"A COMPARATIVE STUDY BETWEEN THE EFFECTS OF PROPOFOL AND ETOMIDATE IN ADULTS UNDERGOING SURGERIES UNDER GENERAL ANAESTHESIA"

Dissertation submitted in partial fulfillment

of the requirements for

Award of the degree

M.D. (Anaesthesiology)

Branch X

KILPAUK MEDICAL COLLEGE

CHENNAI-10

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CHENNAI, TAMILNADU

APRIL 2019.

CERTIFICATE

This is to certify that this dissertation entitled: **A COMPARATIVE STUDY BETWEEN THE EFFECTS OF PROPOFOL AND ETOMIDATE IN ADULTS UNDERGOING SURGERIES UNDER GENERAL ANAESTHESIA** submitted by **Dr.M.SUBHASHINI** in partial fulfillment for the award of the degree Doctor of Medicine in Anaesthesiology by **The TamilNadu Dr.M.G.R. Medical University, Chennai** is a bonafide work done by her at **KILPAUK MEDICAL COLLEGE, CHENNAI** during the academic year 2016-2019.

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CERTIFICATE II

This is to certify that this dissertation entitled: "**A COMPARATIVE STUDY BETWEEN THE EFFECTS OF PROPOFOL AND ETOMIDATE IN ADULTS UNDERGOING SURGERIES UNDER GENERAL ANAESTHESIA** submitted by **Dr.M.SUBHASHINI,** post graduate in anaesthesiology with registration number **201620155** for the award of **MD.ANAESTHESIOLOGY** in the **Branch-X**. I personally verified the urkund.com web site for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conculsion pages and result shows 11 percentage of plagiarism in the dissertation.

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DECLARATION BY THE GUIDE

This is to certify that this dissertation entitled: "**A COMPARATIVE STUDY BETWEEN THE EFFECTS OF PROPOFOL AND ETOMIDATE IN ADULTS UNDERGOING SURGERIES UNDER GENERAL ANAESTHESIA"** submitted by **Dr.M.SUBHASHINI** in partial fulfillment for the award of the degree Doctor of Medicine in Anaesthesiology by **The Tamilnadu Dr.M.G.R. Medical University, Chennai** is a bonafide work done by her at **KILPAUK MEDICAL COLLEGE, CHENNAI** during the academic year 2016- 2019, under my guidance and supervision.

Prof. Dr. Valli Sathyamoorthy, M.D,D.A

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DECLARATION

I, **Dr. M. SUBHASHINI,** solemnly declare that this dissertation, entitled: **"A COMPARATIVE STUDY BETWEEN THE EFFECTS OF PROPOFOL AND ETOMIDATE IN ADULTS UNDERGOING SURGERIES UNDER GENERAL ANAESTHESIA"** has been prepared by me, under the expert guidance and supervision of **Prof. Dr.Valli Sathyamoorthy M.D.,D.A**, Professor, Department of Anaesthesiology, Kilpauk Medical College and Hospital, Chennai and submitted in partial fulfillment of the regulations for the award of the degree **M.D.(Anaesthesiology)** by **The Tamil Nadu Dr. M.G.R. Medical University** and the examination to be held in April 2019.

This study was conducted at Kilpauk Medical College Hospital and Government Royapettah Hospital, Chennai. I have not submitted this dissertation previously to any university for the award of any degree or diploma.

Place: Chennai **DR.M.SUBHASHINI**

Date:

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I wish to thank all the patients whose willingness and patience made this study possible.

I finally thank God Almighty for His blessings in successfully completing the study.

CONTENT

LIST OF ABBREVATIONS

ASA	-	American Society of Anesthesiology
BP	-	Blood Pressure
CNS	-	Central Nervou System
µg	-	Microgram
mg	-	Milligram
kg	-	Kilogram
L	-	Litre
ml	-	Millilitre
i.v	-	Intravenous
i.m	-	Intramuscular
MAP	-	Mean Arterial Pressure
EEG	-	Electroencephalogram
ECG	-	Electrocardigram
HR	-	Heart Rate

INTRODUCTION

INTRODUCTION:

Induction agents are drugs that, when given intravenously in an appropriate dose, cause rapid loss of consciousness. They are used to maintain anesthesia by intravenous infusion, as the sole drug for short procedures done under local anesthesia and also to provide conscious sedation in intensive care unit.

Propofol is 2, 6-diisopropylphenol is one of the most popular**.** induction agent with its favourable characteristics like rapid and smooth induction, recovery and decreased incidence of nausea and vomiting. While on the other side, it decreases blood pressure, causes dose dependent depression of ventilation and pain on injection.

Etomidate is a carboxylated – imidazole is characterized by hemodynamic stability, minimal respiratory depression and cerebro-protective effects. The effect of increased coronary perfusion along with negligent sympathetic response makes it an ideal induction agent of choice in all ischemic heart disease patients.

However, pain on injection, thrombophlebitis and myoclonus are some undesirable adverse effects.

AIM AND OBJECTIVES

AIM OF STUDY:

The aim of the study is to compare the hemodynamics and various other effects of Propofol and Etomidate in adults undergoing surgeries under general anesthesia.

OBJECTIVES OF THE STUDY:

The objectives of the study is to compare the haemodynamic and other effects of Propofol and Etomidate during induction and intubation in adults undergoing surgeries under general anesthesia by assessing the following parameters ;

1. Mean arterial pressure.
2. Changes in heart rate.
3. Pain on injection.
4. Apnoea using calculated doses of propofol and etomidate.
5. Myoclonic movements.

GENERAL ANAESTHESIA

GENERAL ANAESTHESIA:

- General anaesthesia is described as a reversible state of unconsciousness with inability to respond to a supra maximal surgical stimulus.
- In modern anaesthetic practice this involves the triad of unconsciousness, analgesia and muscle relaxation.

HISTORICAL PERSPECTIVE:

- The era of modern anaesthesia and revolution in the medical care of the surgical patient begun after October 16th 1846, when William T.G.Morton, a Boston dentist and medical student, performed the first public demonstration of general anaesthesia using Diethyl Ether on Gilbert Abbott who underwent surgical excision of a neck tumor at the Massachusetts General Hospital, now known as **The Ether dome**.
- Chloroform popularized by James Young Simpson was practiced by John Snow who used it to deliver the last two children of Queen Victoria. He gave analgesic doses of chloroform on a folded handkerchief and this technique was soon termed “chloroform a la reine”.

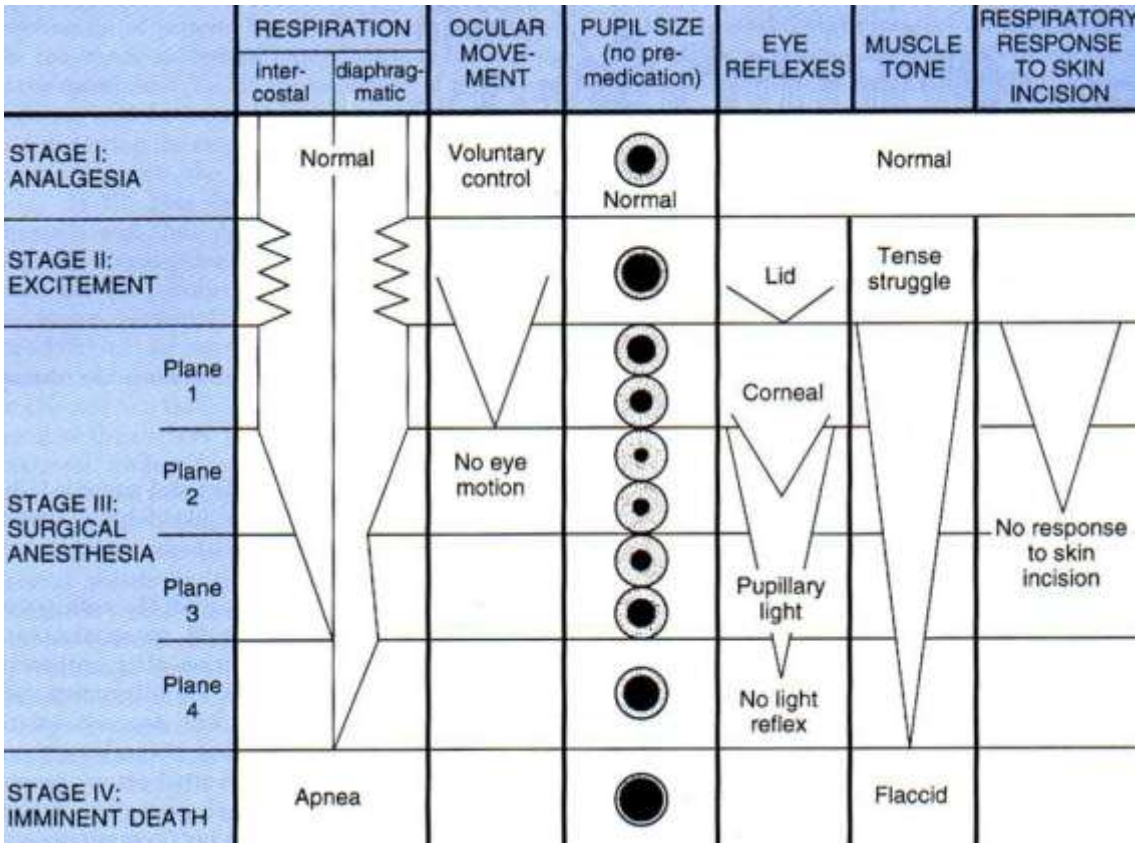
  Victoria abhorred the pain of childbirth and enjoyed the relief that chloroform provided. She wrote in her journal, “Dr.Snow gave that

blessed chloroform and the effect was soothing, quieting and delightful beyond measure".

- In 1934, the anaesthetic properties of cyclopropane were discovered accidentally by Ralph Waters, a chemist analyzing impurities in propylene.
- In 1956, came the introduction of Halothane by Charles Suckling, a nonflammable volatile halogenated alkane that quickly became the dominant anesthetic.

STAGES OF THE GENERAL ANAESTHESIA

- Traditional description of stages and signs of general anaesthesia is also called as "Guedel's stages of anaesthesia", described by Guedel in 1920 with using Ether.
- There are four stages of general anaesthesia.



Stage I: Stage of Analgesia

- Starts from beginning of anesthetic inhalation and lasts upto the loss of consciousness.
- Pain is progressively abolished during this stage.
- Patient remains conscious, can hear and see and feels a dream-like state.
- Reflexes and respiration remains normal.
- It is difficult to maintain, hence use is limited to short procedures only.

Stage II: Stage of Delirium and Excitement

- From loss of consciousness to beginning of regular respiration.
- Eyelash reflex disappear.
- Excitement-patient may shout, struggle and hold his breath.
- Muscle tone increases, jaws are tightly closed.
- Breathing is jerky, vomiting, involuntary micturition or defecation may occur.
- Potentially dangerous responses to painful stimulus or operative procedures, can occur during this stage and includes vomiting, laryngospasm and uncontrolled movement.
- This stage is not found with modern anaesthesia because of the use of pre anaesthetic medication, generous use of opioids, rapid induction and newer inhalational agents.

Stages III: Stage of Surgical anesthesia

- Extends from the onset of regular respiration to respiratory paralysis

This has been divided into four planes:

- Plane 1: Roving eye balls. This plane ends when eyes become fixed.
- Plane 2: Loss of corneal and laryngeal reflexes.

- Plane 3: Pupil starts dilating and light reflex is lost. This is the desired plane for surgery.
- Plane 4: Intercostal paralysis, shallow abdominal respiration and dilated pupil.

Stage IV: Medullary /Respiratory Paralysis

- Cessation of breathing , failure of circulation and impending death.
- Pupils widely dilated, muscles are totally flabby, pulse will be imperceptible and blood pressure will be low.

THE CARDINAL FEATURES OF MODERN GENERAL ANAESTHESIA:

- Analgesia.
- Lack of awareness and amnesia.
- Immobility and muscle relaxation.
- Abolition of somatic and autonomic reflexes.

As no single agent can provide all desirable effects both rapidly and safely, several categories of drugs are combined (i.v and inhalational anesthesia along with pre anesthetic medications) to produce optimal anaesthesia known as **Balanced Anaesthesia.**

SITES OF ACTION OF GENERAL ANESTHETICS:

Possible target sites are the

1. peripheral receptors,
2. spinal cord,
3. brainstem and
4. cerebral cortex.

Cerebral cortex: Major site for integration, storage and retrieval

Brainstem: Has the Reticular activating system and involved in arousal behaviour.

Spinal Cord: Have direct effect on the spinal motor neurons.

- General anaesthetics act both in the pre synaptic and post synaptic neurons.
- Glutamate is the main excitatory and GABA is the main inhibitory neurotransmitter in the central nervous system.
- The inhibitory neurotransmitter in the spinal cord is Glycine.

MOLECULAR TARGETS:

The general anesthetics acts on the Voltage gated ion channels and Ligand gated ion channels.

THEORIES OF GENERAL ANESTHESIA:

There are three main theories of general anaesthesia

- Lipid theory.
- Protein theory.
- Biochemical theory.

LIPID THEORY

Lipid theory suggests that the anesthetic acts non -specifically on the lipid portions of the neuronal membrane to cause a general disturbance that causes the ion channels to change structure thereby changing their function.

There are various lipid theories:-

1. Meyer- Overton theory
2. Pauling and Miller theory/Hydrate theory
3. Membrane expansion theory
4. Membrane Fluidization theory/Lateral Phase Separation Theory

MEYER –OVERTON HYPOTHESIS:

- Meyer and Overton were separate studies,that identically postulated that anesthetic potency varies with the lipid solubility.
- The more lipid soluble a drug is the greater will be its anesthetic potency.

- This theory does not suggest any particular mechanism, but reflects the capacity of an anesthetic agent to enter into CNS and attain sufficient concentration within the neuronal membrane.
- It is now known, that not all highly lipid soluble substances are anesthetics and some potent anesthetics are not lipid soluble.

