“A PROSPECTIVE RANDOMISED COMPARATIVE STUDY OF EFFICACY AND SAFETY OF COMBINATION OF INJ.DEXMEDETOMIDINE–PROPOFOL AND INJ.FENTANYL-PROPOFOL FOR THE INSERTION CONDITIONS OF PROSEAL LARYNGEAL MASK AIRWAY”

By

Dr.PRASHANTH VADIGERI.

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Dr. PRASHANTH VADIGERI

ABBREVIATIONS

- ASA – American society of anaesthesiologist
- BMI – Body mass index
- MPC – Mallam patti class (for airway assessment)
- RR – Respiratory rate
- RT – Ryle's tube
- LMA – Laryngeal mask airway
- cLMA – Classic Laryngeal mask airway
- COPA – Cuffed oropharyngeal airway
- PLMA – Proseal laryngeal mask airway
- cm H_2o – centimetre of water
- mmHg – millimetre of mercury
- AMP - adenosine mono phosphate
- mcg – microgram
- Vd – volume of distribution
- I.V. – Intravenous
- TCI – Target controlled infusion
- SBP – systolic blood pressure
- DBP – diastolic blood pressure
- MAP – mean arterial pressure
- D-P – Dexmedetomidine-Propofol
- F-P – Fentanyl-Propofol

ABSTRACT

- **INTRODUCTION** Insertion of LMA requires adequate mouth opening and minimal upper airway reflexes. Propofol in high doses will provide adequate conditions to insert LMA but causes cardio respiratory depression. To decrease the dose requirement of Propofol, opioids are used, but the incidence of apnoea increases and the duration of apnoea is also prolonged.

- Dexmedetomidine, a highly selective α_2-adrenoceptor agonist, is a frequently used drug along with routine anaesthetic drugs. It maintains haemodynamic stability and is a good sedative, anxiolytic, analgesic neuroprotective agent. Other claimed advantages include minimal respiratory depression with cardioprotection, and renoprotection, thus making it useful at various situations including offsite procedures.

- Fentanyl, an opiod analgesic which provide cardiovascular stability, even in critically ill patients. It has been used as premedication and is known to attenuate haemodynamic responses while intubation and PLMA insertion.

- The current study will be undertaken to compare the adequacy of anaesthesia provided by Propofol in combination with Dexmedetomidine and Propofol in combination with Fentanyl for elective surgical procedures.

AIM : *PRIMARY OBJECTIVES*

- To assess the insertion condition of PLMA
- To study haemodynamic effects during insertion of PLMA

METHODS:

Study Design: Prospective Randomised clinical trial

Study Period: One and half years from December 2015 to August 2017.

Sample Size: With anticipated mean difference of apnoea between the two study as 20% and anticipated SD as 0.3, the minimum sample per group is 47, with 80% power and 5% level of significance. Total sample size is 47+47=94.

All data will be recorded as a +/- SD and statistical analysis will be done using

- Student ' t ' test
- Chi square test
- Fisher's exact test

Procedure and RESULTS: Newly developed supraglottic airway PLMA, now increasingly used with added advantages for better glottic seal and provision of drain tube insertion.

In a prospective, randomized, comparative, open study 94 ASA class I and II patients undergoing short surgical procedures were allotted in 2 different groups. One receiving Dexmedetomidine (group D-P) and the other receiving Fentanyl (F-P). Study drug was given at a dose of 1 mcg/kg over 10 minutes by an infusion pump . After standard premedication, all the patients were induced with Inj. Propofol up to a dose of 2.5 mg/kg fixed in protocol, till the end point of centralization of pupils was achieved. PLMA was introduced with the help of introducer technique described. Every unsuccessful attempt was topped up with Propofol 0.5 mg/kg, followed by successive attempt.

