolic blood pressure was 8.06% in Group I, whereas in Group II it was 13.46%.

In both groups, there was a fall in mean arterial pressure. After administration of Propofol injection, the P value < 0.001 was statistically highly significant, and at 1 minute after intubation, the P value was 0.037 which was statistically significant. The maximum mean percentage change in mean arterial pressure was 6.87% in Group I, whereas in Group II it was 12.03%.

The results of this study demonstrate that dose-dependent alterations in haemodynamics occur, since Group I received lower dosages of Propofol than Group II. A comparable finding of dose-dependent haemodynamic alterations was reported by Djaiani and Ribes,[52] who found that priming with Propofol reduced mean arterial pressure by 15% as opposed to the 23% reduction in the control. Similarly, Kataria et al.[57] reported a noteworthy decrease in post-induction systolic blood pressure (10.1%) and diastolic blood pressure (10.8%) in comparison to the control group, which demonstrated a decrease of 16% and 18% in systolic and diastolic blood pressure, respectively. These results support the concept of dose-dependent haemodynamic changes.

After receiving Propofol intravenously and one minute after being intubated, the mean arterial pressure in Group I was statistically significantly lower than that of Group II ($P < 0.001$ and 0.037, respectively). This is consistent with the findings of Djaiani and Ribes,[52] Anil et al.,[51] and Suganya et al.[49] regarding a dose-dependent drop in blood pressure. Group II experienced a more significant decrease in blood pressure with a higher dosage of Propofol than Group I, which was made feasible by the preloading with Ringer lactate and led to a more stable haemodynamic state.

The reduced induction dose of propofol has been observed in other techniques such as the priming technique, midazolam premedication, and dexmedetomidine infusion, but these methods have notable limitations and side effects that differentiate them from Ringer lactate preloading. The priming technique, which involves administering a small sub-induction dose of propofol before the full induction dose, can cause patient discomfort or mild sedation during the priming phase. Additionally, it poses a risk of oversedation or apnea if the priming dose is miscalculated, without addressing the underlying haemodynamic effects of propofol.[49, 51, 52, 62, 63] In contrast, Ringer lactate preloading addresses haemodynamic stability directly by maintaining intravascular volume, avoiding the procedural complexities and risks of oversedation inherent to priming.[1, 8]

Similarly, midazolam premedication reduces propofol requirements by enhancing sedation but is associated with delayed postoperative recovery, drowsiness, and an increased risk of respiratory depression, particularly in elderly or high-risk patients.[64] There is also a potential for paradoxical agitation or excitement in some individuals. Ringer lactate preloading, by comparison, is devoid of these pharmacological side effects, ensuring quicker recovery and eliminating risks of respiratory compromise or postoperative sedation.[1, 8]

The use of dexmedetomidine, an α2-adrenergic agonist, has been effective in reducing propofol requirements by providing sedation and analgesia, but it is frequently associated with significant bradycardia and hypotension, especially at higher doses. It also requires close haemodynamic monitoring, adding to procedural complexity, and its cost can limit widespread use in resource-constrained settings.[65] In contrast, Ringer lactate preloading is a low-cost, simple intervention that not only avoids bradycardia

or hypotension but actively improves haemodynamic stability, making it more practical and safer for routine clinical application.[1, 8]

This study highlights the unique benefits of Ringer lactate preloading as a non-pharmacological, cost-effective, and widely applicable method for reducing the induction dose of propofol while ensuring haemodynamic stability, distinguishing it from other techniques that carry notable risks and side effects.

In both groups, the majority of patients did not have any complications. However, from the various complications, in Group I there was apnoea in 3.3%, involuntary movement in 3.3%, and cough in 16.7% of patients. In Group II there was apnoea in 6.7% and cough in 10% of patients. P value was 0.590 which was statistically not significant.

A higher incidence of apnoea was observed in Group II (6.7%) when compared to Group I (3.3%) and this is probably due to the cardiorespiratory depressant effect which is dose-dependent. A similar observation was made by Djaiani and Ribes[52] as the control group had more complications than the intervention group.

Involuntary movement was seen in Group I (3.3%) though not statistically significant. This is probably due to factors such as individual patient variability, depth of anaesthesia, and additional premedications. However, the low incidence (3.3%) and lack of statistical significance suggest that the effect of preloading on involuntary movements may not be substantial.

The occurrence of cough in Group I (16.7%) during induction with Propofol, though not statistically significant, may be due to several factors. While Ringer lactate preloading aims to stabilize haemodynamics and reduce the required dose of Propofol, the presence of cough could be influenced by other variables such as the direct irritant effect of Propofol on the respiratory tract, patient sensitivity, or variations in anaesthesia technique. Sebel et al.[66] review the pharmacology of Propofol, including its side effects such as respiratory irritation and cough during induction. Klement et al.[67] discuss how the rate of injection and concentration of Propofol can impact the incidence of adverse effects, including cough.

# CONCLUSION

# CONCLUSION

The study concluded that preloading with Ringer lactate significantly reduces the dose of Propofol required to achieve the loss of eyelash reflex and patients in the preloading group demonstrated a faster onset of anaesthesia compared to the control group. Additionally, the haemodynamic stability observed in the preloading group was superior.