Limitations of Meyer Overton Hypothesis:

This theory does not explain the cut –off phenomenon

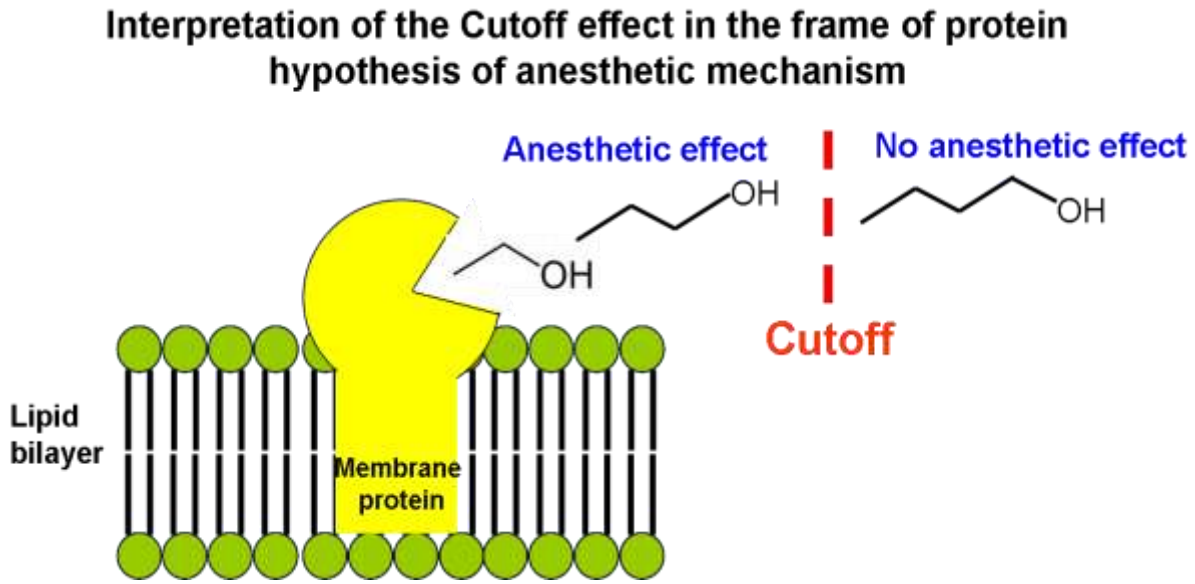


Figure A: The Meyer-Overton rule predicts the constant increase of anesthetic potency of n-alkanols with increasing chain length. However, above certain length the potency vanishes.

PAULING AND MILLER THEORY/HYDRATE THEORY

- This theory was given in 1961

- According to this theory simple molecules like water may be linked together by hydrogen bonding to form ice like structures which are occupied by an anesthetic agent to form anesthetic hydrate crystals.
- These hydrate crystals could then impede ionic mobility, electrical charge, chemical and enzymatic activity of the brain to produce depression and unconsciousness.
- This theory does not explain anesthesia produced by barbiturate and some other anesthetics.

MEMBRANE EXPANSION THEORY

- This theory postulates that anesthetic molecules penetrate into the hydrophobic region of cell membrane and causing it to expand. The mechanism of membrane expansion has not been fully explained but may be attributed to formation of hydrates.

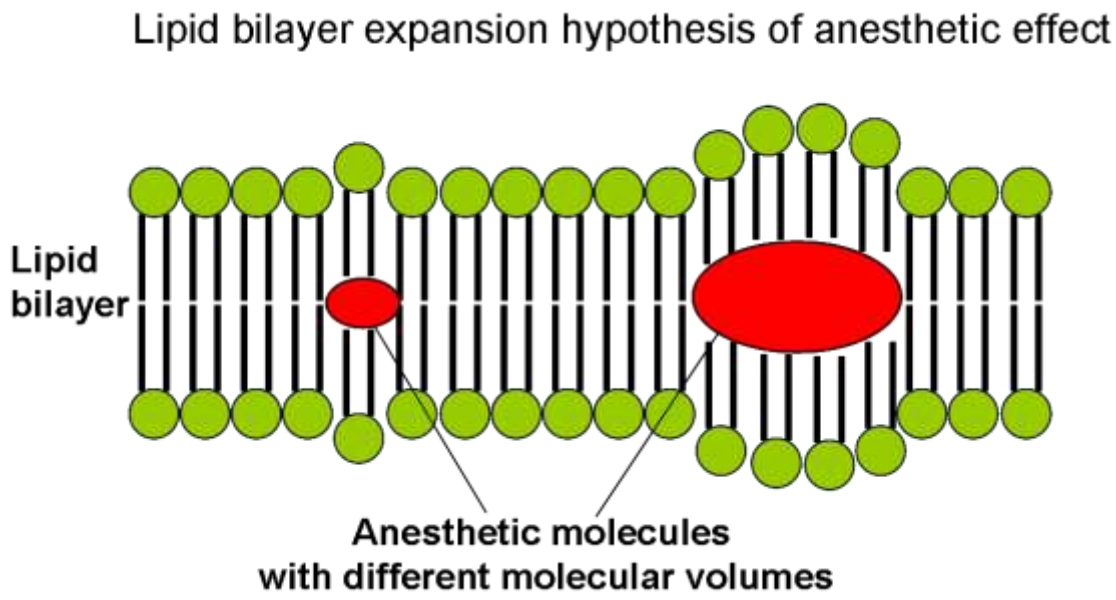


Figure B : Bulky and hydrophobic anesthetic molecules accumulate inside the neuronal cell membrane causing its distortion and expansion (thickening) due to volume displacement. Membrane thickening reversibly alters function of membrane ion channels thus providing anesthetic effect. Actual chemical structure of the anesthetic agent per se was not important, but its molecular volume plays the major role: the more space within membrane is occupied by anesthetic - the greater is the anesthetic effect.

MEMBRANE FLIUDISATION THEORY

- This theory postulates that the anesthetic drugs dissolve in the membrane lipids and causing loosening or fluidization of lipid bilayer region of the membrane.
- It is also known as Lateral Phase Separation Theory.

Most of these lipid theories are outdated now.

PROTEIN THEORY

- Protein theory suggests that the anesthetic agent must act specifically with hydrophobic pockets on certain membrane proteins to produce the effect by acting as a lock and key.
- It was initially hypothesized that general anesthetic binds to its target ion channel by a key-lock mechanism and changes its structure dramatically from open to closed conformation or vice versa. However, there is a

significant amount of evidence against direct key-lock interaction of membrane proteins with general anesthetics.

BIOCHEMICAL THEORY

A number of biochemical theories have been postulated and reviewed.

These postulates include –inhibition of glucose metabolism in brain cells.

1. interference in production of ATP.
2. interference in oxygen utilization and cellular respiration.

PROPOFOL

PROPOFOL

Propofol History:

Propofol was introduced in 1970 at United Kingdom. It initially caused anaphylaxis but later re-launched as an emulsion in soya-bean oil in 1986. Presently it is the most widely used intravenous hypnotic agent.

Physical and Chemical properties:

- Propofol is a substituted isopropylphenol-2, 6 di iso-propylphenol. It consists of a phenol ring. The color of the solution is milky white and is available as 1% and 2% concentration.
- The constituents of the formulation are 10 % soya-bean oil, 1.2% purified egg phosphatide and 2.25% glycerol.
- The Propofol emulsion is isotonic and has a pH of 4.5-6.4.

- Propofol is preservative free, hence should be used within 6 hours of opening the vial as the egg lecithin is a good media for bacterial growth. To avoid this, the formulations are added with Disodium edetate or Sodium meta-bisulfite as antimicrobials.
- Propofol should not be mixed with any other drug, with the exception of mixing Propofol with lidocaine to reduce pain on injection. Mixing of Propofol may predispose to the risk of pulmonary embolism.

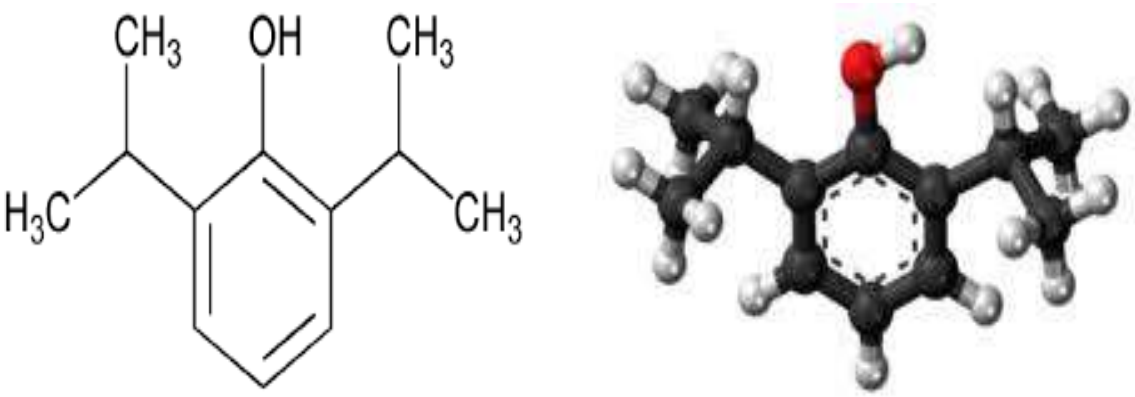
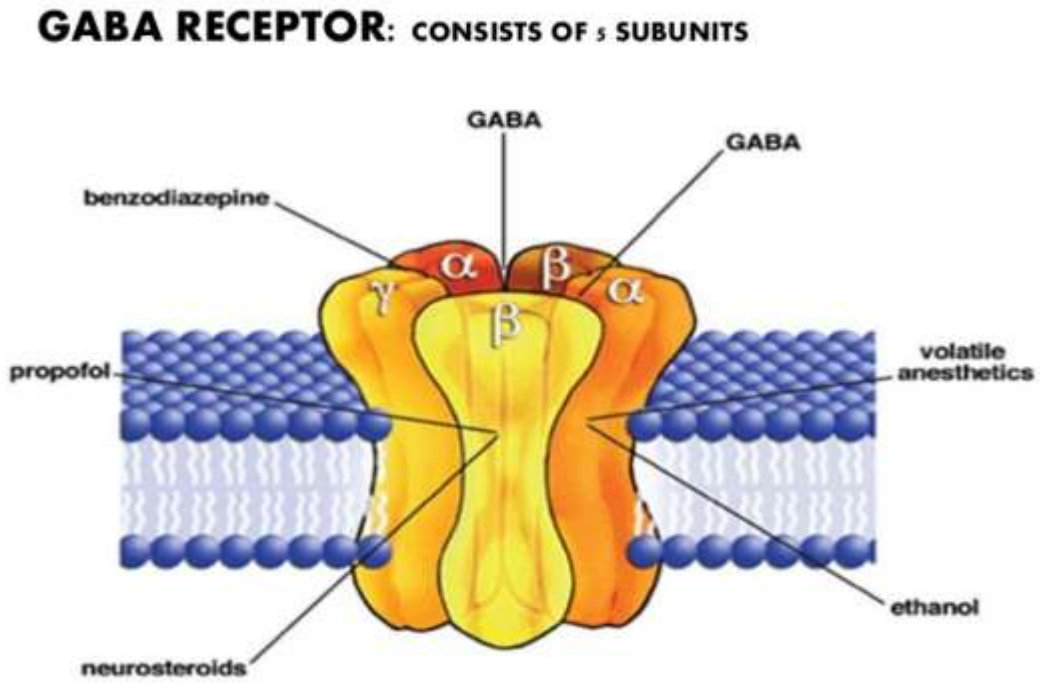


Fig 1; Structure of Propofol

Mechanism of action of Propofol:

- Propofol is a relatively selective modulator of GABA receptors.
- Propofol binds to the beta subunit of GABA-A receptor. It has direct as well as indirect effects on the GABA receptors. At lower concentrations, Propofol has indirect effect –potentiates activation by GABA. At higher concentrations, it activates GABA directly.

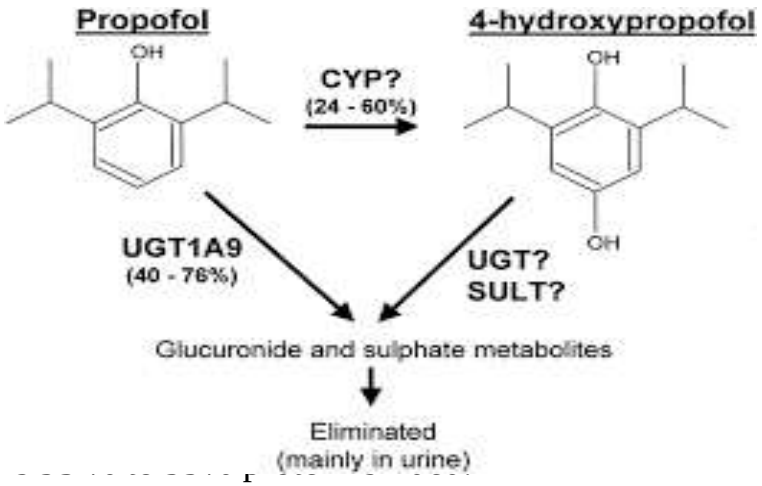
- Activation of GABA receptors increases the trans membrane chloride conductance, which results in hyper polarization of post synaptic membrane and leads to inhibition of the postsynaptic neurons.
- Propofol decreases the dissociation rate of GABA from its receptors, thereby increases the duration of opening of the GABA activated chloride channel which results in hyper polarization of cell membrane.
- Propofol also inhibits NMDA glutamate receptors, increases dopamine in nucleus accumbens (sense of well-being) and also decreases serotonin in area postrema (anti emetic).



Pharmacokinetics:

Propofol is oxidized and conjugated in liver and then excreted through kidneys. The drug also has some extra hepatic clearance likely in the kidneys and lungs.

The clearance of Propofol from the plasma exceeds hepatic blood flow. Tissue uptake as well as hepatic oxidative metabolism by cytochrome p450 removes the drug from plasma.



- Propofol
- Onset of action is 15 to 30 seconds.
- The biological half-life is 30 to 60 minutes.
- Duration of action is 5 to 10 minutes.
- After single bolus dose, level decreases rapidly due to redistribution and elimination with initial distribution half-life of 2 to 8 minutes.

- **The context sensitive half time** is the time required for blood or plasma concentration of a drug to decrease by 50% after discontinuing the drug administration. The context sensitive half time for Prospofol is 10minutes for infusions up-to 3 hours and 40 minutes for infusions between 3 to 8 hours.
- Propofol reduces the EEG activity in the brain in 20 seconds and the peak effect is seen in 90 seconds.
- The decrease in the cardiac output, can impair the drug clearance because of the decreased hepatic blood flow. Hence in the geriatric patients whom, have a greater reduction in cardiac output, the dose has to be necessarily reduced. An 80year old patient needs 50% of the dose in comparison to a 20 year patient to produce the same effect.
- Even though it is cleared hepatically, no dose reduction is needed in hepatic diseases due to efficient extra hepatic clearance.
- Propofol is a competitive inhibitor of cytochrome 3A4 and hence increases the plasma levels of Midazolam and Remifentanil, thereby increasing the duration of action of these drugs.