From this study we came to conclusion that though the insertion conditions were comparable statistically with the use of either Dexmedetomidine or Fentanyl as an adjuvant with Inj. Propofol (up to 2.5mg/kg) for the use of PLMA in short surgical procedures, Dexmedetomidine (1 mcg/kg) can be used with more favorable overall insertion conditions and less chances of coughing and movements; also lower incidence of apnoea than Fentanyl (1mcg/kg). Use of Dexmedetomidine also reduces the requirement of induction and incremental doses of Inj. Propofol. Attenuation of haemodynamic responses is also better with use of Dexmedetomidine as an adjuvant, compared to use of Fentanyl as an adjuvant. Thus Dexmedetomidine has better potential as a co -induction agent used with Propofol for insertion of PLMA in short surgical procedures in given doses with improved overall insertion conditions and better haemodynamic profile than Fentanyl.

KEY WORDS: PLMA, PREMEDICATION ,DEXMEDITOMEDINE , INSERTION CONDITIONS

TABLE OF CONTENTS

LIST OF TABLES AND FIGURES

INTRODUCTION

Airway management is a fundamental aspect of anaesthesia practice and emergency critical care. The first skill that the anaesthesiologist must acquire is procuring and maintaining a patent airway.

Endotracheal intubation, first used in anaesthesia in 1878, is a rapid, simple, safe and non-surgical technique that achieves all the goals of airway management, hence remains the gold standard for airway management. It often requires neuromuscular blockade, stimulates the unwanted reflex activity and may damage the vocal cords and tracheal mucosa [1]. Involvement of rigid laryngoscopy, damage to oropharyngeal structure and haemodynamic responses precludes the global utility of the tracheal tube and requires a better alternative [2]. An alternative method, in fasting patients who are breathing spontaneously is the use of traditional facemask with or without oropharyngeal airway.

With these problems in mind, Dr. Archie Ian Jeremy Brain developed a new approach. The anaesthetic facemask instead of being applied to the face, was reduced in size so that it could be positioned over the laryngeal opening itself [3]. Brain made a prototype mask using cadaveric pharynx in 1981. He inserted it blindly under deep halothane anaesthesia producing satisfactory lung inflation with gentle positive pressure ventilation. Compared to facemask it reduces requirement of fresh gas flow, allows more effective scavenging, facilitates monitoring of end tidal carbon dioxide concentration. Though supraglottic airways provide an adequate airway, the risk of

aspiration always remains. Hence Proseal Laryngeal Mask Airway (PLMA) was introduced.

PLMA has a softer silicone cuff reducing the throat irritation. It has a high seal pressure hence provides a tighter seal against the glottic opening. PLMA has a dorsal cuff, in addition to the peripheral cuff of LMA, which pushes the mask anterior to provide a better seal around the glottic aperture [4] with a tighter seal without increasing pressure on the mucosa and permits high airway pressures without leak. It also facilitates easy insertion of gastric drain tube that helps in confirmation of proper placement of PLMA and aspiration of gastric contents.

Successful insertion of PLMA without any untoward effects such as gagging and coughing requires adequate depth of anaesthesia and suppression of upper airway reflexes but neuromuscular blocking drug is not required [5]. Propofol is a well-known intravenous induction agent with rapid induction and recovery [5].

For the use of PLMA different induction agents used over a period of time for rapid and smooth insertion of PLMA with minimum alteration of haemodynamic responses and insertion conditions are Propofol[5], Thiopentone[6], Sevoflurane[5] etc. Propofol is non-opioid, non-barbiturate, sedative-hypnotic agent with rapid induction and recovery time and anti-emetic effect [7]. Propofol 2.5 – 3.0 mg/kg is considered as the induction agent of choice for PLMA insertion [8]. It is used to facilitate insertion of laryngeal mask airway, because it has a short duration of action and a rapid recovery. In addition, it is known to cause dose dependent cardio-respiratory depression, injection site pain. It has no analgesic property [7]. It depresses pharyngeal and laryngeal reflexes [9].