# LIMITATIONS

# LIMITATIONS

The study on the effect of Ringer lactate preloading on the induction dose requirement of Propofol and its haemodynamic stability at a tertiary center has several limitations. The relatively small sample size and single-center design limit the generalizability of the findings. Future research should address these limitations by including larger, multicenter trials, standardized protocols, long-term follow-up, and broader patient populations.

# RECOMMENDATIONS

# RECOMMENDATIONS

Ringer lactate preloading on the induction dose requirement of Propofol is recommended according to this study. Future research should aim to include larger, multicenter trials to enhance the generalizability of the results across diverse clinical settings and patient populations. It is crucial to standardize anaesthetic protocols and haemodynamic monitoring techniques to ensure consistency and reliability in data collection. By addressing these areas, future studies can provide more definitive evidence on the efficacy and safety of Ringer lactate preloading in optimizing Propofol induction and maintaining haemodynamic stability.

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# REFERENCE


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# APPENDICES

# PROFORMA

**PATIENT CODE:** **CASE NO.**

Name : Age: Sex: M / F Date:

Weight : Height: BMI:

Mallampati grading: ASA grading:

Ward: IP/OP No.:

Surgical Diagnosis:

Proposed Surgery:

Total Dose of Intravenous Propofol Required ( 2 mg/kg ): mg

Dose Of Intravenous Propofol Given: mg

Visualization of Loss of Eyelash Reflex: seconds

| Parameters | Baseline | After IV administration of Propofol | At intubation (0 min) | Post intubation (min) | | | |
|---|---|---|---|---|---|---|---|
| | | | | 1 | 3 | 5 | 10 |
| HR | | | | | | | |
| SBP | | | | | | | |
| DBP | | | | | | | |
| MAP | | | | | | | |

**Complications**

| | |
|---|---|
| Apnoea | |
| Vomiting | |
| Involuntary movement | |
| Laryngospasm | |
| Coughing | |
| None | |

**Signature :**

**Name :**

# CONSENT FORM

## [Effect of Ringer Lactate preloading on induction dose requirement of Propofol and its haemodynamic stability at tertiary center]

Department of Anaesthesiology

National Medical College Teaching Hospital, Tribhuvan University, Birgunj, Nepal

I, ……, male/female of …… years of age, hereby confirm that I have read and understood the information sheet and consent form for this research being conducted by ……, and have had the opportunity to ask questions about it.

I hereby declare that,

1. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
2. I understand that the researchers, the IRC, and other regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted about it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information that will be published or released to third parties.
3. I agree not to restrict the use of any data or results that arise from this study provided that such use is only for scientific purpose(s).
4. I agree to take part in this study.

| **Signature (or Thumb impression) of the research participant/Legal Guardian** | **Signature (or Thumb impression) of Witness** |
|---|---|
| Signature: …… | Signature: …… |
| Name: …… | Name: …… |
| Date: …… | Date: …… |

**Investigator's**

Signature: ……

Name: …….. Date:……

# CONSENT FORM IN LOCAL BHOJPURI LANGUAGE

# सूचित सहमति

## Effect of Ringer Lactate preloading on induction dose requirement of Propofol and its haemodynamic stability

### नेशनल मेडिकल कॉँलेज, बीरगंज , नेपाल

- हम....., उम्र ....., डॉ. हम आगे समझ गईल बानी कि हमरा के अध्ययन में शामिल कईल गईल बा। अध्ययन के विवरण के साथे-साथे प्रीलोडिंग के उद्देश्य, संभावित जटिलता के बारे में हमरा के ओह भाषा में बतावल गइल बा । हम समझ गईनी कि जवन मेडिकल रिकॉर्ड हमार नाम के खुलासा करी उ गोपनीय रही।
- हमरा के बतावल गइल बा कि अध्ययन का दौरान प्रथा के मानक में कवनो बदलाव ना होखी आ अनिच्छा के अभिव्यक्ति से इलाज के मानक में कवनो बदलाव ना होखी. एह सब पर विचार करे के हमरा के पर्याप्त मौका दिहल गइल बा।
- ई काम, हम अपना मन के हिसाब से कइले बानी आ जरूरत के हिसाब से पहिले से सूचना देके कबो भी एह संस्था से बाहर निकलब।
- हम एही से आपन सहमति देत बानी / सहमति देत बानी आ पुष्टि करत बानी कि हम सहमति देत बानी।

**प्रतिभागी के/प्रतिभागी के अभिभावक के**

**प्रतिभागी के अंगूठा बा**

सही : .....

नाम-थर : .....

मिति : २०८० /...../.....

**लपचे के मुहर लागल बा**

| | |
|---|---|
| | |
| दाँया | बाँया |

**गवाह के ह**

सही : .....

नाम-थर : .....

मिति : २०८० /...../.....

**शोधकर्ता के ह**

सही : .....

नाम-थर : .....

मिति : २०८० /...../.....