Effects on Organ System:

Central nervous system:

- Propofol decreases the cerebral metabolic rate of oxygen (CMRO2).

- it decreases the cerebral blood flow.
- it decreases the intracranial pressure.
- it also decreases the early component of somato sensory and motor evoked potential.

Cardiovascular system:

- Propofol decreases the systemic blood pressure.
- Propofol inhibits the sympathetic vasoconstriction, leading to vascular smooth muscle relaxation.
- Propofol has negative inotropic effect due to decrease in Intra-cellular calcium availability caused by inhibition of the trans-sarcolemmal calcium influx.
- Propofol infusion causes decrease in myocardial blood Flow and oxygen consumption.
- Propofol causes bradycardia and may also cause asystole.

Respiratory system:-

- Propofol produces dose-dependant depression of ventilation.
- Propofol infusion decreases the tidal volume and frequency of breathing.
- Propofol produces bronchodilation.

Hepatic and renal system:

- prolonged Propofol infusion may result in hepatocellular injury accompanied by lactic acidosis, bradyarrhythmias and rhabdomyolysis. This is termed as **Propofol infusion syndrome**.
- Prolonged infusion may also result in excretion of green color urine, which reflects the presence of phenol ring in the urine.

Eye:

- ✓ Immediately after induction, it decreases the intra ocular pressure.

CLINICAL USES:

- Induction of anesthesia at dose of 1 to 2.5 mg per kg i.v
- Intravenous sedation at dose of 25 to 75 microgram per kg i.v. Along with opioids it is the agent of choice for total intravenous anaesthesia (TIVA). Propofol may be used in icu for sedation.
- Maintenance of anesthesia at dose of 50 to 150 microgram per kg i.v
- Propofol is used commonly in day care procedures.
- Antiemetic effect- Sub hypnotic doses of Propofol 10 to 15mg i.v can be used in the post anesthesia care unit to treat nausea and vomiting.

Propofol is found to be very effective against the chemotherapy induced nausea and vomiting.

- Propofol has anti pruritic effect,as it depresses the spinal cord activity in the dose of 10 mg i.v. It is effective in the treatment of pruritis associated with neuraxial opioids and cholestasis.
- Propofol have anti convulsant property.1 mg /kg i.v decreases seizure duration.
- It is the agent of choice for induction in susceptible individuals for malignant hyperthermia.

CONTRAINDICATIONS:

- Use is contraindicated in any hypersensitivity to Propofol injectable emulsion or any of its components, example-if allergic to eggs, egg products, soya beans or soy products.

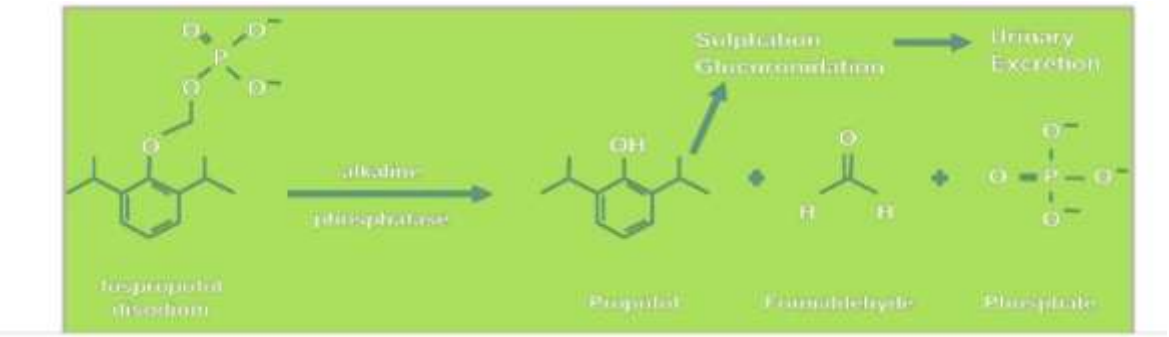
SIDE EFFECTS:

- Pain on injection is the most common side effect associated with Propofol. Using large veins, avoiding veins in the dorsum of hand and use of i.v lidocaine prior to Propofol injection will reduce the pain.
- Bacterial growth- Propofol strongly supports the growth of E.coli and Pseudomonas aeruginosa.
- Hypotension-this is the most significant side effect on induction.

- Abuse potential- intense dreaming activity, amorous behavior and hallucinations has been seen during recovery from the Propofol effect. Addiction is reported.
- Allergic reactions- allergic components of Propofol are due to phenyl nucleus and Disopropyl side chain.

FOSPROPOFOL

- Water soluble prodrug of Propofol
- Reduces the disadvantages of lipid emulsion of Propofol
- Produces more complete amnesia and conscious sedation than midaz+fentanyl.
- Slower onset and recovery than Propofol



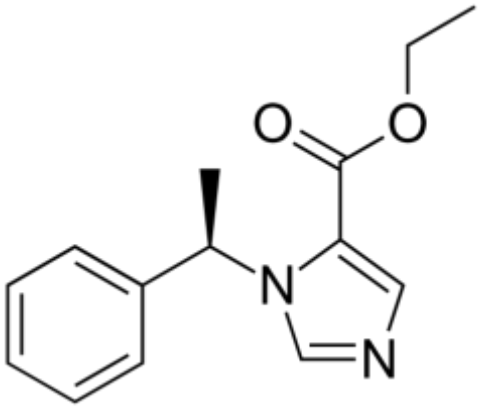
ETOMIDATE

ETOMIDATE

HISTORY:

- ✓ Etomidate was first discovered by Janssen Pharmaceuticals in 1964.
- ✓ The drug was first introduced as an anti-fungal agent. Later introduced as i.v anesthetic agent in Europe (1972), in USA (1983) and in India (2013)

PHYSICAL AND CHEMICAL PROPERTIES:



- ✓ Etomidate is a carboxylated imidazole –containing compound.
- ✓ Etomidate is chemically not related to any other drug and used as an i.v induction agent.

- ✓ It is a R-1-(1-ethylphenyl) imidazole-5-ethyl ester. Etomidate is acidic in nature with a pH 6.9 .It is poorly water soluble and soluble in 35%propylene glycol.
- ✓ Etomidate is available as milky white solution in 35% propylene glycol
- ✓ Etomidate is presently available with medium and long chain triglycerides for preventing pain during injection.

MECHANISM OF ACTION:

- ✓ Etomidate is a relatively selective modulator of GABA –A receptors.
- ✓ GABA-A receptors are the site of action for Etomidate.
- ✓ Etomidate binds to the specific site or sites on the GABA –A receptors and increases the affinity of the inhibitory neurotransmitters to this receptors.

PHARMACOKINETICS:

- Etomidate is 76% protein bounded.
- Onset of action is within 30 to 60 seconds.
- Peak effect is attained in one minute.
- Duration of the action of the drug is 3 to 5 minutes and terminated by its redistribution.

- Metabolism is by hepatic and plasma esterases, by the rapid**.** hydrolysis of the ethyl ester **.**side chain to its carboxylic acid ester that results in a water soluble, pharmacologically inactive compound. The distribution half-life is 3 minutes.(Anesthesia)
- Redistribution half-life is 30 minutes (Sedation).
- Elimination half-life is three hours (drowsiness).
- Etomidate clearance is not affected by hypovolemia.

EFFECTS ON ORGAN SYSTEM:

Central Nervous System:

- Etomidate reduces cerebral blood flow by 34% and cerebral metabolic rate of oxygen by 45% but causes no change in mean arterial pressure.
- Cerebral perfusion pressure is maintained or increased with improved cerebral oxygen supply demand.
- Etomidate acutely decreases intra-cranial pressure by 50% if elevated but the effect is transient.

Cardiovascular system:

- Induction with Etomidate has a very hemodynamically stable status even in hemorrhagic shock.
- Maintains the myocardial O2 supply to demand ratio.

- It has no analgesic effect. Hence needs to be given with opioids to obtund intubation response.
- Negligent effect over the sympathetic tone.
- Respiratory system;-at induction dose produces brief hyperventilation, then brief apnoea (transient apnoea upto 90 seconds)
- Ventilatory response to hypercarbia is decreased.
- Minimal changes in respiratory rate and tidal volume.
- Slight elevation in arterial carbon dioxide tension (PaCO2).

Endocrine effects:

- dose dependent inhibition of 11 B-hyroxylase, decreased cortisol and mineralocorticoids.
- suppression occurs at lower dose than hypnosis by more than 20 times. So suppression lasts much longer up to 72 hrs.
- can be used to treat hypercortisolemia.

Other effects:-

- No histamine release.
- Very rare allergic reactions.
- Hepatic and renal blood flow decreased but clinically accepted.

CLINICAL USES:

- ✓ As Sedation (PSA).
- ✓ As Conscious Sedation.
- ✓ As a Hypnotic Agent.
- ✓ As Anesthetic Agent (preferred in cardiac patients).
- ✓ In Rapid Sequence Intubation (RSI).
- ✓ In Cardio-version.
- ✓ In ICU as infusion for both ventilated/non ventilated patient.
- ✓ As eSAM (Etomidate Speech And Memory Test) (To determine speech**.** lateralization in**.** patient prior to performing lobectomies to remove**.** epileptogenic centre in brain)

DOSES IN DIFFERENT SITUATIONS:

- sedation-0.1mg/kg up to three divided doses.
- General anaesthesia s-0.3 to 0.4 mg/kg i.v over 30 to 60 seconds.
- ICU as a continuous infusion -0.04 to 0.05 mg/kg/hr with continous monitoring.
- Cushing syndrome or low cortisol level patient -0.2mg/kg.
- Pregnancy- 0.2 mg/kg.
- Geriatric patient- 0.2mg/kg

- Pediatric patient -0.1 to 0.3mg/kg

CONTRAINDICATIONS:

- To be avoided in sepsis with unstable hemodynamic patients.
- Abnormally low blood pressure even with treatment.
- Decreased function of the adrenal gland.
- Hypersensitivity to Etomidate.
- Paediatric patients less than 10 years of age.
- In geriatric patient with caution.

SIDE EFFECTS:

- Pain on injection transiently in up-to 80% patients.
- Skeletal muscle movements mainly myoclonic peripheral limb movements up-to 30% patients.
- Adrenal suppression in about 10% patients.
- Nausea and vomiting is highly common.
- Hiccups.

REVIEW OF LITREATURE

REVIEW OF LITREATURE:

Maruyama k, Nishikawa Y, Nakagawa H, et al:

- Did a study to examine whether pretreatment with iv Atropine could prevent bradycardia and hypotension during induction of total iv anesthesia with Propofol and remifentanil in a prospective randomized placebo controlled manner.
- Seventy patients aged 24 to 78 years were randomly divided into two groups and received 0.5 mg Atropine or placebo saline 1min before induction of i.v anesthesia with Remifentanyl at 0.4 mcg /kg/min, Propofol at a target blood concentration of 3mcg/kg/min and Vecuronium1.5mg/kg. Immediately after intubation, the infusion rates of Remifentanil and Propofol were reduced and kept at 0.1 mcg/kg/min and 2mcg/kg/min respectively for ten min.
- Non-invasive blood pressure and heart rate were measured and recorded very minute. Intravenous Atropine could prevent a fall in heart rate but not a fall in blood pressure. Our data suggested that a fall in heart rate induced by Propofol and Remifentanil anesthesia was mainly caused mainly by centrally mediated sympatholytic and/or vagotonic action of Propofol and Remifentanil, where as a fall in blood pressure was mainly the result of their direct vasodilation actions.

Nyman Y, Von Hofsten K, Palm C et al:

- Did a prospective, double blind, randomized trial study to compare the incidence of injection pain during intravenous induction of anesthesia between Propofol with added Lidocaine and the new Etomidate formulation in paediatric patients.
- A total of 110 paediatric patients aged 2-16 years scheduled for out - patient surgery were planned to be included in the Study Primary end point of the study was the incidence of anesthesia as assessed by a four point scale. The occurrence of myoclonic muscular activity was registered as a secondary end point. An interim analysis after 80 patients was requested by the Ethics Committee.
- The study concluded that the use of the new lipid formulation of Etomidate was associated with significantly less pain on injection than Propofol with added. Lignocaine in children.
- These findings may warrant a change in clinical practice in order to avoid unnecessary pain in children.

Mayer M,Doenicke A,Nebauer AE, et al:

- **Di**d a prospective, randomized clinical study to compare the effects of Propofol and Etomidate for their effects on hemodynamic and various adverse effects on patient scheduled for elective surgeries during the

induction of general anesthesia. 100 patients of ASA 1 and 2 were selected.

- Following pre medication with 2mg Lormetazepam given orally in 50 patients per group, anesthesia was induced with either 0.51 mg/kg of Etomidate in lipid emulsion or 3.04mg/kg of Propofol .
- No opioid or benzodiazepines was given i.v before induction .After injection of the tested drug, the cannula was removed. Changes in blood pressure and heart rate as well as signs of discomfort during and after injection (pain, burning, tension, cold).Venous sequel were assessed for five days after injection to register signs of thrombophlebitis.
- The study concluded that Etomidate formulated in a medium chain lipid emulsion causes significant less discomfort for the patients than Propofol, which is in a long chain formulation. Myoclonus, however, occurred significantly more with Etomidate than with Propofol.

Grundmann U, Silomon M, Bach F, et al

- Nitrous oxide (N2O) has been suggested to contribute to bowel distension, resulting in worsened operating conditions for laparoscopic surgery, and to increase incidence of postoperative nausea and vomiting. Therefore, their objective was to assess the feasibility of two remifentanil-based anaesthetic regimens free from N2O with special regard to recovery profile, postoperative analgesic demand and side effects in patients undergoing

laparoscopic cholecystectomy. Fifty patients (ASA I-II, 23-65 yr) were randomly assigned to receive remifentanil-based anaesthesia in conjunction with (group R/P) or desflurane (group R/D). After standardised induction of anaesthesia, analgesia was continued with remifentanil in all patients. For maintenance of hypnosis, Propofol or desflurane were used in concentrations to ensure loss of consciousness, lack of awareness, and maintenance of heart rate and blood pressure within +/- 25% of initial values. At the end of surgery all anaesthetics were discontinued without tapering and early emergence and recovery were recorded. Pain scores were assessed by using a visual analogue scale. Patient-controlled analgesia with i.v. piritramide was used for treatment of postoperative pain and recorded for 90 min in the postanaesthesia care unit (PACU). In addition, side effects were noted.