Propofol decreases blood pressure and heart rate, as it directly suppresses peripheral vascular resistance, decreases myocardial contractility and reduces sympathetic tone [7]. When used alone for laryngeal mask insertion, it still causes undesirable events such as swallowing, coughing, gagging, laryngospasm, limb and head movements [10, 11]. To achieve better insertion conditions with minimum haemodynamic responses and respiratory depression, various adjuvants have been tried with Propofol as Midazolam, Ketamine, low dose muscle relaxants, Mivacurium [11], Alfentanyl [11,13], Fentanyl [11,12,]. The addition of an opioid such as Alfentanyl has been shown to improve the success rates of LMA insertion. However, opioids may increase the incidence and duration of apnoea, due to respiratory depressant effect, and may enhance the depressant effect of Propofol on blood pressure and heart rate [13]. Dexmedetomidine is a pharmacologically active dextro isomer of medetomidine, which displays specific and selective α-2 adrenoceptor agonism. It is found to reduce dose requirement of Propofol to produce unconsciousness and loss of eyelash reflexes [14, 15]. Dexmedetomidine over a period of time has been studied with Propofol as a co-induction agent to assess the haemodynamic response, Propofol dose requirement and overall insertion condition of laryngeal mask airway [15, 16, 17].

In this study, we aim to evaluate the effects of Dexmedetomidine versus Fentanyl with Propofol as an induction agent on the insertion conditions, haemodynamic conditions during insertion of PLMA and total dose and incremental dose requirement of Propofol.

AIMS AND OBJECTIVES

1. To assess the insertion condition of PLMA.
2. To study haemodynamic effects during insertion of PLMA.
3. To assess requirement of total and incremental doses of Propofol.
4. To assess the adverse effects like swallowing, coughing, gagging, laryngospasm, lacrimation, head and limb movement.

HISTORY AND REVIEW OF LITERATURE

In 1878, endotracheal intubation was first used as rapid, simple and safe non-surgical way of airway management with its own set of problems such as requirement of neuromuscular blocking agent stimulation of unwanted reflex activity and possibility of vocal cord damage and tracheal mucosa [1].

Keeping in mind the problems associated with endotracheal intubation, **Dr. A I J Brain** developed a new approach. The anaesthetic facemask, instead of being applied to the face, was reduced in size so that it could be positioned over the laryngeal opening itself [3]. Brain made a prototype mask using cadaveric pharynx in 1981, inserted blindly under deep halothane anaesthesia providing satisfactory lung inflation with gentle positive pressure ventilation.

With the invent of new type of airway known as laryngeal mask airway, **Brain et al**, in 1985 studied the role of LMA in all type of inhalational anaesthesia. They proved its value in some cases of difficult intubation and said that it may contribute significantly to the safety of general anaesthesia [18].

R.A. Martlew et al 1996, in their study they compared Propofol requirement in children posted for minor surgical procedures under general anaesthesia. The study was intended to assess the effect of premedication on dose requirement Propofol for insertion of LMA. They divided 110 patients in two group 50 patients in non pre-medicated and 60 patients in pre-medicated. Patients were pre-medicated with oral Midazolam 0.5 mg/kg. In both groups they gave gradually increasing doses of Propofol. Conditions were considered satisfactory when jaw was relaxed; there was no coughing, swallowing,

laryngospasm, minimal or no limb movement. If the conditions were unsatisfactory in incremental dose of Propofol was given. Finally they concluded that the effective dose of Propofol for induction in non pre-medicated patients exceeds 5 mg/kg, whereas in pre-medicated it was reduced to less than 4 mg/kg. The relatively higher doses of Propofol required in this study was due to the higher volume of distribution compared to adults [19].

Maltby et al in 2002 from university of Calgary, Canada, carried out a study including 109 patients ASA 1 – 3, which were obese with BMI more than 30, scheduled for elective laparoscopic surgery. They studied the effectiveness of PLMA against endotracheal intubation in obese patients posted for laparoscopic Cholecystectomy. In that they concluded that adequate pulmonary ventilation without gastric distension can be achieved with both PLMA and endotracheal intubation, but PLMA may prove to be acceptable alternative to tracheal intubation in obese patients [20].

Similarly in a study conducted by **M Zoremba et al**, in 2002 in Germany over 134 moderately obese patients posted for minor peripheral surgeries, comparison was done between tracheal intubation and laryngeal mask airway. To conclude they said that, in moderately obese patients undergoing minor surgery, use of the LMA may be preferable to orotracheal intubation with respect to postoperative saturation and lung function [21].

Dr. V. Priya, in 2002 Tata memorial hospital, Mumbai, conducted a study on 50 ASA 1 and 2 patients divided in two groups containing 25 patients each, undergoing elective breast surgeries. They compared the conditions of insertion after induction with either inhalation of Sevoflurane 8 % with 100% oxygen or intravenous Propofol mean

dose of 2.45 mg/kg. They concluded that Propofol was superior to Sevoflurane for insertion of LMA, using loss of eyelash reflex as end point of induction. Sevoflurane may be considered as an alternative to Propofol as an induction agent for LMA insertion when adequate jaw relaxation considered as an end point of induction [22].

Bimla Sharma et al, in their study done in 2003, in a group of 100 patients ASA 1- 3, of 18 to 85 years of age scheduled for elective laparoscopic surgeries assessed the use of PLMA. They assessed their effects in relation to stable haemodynamics, good oxygenation and good ventilation. Residual gastric fluid could be aspirated with use of gastric tube. Further it was useful in cases of anticipated difficult airway [23].

Goyagi T. And colleagues in 2003, in the background that Fentanyl is a potent depressant of upper airway reflexes, studied Fentanyl as an adjuvant with Propofol as an induction agent used for insertion of laryngeal mask airway against a controlled group and both were without premedication. After administration of study drug they induced patient with Inj. Propofol at the rate of 100 mg/min. 90 second after LMA was inserted. The total dose of Propofol recorded, the dose of Propofol started with 2.5 mg/kg and adjusted according to Dixon's up and down method with a step of 0.25 mg/kg. Towards end they concluded that pre-administration of Fentanyl 2 mcg/kg decreases the Propofol requirement for LMA insertion [24].

A study was conducted by **M Kodaka et al** in 2003 in Japan, on 64 ASA I and II patients aged 20-60 yrs., to determine the effective concentration for 50% of the attempts to secure laryngeal mask airway insertion (EC_{50LMA}) of Propofol using a target controlled infusion (TCI) and investigated whether Fentanyl influenced these required

concentrations, respiratory rate and bispectral index. Sixty-four elective non pre-medicated patients were randomly assigned to four groups (n = 16 for each group) and given saline (control) or Fentanyl 0.5, 1 or 2 mg kg ±1. Propofol target concentration was determined by a modification of Dixon's up-and-down method. Laryngeal mask airway insertion was attempted without neuromuscular blocking drugs after equilibration had been established for >10 min. Movement was defined as presence of bucking or gross purposeful muscular movement within 1 min after insertion. EC50LMA values were obtained by calculating the mean of 16 patients in each group. They concluded that, Fentanyl 0.5microgm/kg with Propofol TCI is inferred to be a sufficient dose to decrease EC_{50LMA} with minimum respiratory depression and without a high BIS value [25].

A study was conducted by **F Uzumcugil et al 2008**, on 52 ASA I and II patients aged 26 – 65 years, scheduled for minor urological procedures, for comparing Dexmedetomidine - Propofol and Fentanyl - Propofol for insertion of LMA. Those patients were divided in two groups, one group received Inj. Fentanyl 1 mcg/kg in 10 ml of normal saline, Group 2 received Inj. Dexmedetomidine 1 mcg/kg in 10 ml of normal saline over 2 minutes.30 seconds later anaesthesia induced with Inj. Propofol 1.5 mg/kg and 90 seconds after administration first attempt of insertion was tried. For maintenance of anaesthesia they used O_2 + N_2O + Sevoflurane 1.5 %. They recorded apnoea time, respiratory rate, systolic blood pressure, mean blood pressure, at regular intervals. For LMA insertion they observed jaw mobility, coughing, movement and other events such as spontaneous ventilation breathe holding, expiratory stridor and tearing in 3 point scores and score less than 2 considered acceptable. They found number of apnoea and apnoea time were more in group 1 than group 2, reduction in SBP and MBP was more in

group 1 than group 2.They concluded that former combination provides more successful LMA insertion comparable to Fentanyl, while preserving respiratory functions more than Fentanyl [15].