- Early emergence from anaesthesia did not differ between the groups. In group R/P, time to eye opening, spontaneous respiration and extubation was 4.4 +/- 2.9 min, 5.2 +/- 3.4 min and 5.5 +/- 3.3 min respectively, compared with 4.7 +/- 2.7 min, 5.3 +/- 2.4 min and 5.7 +/- 2.5 min in group R/D. While pain scores did not differ between both groups on admission to the PACU, patients receiving desflurane required more i.v. piritramide as compared to those receiving Propofol, 22.0 +/- 6.5 mg and 17.9 +/- 7.0 mg, respectively ($P<0.05$). Nausea was less frequent after Propofol (16% vs. 48%, $P<0.05$).

- They concluded by saying, in patients undergoing laparoscopic cholecystectomy, remifentanil-based anaesthetic regimens in conjunction with Propofol or desflurane are suitable and allow for rapid recovery from anaesthesia. However, the use of Propofol results in less postoperative analgesic consumption and nausea as compared to desflurane.

Shinn HK, Lee MH, Moon SY, et al.

- Did this study to compare sevoflurane with Propofol for intraoperative haemodynamic changes with postoperative recovery profile in patient's undergone laparoscopic cholecystectomies under general anaesthesia.
- In this prospective randomized study, sixty patients of either sex, 18-60 years with ASA grade 1 and 2 scheduled for laparoscopic cholecystectomies under general anaesthesia were randomly allocated into two groups. In Group S, patients were maintained on sevoflurane anaesthesia (0.5-2.5%) while in Group P, patients were maintained with Propofol infusion (75-125 µg/kg/min) along with O2 (50%) and N2O (50%). The intraoperative haemodynamic parameters, recovery characteristics and postoperative nausea and vomiting (PONV) were observed in both groups.
- The mean baseline haemodynamic parameters (HR, SBP, DBP, MBP, SpO2 and EtCO2) were comparable in both groups, (P>0.05). No

significant difference in HR was at observed any time interval, P>0.05, however, SBP, DBP and MBP were significantly lower in Propofol group at different time intervals, P<0.05, but clinically not significant and patients remained haemodynamically table in both groups. The mean time for all recovery characteristics were significantly shorter in sevoflurane group as compared to Propofol group, (P<0.01). However the incidence of PONV was significantly more in sevoflurane group.

- Here is the conclusion of his study. Sevoflurane can be used as an effective alternative to Propofol for maintenance of anaesthesia in day care laparoscopic procedures as it has better recovery profile with stable haemodynamic parameters.

Frazee BW, Park RS, Lowery D, et al

- They sought to evaluate the use of propofol (2, 6-diisopropylphenol) for ED procedural sedation, particularly when administered in a routine fashion for a variety of indications.
- This was a prospective observational study conducted in an urban teaching ED. Propofol was administered by handheld syringe and combined with fentanyl. Measurements included propofol and fentanyl dose, serial vital signs, pulse oximetry, adverse events, and patient and physician satisfaction.

- One hundred thirty-six subjects (18 to 69 years) were enrolled. Procedures included 82 (60.3%) abscess incision and drainages and 47 (34.6%) orthopedic reductions. Adverse events occurred in 14 cases (10.3%; 95% confidence interval 5.2% to 15.4%), including hypotension in 5, hypoxemia in 7, and apnea in 5. One patient required intubation. Both patient and physician satisfaction were excellent.
- Their conclusion was, ED procedural sedation with propofol was effective and well accepted by patients and physicians. However, it produced a significant incidence of hypotension, hypoxemia, and apnea.

Morel J, Salard M, Castelain C, et al.

- Here is the abstract of their study. "The consequences of inhibition of cortisol synthesis by a single dose of Etomidate on subsequent vasopressor drug usage and the duration of relative adrenal insufficiency (RAI) after cardiac surgery are not known."
- This was a prospective, randomized, double-blinded controlled trial of 100 patients undergoing elective cardiac surgery and receiving either Etomidate or propofol at induction of anaesthesia. A short corticotropin test was performed 12, 24, and 48 h after anaesthesia induction. RAI was defined as a response <250 nmol litre(-1).
- The mean (sd) norepinephrine infusion rate during the first 48 postoperative hours was 0.11 (0.01) and 0.11 (0.01) µg kg(-1) min(-1) in

the Etomidate and propofol groups, respectively (P=0.89). Time to norepinephrine withdrawal was similar between the groups. The incidence of RAI was higher in the Etomidate group at 12 h (100% vs 41%, P<0.001) and 24 h (85% vs 25%, P<0.001).

- The conclusion from their study is, "A single bolus of Etomidate blunts the hypothalamic-pituitary-adrenal axis response for more than 24 h in patients undergoing elective cardiac surgery, but this was not associated with an increase in vasopressor requirements.

Nyman Y, von Hofsten K, Ritzmo C, et al.

- In children, the incidence of injection pain at i.v. anaesthetic induction with Etomidate-Lipuro is low when compared with Propofol mixed with lidocaine (5%). However, the incidence of involuntary myoclonic movements (MM) after induction of anaesthesia is higher compared with Propofol (85% *vs* 15%). In adults, the incidence of MM is reported to be significantly reduced if a small priming dose is administered immediately before the main injection of Etomidate. The aim of this prospective, randomized, double-blind, placebo-controlled clinical trial was to investigate if a small priming dose of Etomidate effectively can reduce the incidence of MM also in children.
- Eighty ASA I–II children (1–15 yr) were randomized to receive either a small priming dose of Etomidate (0.03 mg kg^{-1}) or a lipid emulsion

placebo. A standardized induction dose of Etomidate (0.3 mg kg^{-1}) was administered 60 s after the priming dose. The occurrence and severity (observational score 0–3) of MM was defined as the primary endpoint of the study and was recorded during a 2 min period after induction of anaesthesia. A *post hoc* analysis was performed regarding the incidence of MM with respect to age.

- No difference in the occurrence or severity of MM was found between the two study groups, the total incidence of MM being 73.8% (95% confidence interval: 62.7–83.0%). The incidence of MM (score > 0) was found to be statistically higher in the age group 5–10 yr compared with <5 yr; and >10 yr (*P*=0.0008 and 0.01730, respectively). The MM scores were highest in patients aged 5–10 yr (*P*=0.0021).
- Children in the age range of 5–10 yr appear to be especially prone to react with involuntary MM after i.v. induction of anaesthesia with Etomidate. The use of a small, non-sedative, priming dose did not influence the incidence of involuntary MM after i.v. induction of anaesthesia with Etomidate in children 1–15 yr of age.0

Aono H, Hirakawa M, Unruh GK, et al.

- The mechanisms of arterial hypotension following intravenous anesthetic induction agents are multifactorial. The purpose of this study was to evaluate and compare the effects of thiopental, Propofol and Etomidate on hemodynamics, sympathetic outflow and arterial baroreflex sensitivity

using not only neuraxis-intact but also totally baro-denervated rabbits. A total of 60 rabbits was anesthetized with urethane, tracheotomized, and mechanically ventilated with oxygen in nitrogen (FiO2 0.5). The left renal sympathetic nerve was isolated and placed on a bipolar electrode to record renal sympathetic nerve activity (RSNA). Thirty animals underwent a surgical preparation of total baroreceptor denervation. Bolus injections of an anesthesia induction dose of thiopental 4 mg/kg and twice the induction dose of Propofol 4 mg/kg significantly decreased RSNA to the same extent (19.4+/-6.7 and 19.7+/-5.2% reduction, mean +/- SEM) and mean arterial pressure (MAP) also to the same extent (19.5+/-4.6 and 22.1+/-3.1% reduction) in the neuraxis-intact animals. RSNA was increased (34.5+/-6%) without reduction of MAP by an induction dose of Etomidate, 0.3 mg/kg. Sympathetic barosensitivity was attenuated even 10 min after thiopental at 4 mg/kg or Propofol at 4 mg/kg (68% and 54% of control, respectively). Propofol at 2 mg/kg (induction dose) and Etomidate at 0.6 mg/kg decreased RSNA and MAP only in the baro-denervated animals. It was found from the barosensitivity study that patients can be hemodynamically unstable even though blood pressure has returned to normal after thiopental and Propofol administration. Data suggest that Etomidate can even stimulate the sympathetic nervous system and increase sympathetic outflow. It was also clearly found from the baro-denervated animal study that thiopental was stronger than

Propofol in directly suppressing sympathetic outflow at the induction dose.

Hughes RL, MacKenzie JE.

- In the decerebrate rabbit Etomidate caused dose-related decreases in mean arterial pressure and preganglionic sympathetic nerve activity. There were no significant alterations in heart rate. Etomidate was found to have no effect on the baroreceptor reflex. In pithed animals the effects of Etomidate were of short duration and of a lesser magnitude than in the decerebrate animal. It was concluded that the additional effects in the decerebrate rabbit were a result of depression of central cardiovascular control. It was found that Etomidate was largely without effect on the cardiovascular system at normal anaesthetic doses (0.5-1 mg-kg-1). However, larger doses (2-8 mg kg-1) produced marked depression of central cardiovascular control, the myocardium and the peripheral vasculature.

Wu J, Yao S, Wu Z, et al.

- This prospective study compared the safety, recovery time and side effects of six distinct general anesthesia regimens for first-trimester surgical abortion.
- Two hundred forty women scheduled for surgical abortion at 6 to 8 weeks of gestation were randomized into three groups (n=40) of Propofol: group P (2 mg/kg Propofol alone), group PF (2 mg/kg Propofol+1 mcg/kg

fentanyl), group PMF (2 mg/kg Propofol+1 mcg/kg fentanyl+0.02 mg/kg midazolam) and three groups (n=40) of Etomidate: group E (0.2 mg/kg Etomidate alone), group EF (0.2 mg/kg Etomidate+1 mcg/kg fentanyl) and group EMF (0.2 mg/kg Etomidate+1 mcg/kg fentanyl+0.02 mg/kg midazolam). Vital signs including pulse oxygen saturation (SpO2), mean arterial pressure (MAP) and heart rate were recorded as the primary outcomes. The recovery time and side effects were recorded as secondary outcomes.

- During induction, SpO2 and MAP decreased significantly in all the three groups of Propofol and were significantly lower than those in the groups of Etomidate. Mean recovery times to both eye opening and to obeying commands were significantly shorter in group PF than those in groups P and PMF, while there were no significant differences among the three groups of Etomidate. Compared with the Etomidate groups, the incidence of injection-induced pain was significantly higher, while the scores of myoclonus and postoperative nausea and vomiting were lower, in the three Propofol groups. Moreover, myoclonus scores as well as nausea and vomiting scores were lower in group EMF than in groups E and EF.
- The results of this study suggest that (a) Etomidate is much safer than Propofol for first-trimester surgical abortions and (b) using a lower dose of Etomidate, supplemented with fentanyl and midazolam, is more

beneficial than the use of Etomidate with or without fentanyl in reducing adverse effects like myoclonus and postoperative nausea and vomiting.

Ray DC, Hay AW, McKeown DW.

- Etomidate is often used to induce anaesthesia in sick patients owing to its relative cardiovascular stability. However, Etomidate affects adrenal cortical activity, and there is concern that this could impair outcome in patients undergoing emergency surgery.
- We retrospectively analysed data from 176 patients admitted to an ICU after emergency laparotomy. We retrieved ASA status, surgical diagnosis, induction drug use, blood pressure before and after induction and any vasopressor administration, steroid and vasopressor therapy in ICU and patient outcome. Choice of induction drug was at the discretion of the attending anaesthetist.
- The drugs (numbers of patients) used to induce anaesthesia were Etomidate (52), thiopental (90), Propofol (16), midazolam (12) and ketamine (4). Fifty-two patients (30%) died in hospital. ASA status was the only independent predictor of hospital outcome ($P < 0.001$). Choice of induction drug was related to ASA status. As ASA status worsened, the likelihood of using Etomidate or midazolam/ketamine increased ($P = 0.001$). We found no association between Etomidate and dying in hospital, though our study might not have had sufficient power to show a difference between induction drugs. The relative risks [95% confidence

interval (CI)] of dying in hospital were Etomidate 1.16 (0.72-1.87), thiopental 0.82 (0.52-1.30), Propofol 0.40 (0.11-1.49) and midazolam/ketamine 1.84 (1.09-3.12). Vasopressor and steroid therapy in the ICU was not related to induction drug. The risk of developing hypotension at induction or of receiving vasopressor to treat hypotension was least with Etomidate.

- We found no evidence that Etomidate is associated with worse outcome than thiopental or Propofol in patients undergoing emergency laparotomy, but we cannot be certain that Etomidate is well tolerated in this group of patients. More data are required to address this issue definitively.

Ray DC, McKeown DW.

- In seriously ill patients, Etomidate gives cardiovascular stability at induction of anaesthesia, but there is concern over possible adrenal suppression. Etomidate could reduce steroid synthesis and increase the need for vasopressor and steroid therapy. The outcome could be worse than in patients given other induction agents.
- We reviewed 159 septic shock patients admitted to our intensive care unit (ICU) over a 40-month period to study the association between induction agent and clinical outcome, including vasopressor, inotrope, and steroid therapy. From our records, we retrieved induction agent use; vasopressor

administration at induction; vasopressor, inotrope, and steroid administration in the ICU; and hospital outcome.

- Hospital mortality was 65%. The numbers of patients given an induction agent were 74, Etomidate; 25, Propofol; 26, thiopental; 18, other agent; and 16, no agent. Vasopressor, inotrope, or steroid administration and outcome were not related to the induction agent chosen. Corticosteroid therapy given to patients who received Etomidate did not affect outcome. Vasopressor therapy was required less frequently and in smaller doses when Etomidate was used to induce anaesthesia. We found no evidence that either clinical outcome or therapy was affected when Etomidate was used. Etomidate caused less cardiovascular depression than other induction agents in patients with septic shock.
- Etomidate use for critically ill patients should consider all of these issues and not simply the possibility of adrenal suppression, which may not be important when steroid supplements are used.

Zausig YA, Busse H, Lunz D, et al.

- The current debate about the side effects of induction agents, e.g. possible adrenal suppression through Etomidate, emphasizes the relevance of choosing the correct induction agent in septic patients. However, cardiovascular depression is still the most prominent adverse effect of these agents, and might be especially hazardous in septic patients presenting with a biventricular cardiac dysfunction - or so-called septic

cardiomyopathy. Therefore, we tested the dose-response direct cardiac effects of clinically available induction agents in an isolated septic rat heart model.