Z Begec et al in 2008 conducted a study in a group of 80 patients posted for elective minor surgical procedures. They compared giving Ketamine and Fentanyl prior to Propofol induction for PLMA insertion in children. They used Alfentanyl 20 mcg/kg in one group and Ketamine 0.5 mg/kg in other group. This premedication followed by Inj. Propofol 4 mg/kg for induction, then PLMA was inserted according to instruction manual. They found that though increased secretion and emergence was anticipated in Ketamine group, it was not occurred may be the Propofol masked that effects. Ketamine preserved the haemodynamic stability and in this group there was early return of spontaneous ventilation as compared to Fentanyl. Fentanyl also associated with prolonged apnoea time than Ketamine group [13].

R. Towsend et al in 2009 conducted a study over 160 patients posted for elective surgical procedures. On the observation that PLMA insertion required adequate depth of anaesthesia otherwise it may lead to coughing, gagging, head – limb movement, laryngospasm. There are few studies regarding setting of end point of Induction to reduce the unwanted effects. Some of the issues considered loss of eyelash reflex, apnoea and jaw relaxation, ease of face mask ventilation, dropping a weighted syringe, loss of verbal contact, bispectral index and motor response to jaw relaxation as potential tests for adequate depth. In this study they assessed jaw thrust as a predictor of adequate depth, fixed amount of thrust applied while the other three anaesthetists observed the patients movements and upper airway response to jaw thrust and analysed as optimal or

suboptimal condition. At end of study they suggested that jaw thrust can be used as a reliable predictor of insertion condition for PLMA and could be used as routine test [26].

Patel MG et al, in 2010 studied 60 patients in two groups of 30 patients each to assess Sevoflurane and Propofol as an induction agent for insertion of LMA. They used Inj. Propofol 3 mg/kg and Sevoflurane 85 with 100% Oxygen. PLMA was inserted after giving Fentanyl 2 mcg/kg. They concluded that though induction was faster than Sevoflurane when Propofol used as an induction agent but it was associated with pain at the site of injection. PLMA insertion was comparable with Propofol and Sevoflurane and PLMA can be used safely in laparoscopic surgeries [5].

In 2010 **Suparto et al,** conducted a randomized controlled study to compare the effectiveness of Dexmedetomidine versus Fentanyl in attenuating the sympathetic response to laryngoscopy and tracheal intubation. It is well-known fact that laryngoscopy and intubation causes sympathetic stimulation and increase in heart rate and blood pressure. This study involved 56 patients posted for surgeries under general anaesthesia. Those patients were allocated to receive Inj. Dexmedetomidine 1 mcg/kg and Inj. Fentanyl 1 mcg/kg intravenously prior to induction of anaesthesia. All patients received incremental doses of Propofol, Atracurium and O_2-sevoflurane. Blood pressure, heart rate and adverse events were monitored. There was greater decrease in haemodynamic parameters in patients given Dexmedetomidine, but the pressor response to laryngoscopy and intubation was attenuated significantly in the group receiving Dexmedetomidine compared to Fentanyl. They also concluded that Dexmedetomidine reduced Propofol requirement for induction. Dexmedetomidine also produced lowering of heart rate prior to the onset of physical stimulus like laryngoscopy and intubation [16].

A study was conducted by **Ali et al** 2010, on 50 children ASA I, aged 3-8 yrs., undergoing extra corporeal shockwave lithotripsy to evaluate the effects of Dexmedetomidine vs. Fentanyl as adjuvant to Propofol and concluded that Propofol - Dexmedetomidine combination was accompanied with less Propofol consumption, prolonged analgesia and lower incidence of intra-procedural and post-procedural complications [27].

Ranju Singh et al in 2011 in their study over 100 ASA 1 and 2 patients of age 3 – 12 years assessed use of different adjuvant with Propofol for insertion of laryngeal mass airway in children, and they concluded that although resistance to mouth opening and LMA insertion was equally comparable in both groups, overall insertion condition were better in Fentanyl group than Ketamine group as adjuvant [28].