- A polymicrobial sepsis was induced via cecal ligation and single puncture. Hearts (n = 50) were isolated and randomly assigned to five groups, each receiving Etomidate, s(+)-ketamine, midazolam, Propofol, or methohexitone at concentrations of 1 × 10-8 to 1 × 10-4 M. Left ventricular pressure, contractility and lusitropy, and coronary flow were measured. Cardiac work, myocardial oxygen delivery, oxygen consumption, and percentage of oxygen extraction were calculated.
- All of the induction agents tested showed a dose-dependent depression of cardiac work. Maximal cardiac work dysfunction occurred in the rank order of s(+)-ketamine (-6%) <Etomidate (-17%) <methohexitone (-31%) <midazolam (-38%) <Propofol (-50%). In addition, Propofol showed a maximum decrease in contractility of -38%, a reduction in lusitropy of -44%, and a direct vasodilator effect by increasing coronary flow by +29%.
- Overall, this study demonstrates that these tested drugs indeed have differential direct cardiac effects in the isolated septic heart. Propofol showed the most pronounced adverse direct cardiac effects. In contrast, S(+)ketamine showed cardiovascular stability over a wide range of

concentrations, and might therefore be a beneficial alternative to Etomidate.

Paris A, Philipp M, Tonner PH, et al.

- The intravenous anesthetic Etomidate exhibits structural similarities to specific alpha2-adrenoceptor agonists of the type such as dexmedetomidine. The current study was performed to elucidate the possible interaction of Etomidate with alpha2-adrenoceptors in mice lacking individual alpha2-adrenoceptor subtypes (alpha2-KO).
- Sedative and cardiovascular responses to Etomidate and the alpha2-agonist, dexmedetomidine, were determined in mice deficient in alpha2-receptor subtypes. Inhibition of binding of the alpha2-receptor antagonist [3H]RX821002 to recombinant alpha2-receptors by Etomidate was tested in human embryonic kidney (HEK293) cells in vitro.
- In vivo, loss and recovery of the righting reflex required similar times after intraperitoneal injection of Etomidate in wild-type and in alpha2A-receptor-deficient mice, indicating that the hypnotic effect of Etomidate in mice does not require the alpha2A-receptor subtype. Intravenous injection of Etomidate resulted in a transient increase (duration 2.4 +/- 0.2 min) in arterial blood pressure in wild-type mice (17 +/- 3 mmHg). Etomidate did not affect blood pressure in alpha2B-KO or alpha2AB-

KO mice. In membranes from HEK293 cells transfected with alpha2-receptors, Etomidate inhibited binding of the alpha2-antagonist, [3H]RX821002, with higher potency from alpha2B- and alpha2C-receptors than from alpha2A-receptors (Ki alpha2A 208 microm, alpha2B 26 microm, alpha2C 56 microm). In alpha2B-receptor-expressing HEK293 cells, Etomidate rapidly increased phosphorylation of the extracellular signal-related kinases ERK1/2.

- These results indicate that Etomidate acts as an agonist at alpha2-adrenoceptors, which appears in vivo primarily as an alpha2B-receptor-mediated increase in blood pressure. This effect of Etomidate may contribute to the cardiovascular stability of patients after induction of anesthesia with etomidate.

Kim TK, Park IS.

- This study was conducted to compare the effect of Etomidate with that of thiopental on brain protection during temporary vessel occlusion, which was measured by burst suppression rate (BSR) with the Bispectral Index (BIS) monitor.
- Temporary parent artery occlusion was performed in forty one patients during cerebral aneurysm surgery. They were randomly assigned to one of two groups. General anesthesia was induced and maintained with 1.5-2.5 vol% sevoflurane and 50% N2O. The pharmacological burst

suppression (BS) was induced by a bolus injection of thiopental (5 mg/kg, group T) or Etomidate (0.3 mg/kg, group E) according to randomization prior to surgery. After administration of drugs, the hemodynamic variables, the onset time of BS, the numerical values of BIS and BSR were recorded at every minutes.

- There were no significant differences of the demographics, the BIS numbers and the hemodynamic variables prior to injection of drugs. The durations of burst suppression in group E (11.1±6.8 min) were not statistically different from that of group T (11.1±5.6 min) and nearly same pattern of burst suppression were shown in both groups. More phenylephrine was required to maintain normal blood pressure in the group T.
- Thiopental and Etomidate have same duration and a similar magnitude of burst suppression with conventional doses during temporary arterial occlusion. These findings suggest that additional administration of either drug is needed to ensure the BS when the temporary occlusion time exceed more than 11 minutes. Etomidate can be a safer substitute for thiopental in aneurysm surgery.

Hoka S, Yamaura K, Takenaka T, et al.

- Venodilation is thought to be one of the mechanisms underlying propofol-induced hypotension. The purpose of this study is to test two

hypotheses: (1) propofol increases systemic vascular capacitance, and (2) the capacitance change produced by propofol is a result of an inhibition of sympathetic vasoconstrictor activity.

- In 33 Wistar rats previously anesthetized with urethane and ketamine, vascular capacitance was examined before and after propofol infusion by measuring mean circulatory filling pressure (Pmcf). The Pmcf was measured during a brief period of circulatory arrest produced by inflating an indwelling balloon in the right atrium. Rats were assigned into four groups: an intact group, a sympathetic nervous system (SNS)-block group produced by hexamethonium infusion, a SNS-block + noradrenaline (NA) group, and a hypovolemic group. The Pmcf was measured at a control state and 2 min after a bolus administration of 2, 10, and 20 mg/kg of propofol.
- The mean arterial pressure (MAP) was decreased by propofol dose-dependently in intact, hypovolemic, and SNS-block groups, but the decrease in MAP was less in the SNS-block group (-25%) than in the intact (-50%) and hypovolemic (-61%) groups. In the SNS-block + NA group, MAP decreased only at 20 mg/kg of propofol (-18%). The Pmcf decreased in intact and hypovolemic groups in a dose-dependent fashion but was unchanged in the SNS-block and SNS-block + NA groups.
- The results have provided two principal findings: (1) propofol decreases Pmcf dose-dependently, and (2) the decrease in Pmcf by propofol is

elicited only when the sympathetic nervous system is intact, suggesting that propofol increases systemic vascular capacitance as a result of an inhibition of sympathetic nervous system.

Nyman Y, Von Hofsten K, Palm C et al:

- Did a prospective, double blind, randomized trial study to compare the incidence of injection pain during intravenous induction of anesthesia between Propofol with added Lidocaine and the new Etomidate formulation in paediatric patients.
- A total of 110 paediatric patients aged 2-16 years ,scheduled for out - patient surgery were planned to be included in the. Study Primary end point of the study was the incidence of anesthesia as assessed by a four point scale. The occurrence of myoclonic muscular activity was registered as a secondary end point. An interim analysis after 80 patients was requested by the Ethics Committee.
- The study concluded that the use of the new lipid formulation of Etomidate was associated with significantly less pain on injection than Propofol with added. Lignocaine in children.
- These findings may warrant a change in clinical practice in order to avoid unnecessary pain in children.

Mayer M, Doenicke A, Nebauer AE, et al:

- Did a prospective, randomized clinical study to compare the effects of Propofol and Etomidate for their effects on hemodynamic and**.** various adverse effects on patient scheduled for elective surgeries during the induction of general anesthesia. 100 patients of ASA 1 and 2 were selected.
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- No opioid or benzodiazepines was given i.v before induction. After injection of the tested drug, the cannula was removed. Changes in blood pressure and heart rate as well as signs of discomfort during and after injection (pain, burning, tension, cold).Venous sequel were assessed for five days after injection to register signs of thrombophlebitis.
- The study concluded that Etomidate formulated in a medium chain lipid emulsion causes significant less discomfort for the patients than Propofol, which is in a long chain formulation. Myoclonus, however, occurred significantly more with Etomidate than with Propofol.

Saricaoglu F, Uzun S,Arun O et al:

- Did a study to compare Etomidate–lipuro and Propofol and 50% admixture of these agents at induction with reference to injection pain, hemodynamic changes and myoclonic movements.
- Ninety patients were assigned at random into three**.** Groups. Induction was performed with either 1)Etomidate –lipuro, 2)Propofol or 3)Etomidate-lipuro-Propofol admixture.
- After bi-spectral**.** Index monitoring, all agents were given as infusion with a perfusor at a constant rate of 200 ml/min till the BIS values reduced to 40. Blood pressure and heart rate were measured once in every 30 sec during this period. Patients were asked for pain at injection site and observed visually for myoclonus. The time BIS values decreased to 40, the total amount of induction doses were measured.
- This study concluded that the incidence of hemodynamic changes, myoclonus**.** And pain on injection is significantly lower in**.** group induced with Propofol –Etomidate-lipuro mixture. BIS is 40 times least in the same group and thus the 1:1admixture of Etomidate -lipuro-Propofol is a valuable agent for induction.

Miner JR, Danahy M, Moch A,Biros M, et al:

- A randomized non blinded prospective trial study to compare the efficacy, adverse events and recovery duration of Etomidate and Propofol used in procedural sedation**.** For painful procedures in the**.** Emergency department. Patients received either Propofol or Etomidate Doses, vital signs, nasal end tidal CO2, pulse-oximetry and bi-spectral EEG analysis scores were recorded.
- After the procedure, patients completed visual analog scales about pain perception during the procedure**.** and recall of the procedure.
- 220 patients were enrolled, 214 underwent sedation and analysed, 105 patients received Etomidate and 109 received Propofol. No clinically significant complications were noted.
- The study concluded that Propofol and Etomidate appear equally safe for emergency department procedure procedural sedation. However Etomidate had a lower rate of procedural success and induced myoclonus in 20% of patients.

Ray D C, McKeown DW, et al:

- The study was made in 159 septic shock patients admitted in the ICU over a 40 month period to study the association between induction agent

and its clinical outcome, including vasopressor, inotrope and steroid therapy.

- From the records, retrieved the details regarding induction agent use, vasopressor administration at induction, vasopressor, inotrope and steroid administration in the ICU and hospital. Hospital mortality was 65%.
- The numbers of patients given an induction agent were 74 Etomidate, 25 Propofol, 26 Thiopentone,18 other agent and 16 no agent
- Vasopressor, inotrope or steroid administration and outcome were not related to the induction agent chosen.
- Corticosteroid therapy given to patients who received Etomidate did not affect the outcome.
- Vasopressor therapy was required less frequently and in smaller doses when Etomidate was used to induce anesthesia
- Etomidate caused less cardiovascular depression than other induction agents in patients with septic shock.
- The study concluded that Etomidate use in critically ill patients should consider all these issues and not simply the possibility of adrenal suppression, which was unimportant when steroid supplements were used.

Sarkar, M; Laussen, Peter C. Zurakowski, D[†] et al:

- Made a prospective study in the acute effects of a bolus of Etomidate during induction of anesthesia in children using invasive hemodynamic monitoring.
- 12 children undergoing cardiac catheterization were studied (mean age, 9.2 ± 4.8 years; mean weight, 33.4 ± 15.4 kg); catheterization procedures which included device closure of secundum atrial septal defects (n = 7) and radiofrequency catheter ablation procedures for supraventricular tachycardia (n = 5).
- Using IV sedation, a balloon-tipped pulmonary artery catheter was placed to measure intra-cardiac and pulmonary artery pressures and oxygen saturations. Baseline measurements were recorded and then repeated after a bolus of IV Etomidate (0.3 mg/kg),
- For the entire group, no significant changes in right atrial, aortic, or pulmonary artery pressure, oxygen saturations, calculated Qp:Qs ratio or systemic or pulmonary vascular resistance were detected after the bolus dose of Etomidate.
- The lack of clinically significant hemodynamic changes after Etomidate administration supports the clinical impression that Etomidate is safe in children. Further research is needed to determine the hemodynamic profile of Etomidate in neonates and in pediatric patients with severe ventricular dysfunction and pulmonary hypertension.

Boysen K,Sanchez R,Krintel JJ et al:

- Did a prospective study comparing the induction and recovery characteristics of Propofol, Thiopental and Etomidate, with 20 patients in each group which were compared for anesthesia in women undergoing termination of pregnancy, with respect to:

1. pain on injection (equally often after Propofol and Etomidate, but more rarely after Thiopental);
2. apnea following induction (no difference);
3. involuntary muscular movements (more frequent after Etomidate)
4. blood pressure (larger drop after Propofol);
5. heart rate (greater increase after Thiopental);
6. time to eye opening on command (longer after Propofol);
7. Steward score on eye opening (no difference);
8. coin counting after 15, 30 and 60 min (performance better after Propofol at 15 and 30 min, producing even shorter times than pre-operatively at 60 min);
9. reaction time after 15, 30 and 60 min (performance better after Propofol, producing even shorter times than pre-operatively at 60 min.

- It was concluded that the faster recovery gives Propofol an advantage over Thiopental and Etomidate in outpatient anesthesthesia.

Muzi M, Berens RA,Kampine JP et al:

- Did a study which explored potential mechanisms, contributing to hypotension by recording cardiovascular responses including sympathetic neural activity from patients during induction of anaesthesia with Propofol (2.5 mg.kg-1 plus 200 micrograms.kg-1.min-1) or for comparison, Etomidate (0.3 mg.kg-1 plus 15 micrograms.kg-1.min-1).
- In this study, 25 nonpremedicated, ASA physical status 1 and 2, surgical patients were evaluated. Measurements of R-R intervals (ECG), blood pressure (radial artery), forearm vascular resistance (plethysmography), and efferent muscle sympathetic nerve activity ([MSNA] microneurography: peroneal nerve) were obtained at rest and during induction of anesthesia.
- In addition, a sequential bolus of nitroprusside (100 micrograms) followed by phenylephrine (150 micrograms) was used to obtain data to quantitate the baroreflex regulation of cardiac function (R-R interval) and sympathetic outflow (MSNA) in the awake and anesthetized states.
- Etomidate induction preserved MSNA, forearm vascular resistance, and blood pressure, whereas propofol reduced MSNA by 76 +/- 5% (mean +/- SEM), leading to a reduction in forearm vascular resistance and a significant hypotension.

- Both cardiac and sympathetic baroslopes were maintained with Etomidate but were significantly reduced with Propofol, especially in response to hypotension.
- These findings suggest that Propofol-induced hypotension is mediated by an inhibition of the sympathetic nervous system and impairment of baroreflex regulatory mechanisms. Etomidate, conversely, maintains hemodynamic stability through preservation of both sympathetic outflow and autonomic reflexes.

Ozgul U,Begec Z,Erdogan MA, et al:

- Did a randomised prospective study, with 100 patients aged 18-55 years. They were given 3 nerve blocks (inferior alveolar, lingual, and long buccal) to assess the effect of alkalinisation of the lignocaine solution with sodium bicarbonate.
- All the patients were given 2% lignocaine hydrochloride with adrenaline 1:80,000 and 50 patients were randomly allocated to be given 8.4% sodium bicarbonate in a 1/10 dilution.
- Pain was measured on a visual analogue scale (VAS). No patient given the injection with sodium bicarbonate complained of pain, compared with 39/50 (78%) not given sodium bicarbonate ($p<0.0001$).

- The mean (SD) time (seconds) to onset of local anaesthesia in the group given sodium bicarbonate was 34.4 (9.8) compared with 109.8 (31.6) in the control group ($p<0.001$).
- Our results have confirmed the efficacy of the alkalinised local anaesthetic solution in reducing pain on injection and resulting in quicker onset of anaesthesia.

MATERIALS AND METHODS

MATERIALS AND METHODS

SOURCE OF DATA:

Patients undergoing surgery under general anesthesia at Govt. Kilpauk Medical College Hospital and Govt. Royapettah Hospital , Chennai between February 2018 and July 2018 were assessed for inclusion and exclusion criteria. They were included in the study after obtaining written informed consent.

SAMPLE SIZE: 60

Sample size was determined based on the study "**PROSPECTIVE STUDY OF THE EFFECTS OF PROPOFOL AND ETOMIDATE IN ADULTS UNDERGOING SURGERIES UNDER GENERAL ANAESTHESIA"**

Authored by

V K GOYAL et al.

Published in

Rev Bras Anestesiol 2016; 66(3):237-241

Description:

The formula for determining sample size is given as:

$$n = \left(\frac{Z_{\alpha/2} \cdot \sigma}{E}\right)^2$$

Where

n = Sample size

σ = Population standard deviation

e = Margin of error

Z = The value for the given confidence interval

- The confidence level is estimated at 95%
- Standard deviation 58
- With a z value of 1.96
- The confidence interval or margin of error is estimated at +/-15
- Assuming that 80 percent as power of the study, minimum sample size required for the study was calculated to be 100.

In our study 60 subjects were chosen

(group 1 =30 numbers, group 2=30 numbers)

STUDY DESIGN:

A prospective, Non –Randomized, Double- arm, Single blind controlled study.

INCLUSION CRITERIA:

1) Patients undergoing elective surgeries under general anesthesia.
2) Age between 18 to 50 years.

3) ASA class 1 and 2.

4) Patients who have given valid informed consent.

EXCLUSION CRITERIA:

1. Patients not satisfying inclusion criteria.
2. Patients with a history of allergy to Propofol or Etomidate.
3. Patients with seizure disorder.
4. Presence of primary**.** or secondary steroid deficiency/on steroid medication
5. Impaired ability to communicate (e.g., confusion, poor hearing or language barrier).
6. Patients who were unconscious or severely ill.
7. Pregnant patients.
8. Hypotensive patients.

MATERIALS:

1. Boyles apparatus,
2. Laryngoscope with different blade sizes,
3. Emergency airway crash cart used in case of difficult intubation,
4. Appropriate sized Endotracheal tubes.
5. Drugs for administering premedication ,muscle relaxant,

6. Inj. Propofol availabl as 10mg/ml vial.

7. Inj. Etomidate available as 2mg/ml ampoule.

METHODOLOGY

METHODOLOGY:

- Patients satisfying the above mentioned inclusion criteria were selected and counseled regarding the risks and benefits involved in the study. After obtaining due informed consent, 60 patients were included enrolled and analyzed in the study. They were divided into two groups of 30 in each group based on random number as group 1 and group 2. The patients in Group 1 given Inj. Propofol 1% (2mg/kg of body weight) and the patients in Group 2 received Inj. Etomidate (0.3mg/kg of body weight).
- This study was designed as a prospective, comparative study. Patients were pre-operatively assessed and clinically examined.
- Procedures were explained in detail and written informed consent obtained. Routine monitoring included ECG, Pulse-Oximetry, NIBP. Intravenous cannulation secured with 18G intravenous cannula.
- Premedication given with inj. Glycopyrrolate 0.2 mg i.v, inj. Midazolam 0.02 mg/kg i.v and inj.Fentanyl 2 mg/kg I.V.
- Pre-oxygenation for 5 to 8 minutes**.**
- Induction with calculated dose of Propofol or Etomidate. Pain on injection and myoclonic movements at induction, if occurred were recorded.

- Patient was intubated with appropriate sized cuffed oral endotracheal tube 3 minutes after giving the intubating dose of Inj Vecuronium (0.1 mg/kg) I.V.
- Endotracheal tube was secured after assuring equivalent bilateral breath entry by 5 point auscultatory method by and positive pressure ventilation was initiated.
- Anesthesia was maintained with oxygen and nitrous oxide (70:30), Isoflurane along with intermittent boluses of Vecuronium, as required throughout the surgery.
- At the end of surgery, the residual neuromuscular block**.** was reversed with Neostigmine (0.05 mg/kg) and Glycopyrrolate (0.01 mg/kg) I.V. Patient was extubated when patient was conscious, oriented, reflexes recovered, good muscle power, adequate respiration and with stable haemodynamics.

ASSESSMENT CRITERIA	Group 1	Group 2
Blood pressure		
Heart rate		
Pain on injection		
Myoclonic movements		
Apnoea on induction		

METHOD OF COLLECTION OF DATA

60 patients were enrolled in the study who underwent elective surgeries under general anesthesia and had been assessed individually both intra-operatively and post -operatively.

The heart rate and mean arterial pressure were monitored continuously and recorded before induction, at induction and laryngoscopy followed by 1^{st}, 3^{rd}, 5^{th} and 10^{th} minutes after intubation.

Pain on injection was measured using 4 graded scale:

Grade 0 = no pain,

Grade 1 = verbal complaint of pain,

Grade 2 = withdrawal of arm and

Grade 3 = both verbal complaint and withdrawal of arm

Incidence and degree of pain of myoclonic movements recorded as

Grade 0=no myoclonic movements,

Grade 1=minor myoclonic movements,

Grade 2=moderate myoclonic movements,

Grade 3=major myoclonic movements.

Episodes of apnoea noted.

The obtained results were sent for statistical analysis.

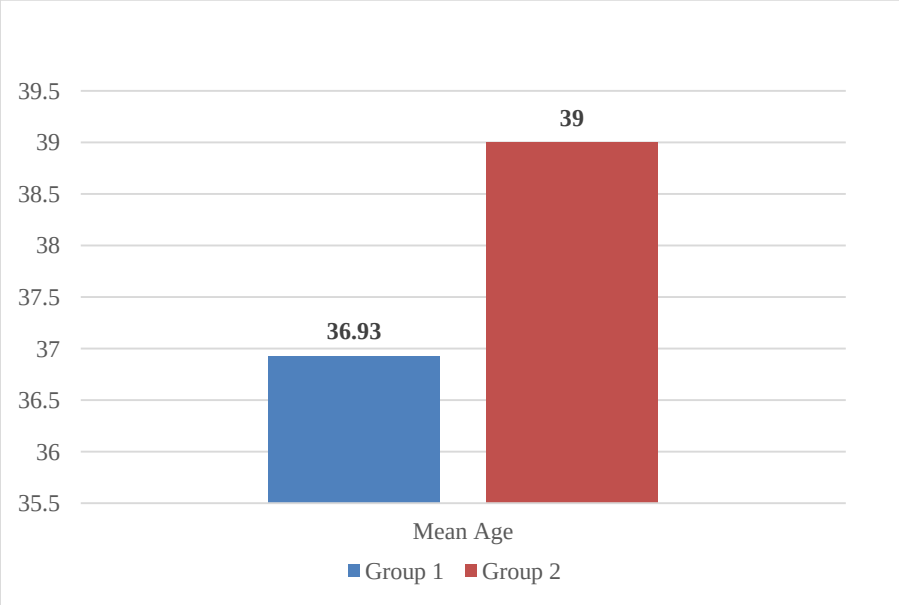
STATISTICAL ANALYSIS

- Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done.
- Continuous variables were analyzed with the unpaired t test and ANOVA.
- Categorical variables were analyzed with the Chi-Square Test. Statistical significance was taken as $P < 0.05$.
- The data was analyzed using SPSS version 16 and Microsoft Excel 2007.
- In this study, an analytical approach was adopted to assess the haemo-dynamic changes and various effects of the Propofol and Etomidate in patients undergoing general anesthesia.
- Data collected from 60 selected subjects were internally compared, tabulated, analyzed and interpreted by using descriptive and inferential statistics based on the formulated objectives of the study.

Table 1: Age Distribution between Two Groups

GROUP	N	AGE	
		Mean (yrs)	Standard deviation
Group 1 PROPOFOL	30	36.93	10.56
Group 2 ETOMIDATE	30	39.00	10.15
P value	P = 0.4420		

Figure 1: Age distribution between two groups:



DISCUSSION:

Table 1 and Figure 1 show that out of 60 patients, 30 were in group 1 and 30 in group 2.

Mean age was 36.93 ±10.56 in group 1 and 39 ±10.15 in group 2.

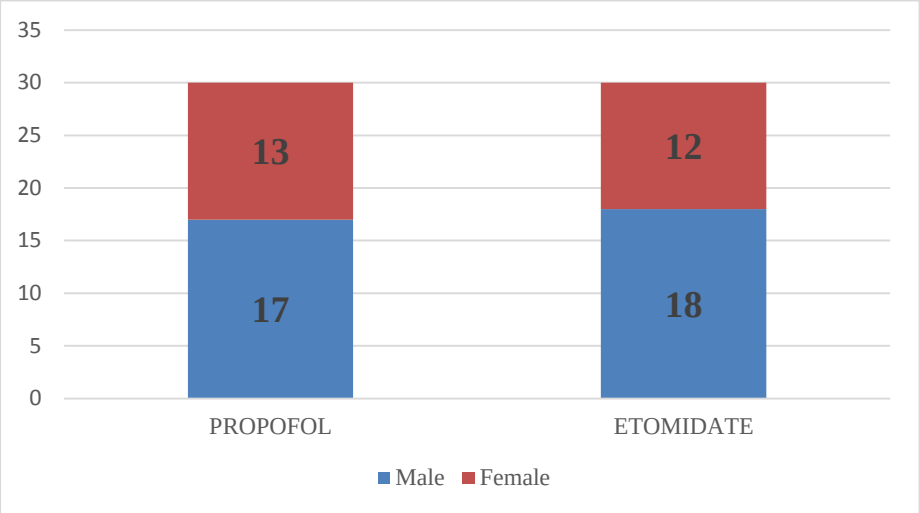
P value is 0.4420.

The difference was statistically non -significant.

Table 2: Sex Distribution between Two Groups

GROUP		Male		Female	
		n	%	N	%
Group 1 PROPOFOL	30	17	56.67	13	43.33
Group 2 ETOMIDATE	30	18	60	12	40
P value	P =0.551				

Figure 2: Sex distribution between two groups:



DISCUSSION:

Table 2 and Figure 2 show that 30 each were in group 1 and 2.

In group 1 - 17 were males and 13 were females

In group 2- 18 were males and 12 were females.

The percentage of age distribution in group 1 for male is 56.67% and for female is 43.33% and

In group 2 for male is 60% and for female is 40%.

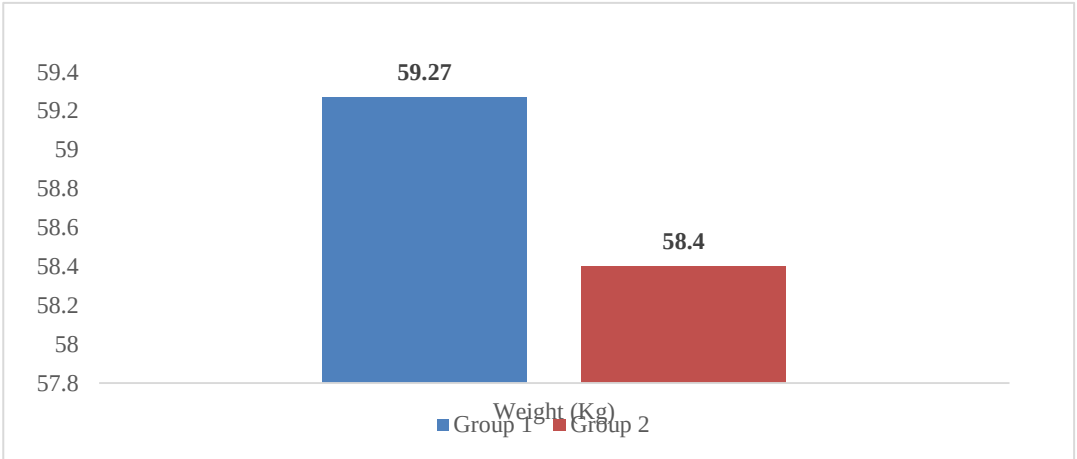
P value is 0.551.

The difference is statistically non-significant.

Table 3: Weight Distribution between Two Groups

GROUPS	**n**	**Weight**	
		Mean (mg)	Standard deviation
Group 1 PROPOFOL	30	59.27	5.79
Group 2 ETOMIDATE	30	58.40	5.49
P value	P = 0.5527		

Figure 3: Weight distribution between groups



DISCUSSION:

Table 3 and Figure 3 show that out of 60 patients, 30 were in group 1 and 30 in group 2.

Mean weight was 59.27 ±5.79 in group 1 and 58.40 ±5.49 in group 2.