Asha Gupta et al 2011 conducted a study on 90 patients in the age group of 20-50 years of either sex belonging to ASA grade I and II undergoing elective short surgical procedures. They were randomly divided into 3 groups of 30 each as follows: group PK (Propofol - Ketamine), group PF (Propofol - Fentanyl) and Group PB (Propofol - Butrorphanol). They were given their assigned drugs over 10 seconds i.e. Group PK - Inj. Ketamine 0.5 mg/kg intravenous, Group PF - Inj. Fentanyl 1 mcg kg-1intravenous and Group PB - Inj. Butorphanol 20 mcg/kg intravenous. This was followed immediately by Propofol 2.5 mg/kg intravenously over 15 seconds. If required, further increments of Propofol 0.5 mg/kg were given every 30 seconds until loss of consciousness and loss of eyelash reflex. Insertion of LMA was performed 60 seconds after injection of Propofol by a blinded investigator. Anaesthesia was maintained with 0.75 to 1% of Halothane, 60% and O2 40%. Insertion conditions and haemodynamics were recorded during and

immediately after insertion. They concluded that addition of Butrophanol to Propofol for LMA insertion provides absolute jaw relaxation and excellent insertion conditions with stable haemodynamics Side effects like coughing, gagging, lacrimation and laryngospasm were lower as compared to the other two groups. So, Butorphanol is a good adjuvant with Propofol for LMA insertion [29].

Sudeep Krishnappa et al according to their study published in IJA 2011, assessed optimal anaesthetic depth required for LMA insertion. A fixed dose of Propofol administered rapidly can be insufficient or in excess resulting in airway complications and haemodynamic disturbances. The study was designed to assess whether loss of motor response to jaw thrust can be a reliable indicator of anaesthetic depth for LMA insertion. They included 120 ASA 1, 2 patients scheduled for general anaesthesia on day care basis, allocated in two groups. In one group they tried a fixed dose of Propofol 3 mg/kg and other group was given Propofol sufficient to abolish jaw thrust response. The effects were analysed by recording MAP, heart rate and insertion condition on 3 point scale. After analysing the data statistically they found that loss of motor response to jaw thrust provides satisfactory LMA insertion conditions [30].

In the background knowledge of induction agents used for LMA insertion, different adjuvant have tried by many people to reduce the requirement of induction agent so as to reduce the complications associated with it, especially in children. Ina study conducted by **Ranju Singh** et al, 2011, they compared two adjuvant Ketamine and Fentanyl along with Propofol as an induction agent. They included 100 paediatric patients of 3 – 12 years of age and allocated to receive either Fentanyl 2 mcg/kg or Ketamine 0.5 mg/kg intravenously before induction of anaesthesia with Inj. Propofol 3.5

mg/kg. Haemodynamic parameters were recorded at regular intervals. LMA inserted and the insertion conditions were assessed on 6 parameters on a three point scale. Duration and incidence of apnoea also recorded. They concluded that the combination of Fentanyl – Propofol gives better insertion condition LMA than Ketamine – Propofol. Resistance to mouth opening and LMA insertion was comparable in both groups, though coughing, swallowing and movements were significantly higher in Ketamine group [28].

Insertion of laryngeal mask airway requires optimal balance of anaesthesia. Though Propofol considered as induction agent of choice for insertion of LMA it requires different opioid as adjuvant. **Akanksha dutt et al** 2012, studied two different doses of Fentanyl, 1 mcg/kg and 2 mcg/kg with Propofol 2.5 mg/kg as an induction agent, in 104 patients scheduled for elective surgical procedures. Optimal ventilation and insertion conditions were assessed on three point scale. The combination of Propofol and Fentanyl facilitated classic LMA insertion. Though optimal conditions for insertion were achieved with both doses of Fentanyl 1 mcg/kg and 2 mcg/kg with Propofol 2.5 mg/kg, Fentanyl 1 mcg/kg provided more stable haemodynamic condition [31].

Though Propofol considered as preferred agent for LMA insertion, it cannot be used as a single agent for induction as it is required in higher doses if used as a sole drug. Thus it may cause other side effects as hypotension, apnoea, myoclonus etc. Different co-induction agents were tried with Propofol to reduce Propofol requirement with preserving the adequate depth of anaesthesia for LMA insertion.