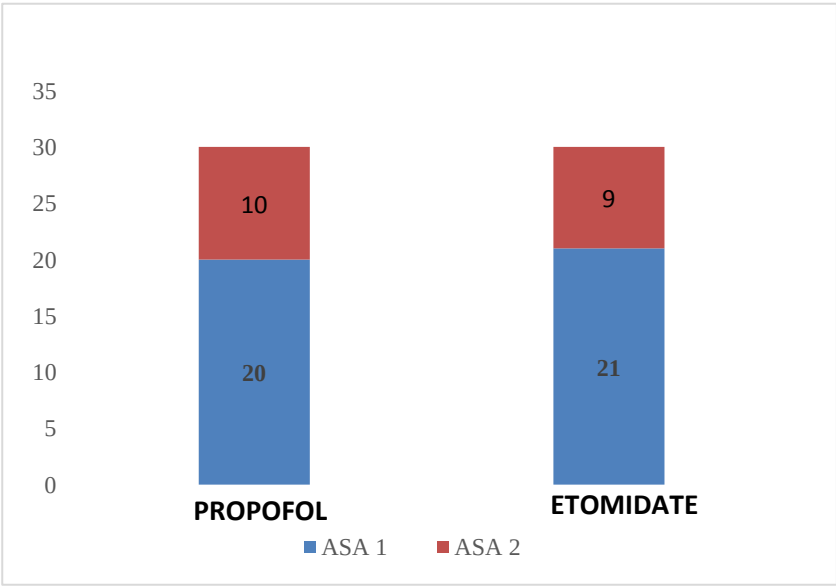
P value is 0.5527.

The difference was statistically non- significant.

Table 4: Comparison of ASA between two groups

ASA		1		2	
		N	**%**	**N**	**%**
Group 1 PROPOFOL	30	20	66.7	10	33.3
Group 2 ETOMIDATE	30	21	70	9	30
P value Chi square test	P=0.781375				

Figure 4: Comparison of ASA between two groups



DISCUSSION:

Table 4 and Figure 4 show that out of 60 patients , 30 were in group 1 and 30 in group 2.

The number of patients with ASA grade 1 was 20 in group 1 and 21 in group 2 while ASA grade 2 was 10 in group 1 and 9 in group 2.

The percentage of ASA grade 1 was 66.7% and 70% in group 1 and group 2 respectively while the percentage of ASA grade 2 is 33.3% and 30% in group 1 and group 2 respectively.

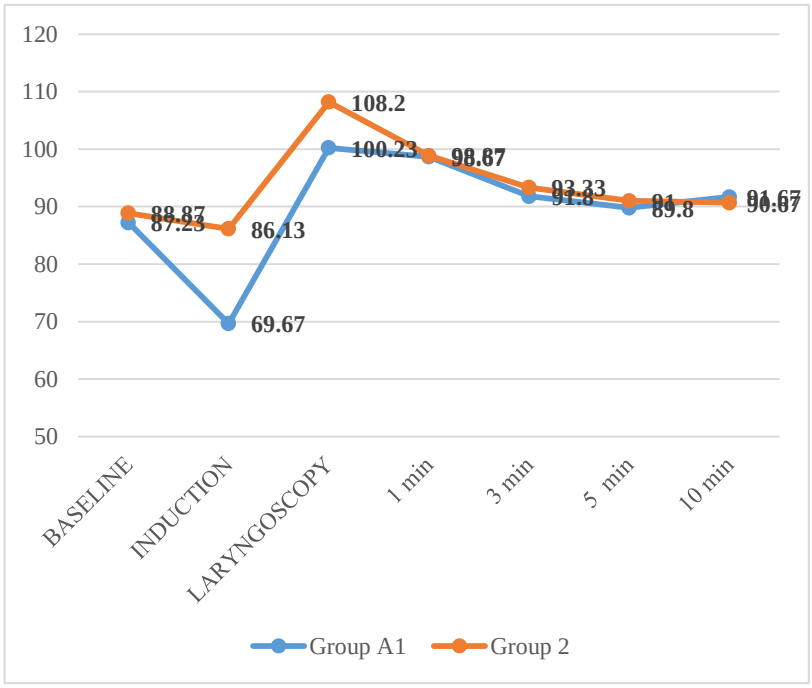
P value is 0.781375.

The difference was statistically non-significant.

Table 5: Comparison of Pre and Post Intubation Map Between Two Groups

Comparison of Pre and Post Intubation Mean(SD) MAP between two groups							
Group	Baseline	Induction	Laryngoscopy	1 Min	3 Min	5 Min	10 Min
Group 1 PROPOFOL	87.23	69.67	100.23	98.67	91.80	89.80	91.67
Group 2 ETOMIDATE	88.87	86.13	108.20	98.87	93.33	91.00	90.67
P value	P = 0.0903	P < 0.0001	P < 0.0001	P = 0.8658	P = 0.0976	P = 0.1826	P = 0.2498

Figure 5: Comparison of Pre and Post Intubation MAP between two groups



DISCUSSION:

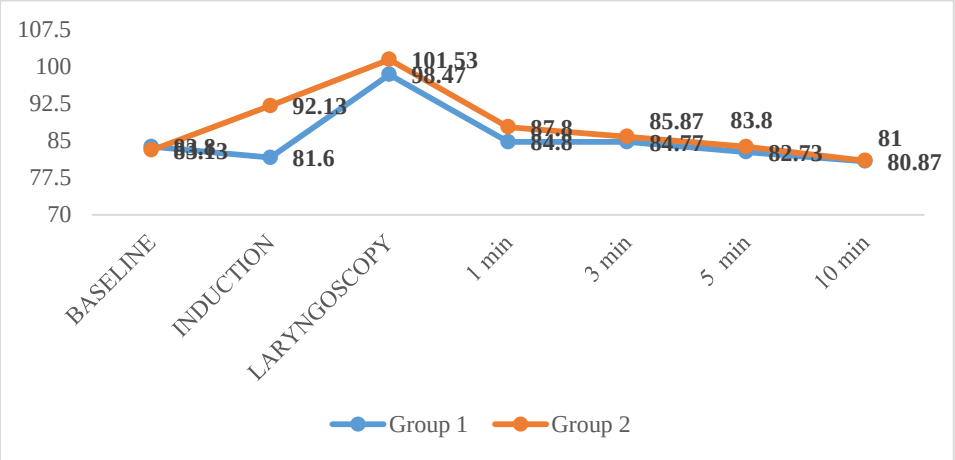
Table 5 and Figure 5 show MAP (Mean arterial pressure) at different time intervals in both groups. In group 1, a significant decrease in MAP from baseline at induction was seen compared to group 2.

The mean arterial pressure of both the groups was comparable. ($p>0.05$).

Table 6: Comparison of Pre and Post Intubation Heart Rate Between Two Groups

Comparison of Pre and Post Intubation Mean(SD) HR between two groups							
Group	Baseline	Induction	Laryngos-copy	1 Min	3 Min	5 Min	10 Min
Group 1 propofol	83.80	81.60	98.47	84.80	84.77	82.73	80.87
Group 2 etomidate	83.13	92.13	101.53	87.80	85.87	83.80	81.00
P value	P = 0.3275	P < 0.0001	P = 0.0018	P = 0.0008	P = 0.1791	P = 0.2227	P = 0.8883

Figure 6: Comparison of Pre and Post Intubation Heart Rate between Two Groups



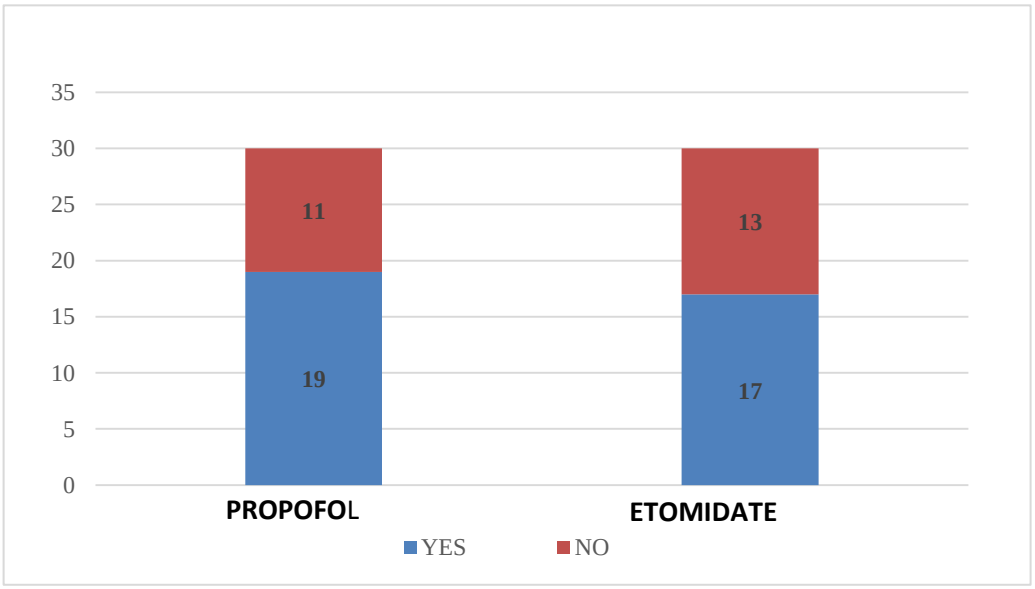
DISCUSSION:

Table 6 and Figure 6 show heart rate in both groups. In group 1, there was significant increase in heart rate from baseline to induction as compared to group 2. (p-0.01)

Table 7: Comparison of Aponea between Two Groups

APONEA		YES		NO	
		N	%	N	%
Group 1 PROPOFOL	30	19	63.3	11	36.7
Group 2 ETOMIDATE	30	17	56.7	13	43.3
P value Chi square test	P =0.60				

Figure 7: Comparison of Aponea between Two Groups



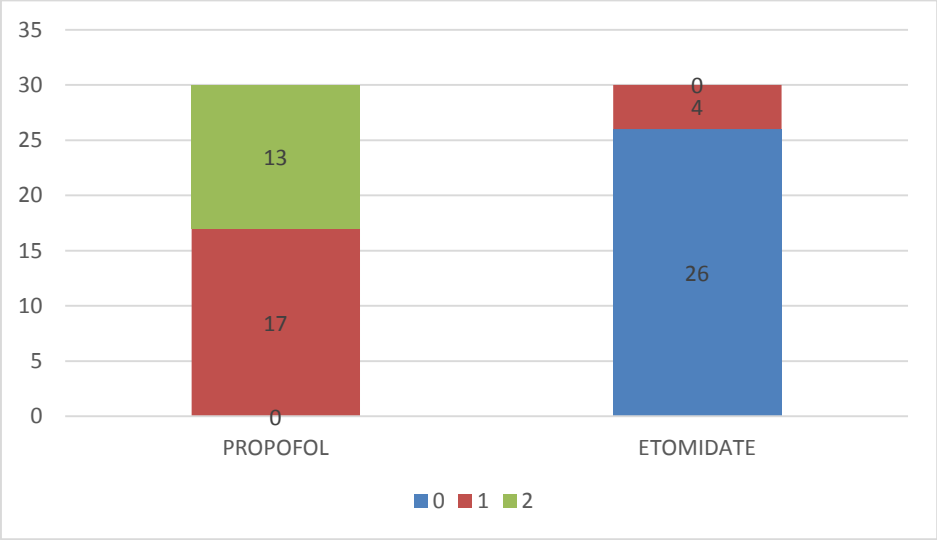
DISCUSSION:

Table 7 and Figure 7 show the number of patients with apnoea in both the groups. The number of patients with apnoea was 19 in group 1 and 17 in group 2 while no apnoea was seen in 11 subjects in group 1 and 13 subjects in group 2.The difference was statistically non- significant with p value of 0.60.

Table 8: Comparison of Grade of Pain on Injection between Two Groups

Pain on Injection		Grade 0		Grade 1		Grade 2	
		n	%	n	%	N	%
Group 1 PROPOFOL	30	0	0	17	56.7	13	43.3
Group 2 ETOMIDATE	30	26	86.7	4	13.3	0	O
P value Chi square test	P<0.0001						

Figure 8 Comparison of Grade of Pain on Injection between Two Groups



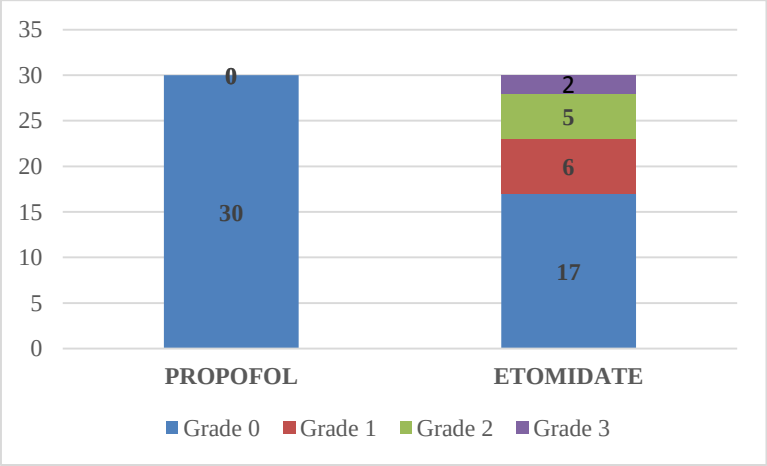
DISCUSSION:

Table 8 and Figure 8 show that in group 1, number of patients with grade 1, grade 2 and grade 3 pain was 17(56.7%), 13 (43.3%) and 0 respectively. In group 2, number of with grade 1, grade 2 and grade 3 was 26 (86.7%), 4 (13.3%) and 0 respectively. The chi square test was applied that showed highly significant value of p<0.0001.

Table 9: Comparison of Grade of Myoclonic Movements on Injection between Two Groups

Myoclonic movements		Grade 0		Grade 1		Grade 2		Grade 3	
		n	%	n	%	n	%	N	%
Group 1 PROPOFOL	30	30	100	0	0	0	0	0	0
Group 2 ETOMIDATE	30	17	56.7	5	16.7	6	20	2	6.7
P value Chi square test	P<0.001								

Figure 9: Comparison of Grade of Myoclonic Movements on Injection between Two Groups



DISCUSSION:

Table 9 and Figure 9 show that all patients in group 1showed grade 0 while in group 2 -17 patients showed grade 0,6 patients showed grade 1, 5 patients showed grade2 and 2 patients showed grade 3 movements. The difference was statistically significant with p value <0.001

DISCUSSION

DISCUSSION:

- The induction of anesthesia may produce hemodynamic variation of mild to moderate degree depending **.**upon many factors.
- In this prospective study, 60 patients were included and they were separated into two groups.
- The systolic blood pressure ,diastolic blood pressure , mean arterial blood pressure and heart rate were monitored continuously and recorded before induction, at induction and during largyngoscopy followed by 1,3,5 and 10 minutes after intubation.
- It was observed that Propofol**9** (Group 1) caused significant hypotension and tachycardia at induction in comparison to Etomidate (Group 2).
- Hypotension occurring with Propofol is mainly due to reduction of sympathetic activity causing vasodilation and by its effect directly on vascular smooth muscles.
- Sudden hypotension and tachycardia has deleterious effects on maintaining the circulation to vital organs in patients with coronary artery disease, Valvular stenosis, uncontrolled hypertension and shock.
- On the other hand hemodynamic stability observed with Etomidate may be due to its unique lack of effect on the sympathetic nervous system and on baroreceptor function.

- Etomidate does not have its limitation to normotensive patients for its hemodynamic peculiarity.
- In various studies, Etomidate has showed less cardiovascular depression and minimized the use of vasopressor agents than other induction agents in sepsis and critically ill patients.
- Although Etomidate can cause adrenal insufficiency in these patients in postoperative period, clinical consequence of that is still unclear over its advantage to prevent hypotension at induction. Mayer et al and Wu et al also cocluded that, Etomidate maintains hemodynamis stability during anesthesia.
- Pain during injection of anesthetic agent is a traumatic experience for the patient and also an embarrassing situation for the anesthesiologist.
- In our study, we observed that, in group 1 percentage of patients with pain of grade 1 was 56.7% (17 patients), grade 2 was 43.3% (13 patients).In group 2,the percentage of patients with pain of grade 0 was 86.7% (20 patients), grade 1 was 13.3% (patients) and grade 2 was nil.
- This showed that pain on injection was more significant with group 1 compared to group 2.Saricaoglu et al. and Wu et al. Too showed same results in their studies.
- In our study, both agents had shown similarity in their respiratory depressant effect.

- In our study, it was found that the occurrence of apnoea was less in the group 2 when compared with group 1 but the difference was non-significant.
- The episodes of apnea were transient and not associated with any fall in oxygen saturation. Boysen et al. study results also found to be in agreement with our study results, that there is insignificant difference in the occurrence of apnoea between the Propofol and Etomidate groups.
- In our study, group 1 patients showed no myoclonic movements but group 2 showed high incidence of myoclonic jerks. The only negative characteristic noted with Etomidate was high incidence of myoclonic jerks. Miner et al and Desai et al also concluded in their study, that there is high incidence of myoclonic movements with the use of Etomidate.

CONCLUSION

CONCLUSION:

In conclusion, Etomidate was found ideal for its hemodynamic stability when compared to Propofol along with less incidence of pain on injection, the only drawback being high incidence of myoclonus.

The study suggests that Etomidate is a better option in patients particularly vulnerable to hemodynamic fluctuation during induction like uncontrolled hypertension, sepsis, critically ill and patients with coronary artery disease.

This study showed significant p value in heart rate at induction, mean arterial pressure at induction, pain on injection and incidence of myoclonus.

Hence the hypothesis proving the study with high clinical significance.

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INSTITUTIONAL ETHICS COMMITTEE
GOVT. KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID. No. 02/2017 Meeting held on 14.11.2017

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval **"A COMPARATIVE STUDY BETWEEN THE EFFECTS OF PROPOFOL AND ETOMIDATE IN ADULTS UNDERGOING SURGERIES UNDER GENERAL ANAESTHESIA"** submitted by Dr.M.SUBHASHINI, Post Graduate in M.D Anaesthesiology,Govt. Kilpauk Medical College, Chennai-10.

The Proposal is **APPROVED.**

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

14.11.2017

DEAN
Govt. Kilpauk Medical College,
Chennai-10.

ME 1 Sec> Ethical Committee

INFORMED CONSENT FORM

STUDY. " A COMPARATIVE STUDY BETWEEN THE EFFECTS OF PROPOFOL AND ETOMIDATE IN ADULTS UNDERGOING SURGERIES UNDER GENERAL ANESTHESIA"

STUDY CENTRE: GOVT. KILPAUK MEDICAL COLLEGE & GOVT. ROYAPETTAH HOSPITAL, CHENNAI

PATIENT'S NAME:

PATIENT'S AGE:

I.P NO :

Patient may check (√) these boxes

I confirm that I understood the purpose of the procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction ☐

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

I understand that the ethical committee members and the regulatory authorities will need not my permission to look at my health records, both in respect of the

current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. ☐

I agree not to restrict the use of any data or results that arise from the study. I agree to take part in the above study and to comply with the instructions given during the study and faithfully co-operate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well-being or any unexpected or unusual symptoms. ☐

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests. ☐

Signature / thumb impression:

Patient's name and address: place & date :

Signature of the investigator:

Study investigator's name: place & date:

PARTICIPANTS INFORMATION SHEET

Investigator : **Dr.M.SUBHASHINI**

Name of the participant :

Title: "**A COMPARATIVE STUDY BETWEEN THE EFFECTS OF PROPOFOL AND ETOMIDATE IN ADULTS UNDERGOING SURGERIES UNDER GENERAL ANESTHESIA"**

You are invited to take part in this research study. We have got approval from the IEC. You are asked to participate because you satisfy the eligibility criteria.

What is the purpose of this research?

In this study, the hemodynamic and various effects of etomidate and propofol will be evaluated so that the patient will have peri operative hemodynamic stability.

BENEFITS:

This study will help us in determining the hemodynamic effects of the patients undergoing surgeries under general anesthesia.

DISCOMFORTS AND RISKS:

Intravenous injection of Propofol may produce pain on injection, hypotension, bradycardia. I.V Etomidate may produce myoclonus.

CONFIDENTIALITY:

Patients who participated in the study and their details will be maintained confidentially in all circumstance.

RIGHT TO WITHDRAW:

Patients will not be forced to complete the study. At any cost, in such circumstances the treatment will not be compromised in any way.

Date :

Signature of the investigator:

Place :

Signature/Thumb impression of the participant

URKUND

Urkund Analysis Result

Analysed Document: Subhashini Plagiarism.docx (D42833347)
Submitted: 10/21/2018 4:40:00 PM
Submitted By: dr.subhamano@yahoo.co.in
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Instances where selected sources appear:

MASTER CHART

S.NO	NAME	AGE	SEX	Wt IN KG	ASA STATUS	MEAN ARTERIAL PRESSU							HEART RATE							PAIN ON INJECTION	APNOEA	MYOCLONIC MOVEME	
						BASELINE	INDUCTION	LARYNGOSCOPY	I MIN	3 MIN	5MIN	10 MIN	BASELINE	INDUCTION	LARYNGOSCOPY	1 MIN	3 MIN	5 MIN	10 MIN	GRADES		GRADES	
1	bharathi	32	male	62	I	88	72	105	102	96	90	92	84	90	100	88	86	84	82	2	YES	0	
2	siva	43	male	70	I	88	70	102	100	94	90	92	88	98	104	86	84	82	80	1	YES	0	
3	gokul	25	male	61	I	84	72	104	102	92	90	94	86	92	102	88	86	84	82	1	YES	0	
4	indhra	32	female	48	II	86	62	98	100	94	86	92	84	94	100	90	90	88	86	2	NO	0	
5	valli	51	female	56	II	89	72	96	102	90	90	88	82	90	102	88	86	84	82	1	YES	0	
6	arumugam	46	male	66	I	90	74	102	98	90	92	94	82	96	100	86	84	82	80	2	YES	0	
7	sundar	24	male	64	I	94	76	106	104	88	88	90	84	80	104	88	86	84	82	1	YES	0	
8	gowri	28	female	52	I	96	74	108	106	92	86	90	88	98	98	86	84	82	80	2	YES	0	
9	ranga	56	male	55	II	82	64	96	98	92	88	92	86	96	98	90	88	86	84	1	NO	0	
10	lalitha	39	female	57	I	90	76	110	108	92	92	94	82	94	100	92	90	88	86	1	NO	0	
1	devi	40	female	54	II	92	74	96	94	96	92	92	82	82	100	88	86	84	82	2	YES	0	
12	hariharan	49	male	72	II	86	68	94	92	92	90	92	84	80	100	86	84	80	78	1	YES	0	
13	kannan	51	male	65	II	88	66	98	96	88	88	90	82	82	98	88	86	86	84	2	YES	0	
14	eswari	27	female	59	I	82	70	102	102	92	90	92	82	84	98	86	84	80	78	1	NO	0	
15	karnan	28	male	58	I	90	72	98	96	90	90	92	82	86	100	90	86	86	84	2	YES	0	
16	thendral	49	female	55	II	84	66	98	98	90	90	90	84	98	102	88	86	84	82	2	YES	0	
17	mathi	31	male	62	I	96	74	120	110	92	90	92	86	96	100	84	84	82	80	1	NO	0	
18	rani	37	female	55	I	90	70	96	94	94	90	94	84	94	100	88	86	84	80	1	NO	0	
19	kalyani	28	female	58	I	86	68	94	94	92	88	90	80	96	104	90	88	84	80	2	YES	0	
20	vijayan	46	male	65	I	84	64	96	96	94	94	92	80	98	102	86	84	82	80	1	YES	0	
21	devan	44	male	66	I	86	70	98	96	90	90	92	82	98	120	88	84	82	80	2	NO	0	
22	maari	39	male	59	II	88	70	98	98	92	92	90	82	98	108	90	88	86	84	1	NO	0	
23	karthi	26	male	67	I	84	68	94	92	92	92	92	82	98	100	86	84	82	80	1	YES	0	
24	vani	33	female	55	I	80	72	102	100	94	90	92	82	88	102	88	86	84	82	1	YES	0	
25	jaya	51	female	53	II	84	66	90	88	92	90	94	82	98	100	90	88	86	84	2	NO	0	
26	srinivasan	22	male	60	I	88	72	98	96	92	88	90	82	86	100	88	86	84	82	1	YES	0	
27	jothi	20	female	54	I	90	74	96	98	92	90	92	80	88	102	86	84	82	80	2	NO	0	
28	malar	30	female	52	I	86	68	110	104	92	90	90	84	90	98	84	84	80	78	1	NO	0	
29	vasanth	52	male	62	II	82	66	102	98	88	88	92	84	98	100	88	88	86	74	2	YES	0	
30	rajan	29	male	56	I	84	60	100	98	90	90	92	82	98	104	90	86	86	74	1	YES	0	

S NO	NAME	AGE	SEX	WT IN KG	ASA STATUS	MEAN ARTERIAL PRESSURE							HEART RATE							EFFECTS OF ETOMIDATE	PAIN ON INJECTION	APNOEA	MYOCLONIC MOVEMENTS
						BASELINE	INDUCTION	LARYNGOSCOPY	1 MIN	3 MIN	5 MIN	10 MIN	BASELINE	INDUCTION	LARYNGOSCOPY	1 MIN	3 MIN	5 MIN	10 MIN		GRADES	GRADES	GRADES
1	Gowthami	28	female	52	I	88	86	108	100	96	94	94	80	82	96	82	82	80	78		0	0 YES	0
2	Renuka	21	female	58	I	90	88	110	98	94	92	92	84	82	98	84	84	82	80		0	0 NO	0
3	Jayanthi	40	female	60	I	86	84	108	102	98	96	96	82	80	98	84	86	82	80		1	0 YES	1
4	Jayashankar	45	male	54	II	84	82	110	100	96	92	92	84	82	98	86	86	84	82		1	0 YES	1
5	Manoj	26	male	62	I	92	90	106	100	96	90	92	86	84	100	86	86	84	82		0	0 NO	0
6	Markandeyan	35	male	65	I	92	88	104	96	90	88	88	84	80	96	82	82	80	78		1	0 NO	0
7	Jothi	38	female	60	I	90	88	120	106	100	98	98	82	80	94	80	80	78	76		0	0 NO	0
8	Sarangabani	28	male	61	I	88	86	110	100	96	96	94	84	82	100	86	84	82	80		0	0 YES	2
9	Lakshmi	31	female	54	I	86	84	116	110	104	102	100	88	82	98	84	84	82	80		0	0 NO	0
10	Kalyani	44	female	56	II	92	90	106	100	96	94	94	82	80	98	82	82	80	80		0	0 YES	2
11	Gangadhar	55	male	60	II	86	84	104	98	94	92	92	84	82	100	86	86	84	82		0	0 YES	0
12	Thilak	56	male	64	II	88	86	102	96	92	90	90	86	84	102	88	88	84	82		0	0 NO	0
13	Mariammal	48	female	58	I	84	82	110	98	90	88	88	82	80	98	84	84	82	80		1	0 YES	1
14	Porvannan	44	male	64	I	82	80	108	98	90	90	90	82	80	96	82	84	82	80		0	0 YES	0
15	Palani	36	male	66	II	86	84	110	100	94	92	92	84	82	98	84	84	82	80		3	0 NO	0
16	Krishnan	38	male	64	I	88	86	106	96	90	88	86	88	86	110	104	104	102	100		0	0 YES	0
17	Shankar	50	male	68	I	90	88	104	94	86	84	84	80	80	100	86	86	84	82		0	0 NO	0
18	Chandru	48	male	58	II	92	90	112	102	98	96	94	82	80	96	82	82	80	78		0	0 YES	0
19	kumar	43	male	56	II	94	90	116	106	98	96	96	82	80	98	84	84	84	82		3	0 NO	3
20	Malliga	52	female	48	I	88	84	108	98	96	88	88	80	80	98	86	86	84	82		0	0 YES	0
21	Manivannan	56	male	52	II	90	82	104	94	88	86	86	84	82	96	82	82	80	78		0	0 YES	0
22	Rajesh	36	male	65	I	84	80	102	92	88	86	84	86	84	100	86	86	84	82		2	0 YES	2
23	Ramkumar	33	male	67	I	88	86	110	100	94	92	92	92	80	104	90	90	88	86		1	0 YES	1
24	Vishwanathan	28	male	55	II	96	90	104	94	88	86	86	80	86	98	84	84	82	80		2	0 NO	2
25	Anudha	24	female	52	I	92	90	116	106	100	98	98	92	80	96	82	82	80	78		2	0 NO	2
26	Geetha	34	female	50	I	90	86	108	98	90	88	88	82	80	98	82	82	80	78		0	1 YES	0
27	Anitha	28	female	54	I	88	86	104	94	88	86	86	82	80	96	82	82	80	78		0	0 YES	0
28	Jansi rani	48	female	51	II	94	90	102	92	86	84	84	84	82	100	86	84	82	80		0	0 YES	0
29	Selvam	47	male	60	I	90	88	110	100	92	90	90	84	82	98	84	82	80	80		0	0 NO	1
30	Praveen	29	male	58	I	88	86	108	98	90	88	88	82	82	96	84	84		80		1	0 NO	2