A study was conducted by **Dr. Tanmoy Ghatak** in 2012, in three groups of patients each containing 60 patients each. They were compared for effects of Ketamine,

Fentanyl and saline with Propofol induction on haemodynamics and laryngeal mask airway insertion conditions in oral pre-medicated children. Study groups received Fentanyl 1 mcg/kg, Ketamine 0.5 mg/kg and normal saline each in 5 ml volume in respective groups. They used oral Clonidine 4 mcg/kg as a premedication 90 minutes before surgery diluted in 5ml of 50 % dextrose solution. Then patients were induced with Propofol 3 mg/kg. Loss of consciousness and loss of eyelash reflex was considered as end point for induction. LMA was introduced according to manufacturer's instruction. End of the study they concluded that Ketamine balanced the cardio depressant effect of Propofol. The combinations were of significant haemodynamic benefits and better LMA insertion conditions compared with placebo. Ketamine – Propofol provided comparable insertion conditions like Fentanyl – Propofol with significantly less prolonged apnoea and haemodynamic stability [32].

Riham Hussein from university of Cairo in 2012 conducted a study in 75 paediatric patients posted for minor surgical procedures done under general anaesthesia. They divided patients in three groups of 25 patients each and assigned them as Fentanyl, Ketamine and Ketamine – Midazolam with respect to the co-induction agent used with Propofol 3 mg/kg. After induction each group was assessed for insertion parameters as, resistance to mouth opening, resistance to LMA insertion, swallowing, coughing, gagging, head and limb movement and laryngospasm. The data was analysed and stated that insertion conditions were better in Fentanyl and Ketamine – Midazolam group than Ketamine group. Although the resistance to mouth opening and LMA insertion were comparable in three groups, coughing, gagging, limb and head movements were considerably more in Ketamine and Ketamine – Midazolam group. Incidence of apnoea

was higher in Fentanyl group than other two groups, while duration of apnoea was prolonged in Ketamine group. Combination of Ketamine and Midazolam in 20:1 ratio with Propofol 3 mg/kg provided better insertion conditions in children with least side effects than Fentanyl and Ketamine group [33].

As this new type of airway device was accepted routinely in different surgical procedures researchers tried for different induction agents either intravenous or inhalational, for the assessment of insertion conditions and stable haemodynamic responses. They used these induction agents either alone or in combination with different adjuvant to improve insertion condition and reduce requirement of single induction agent.

Hashaam B. Gafoor et al in 2012 conducted a prospective randomised double blinded study in groups of 30 patients each. As Etomidate known to produce less hypotension than Propofol, they assessed these two agents as an induction agent for insertion of LMA. They found that though Etomidate can prevent hypotension caused by induction, it may delay the insertion of laryngeal mask airway [34].

In a study conducted in 2013, on 100 ASA 1 and 2 patients, **Rehman A. Et al** compared the haemodynamic responses to conventional endotracheal intubation and laryngeal mask airway. It was a single blind randomised controlled trial done in patients posted for routine elective surgical procedure. In this study they concluded that endotracheal intubation produces statistically significant rise in haemodynamic parameters as compared to classic LMA insertion [35].

Seyedhejazi et al 2013, carried out a study in children to asses different doses of Propofol for insertion of LMA to found out the optimal dose of Propofol required, as

higher doses may cause serious complications while lower doses may not give optimal insertion conditions. They used Propofol 2.5 mg/kg and 3.5 mg/kg in two groups. To conclude they said that there was no superiority over each other compared with the two doses studied [36].

Dawood Aghamohammadi et al in 2013 did a study in 60 ASA 1, 2, 3 patients of 20 – 60 years scheduled for urological procedures. They divided 60 patients in two groups containing 30 patients each. One group received Inj. Succinylcholine 0.1 mg/kg in 2ml 0.9% normal saline post induction and other group received 0.9 % normal saline after induction with Propofol 2 mg/kg. Patients were assessed for ease of insertion, coughing, gagging, limb and head movement. Propofol as a sole induction agent was not helpful in ease of insertion but when used with minimal dose Succinylcholine LMA was easily inserted. Thus Succinylcholine use was associated with less evidence of sore throat and myalgia [37].

Suvadeep Sen et al 2013, based on the studies that Dexmedetomidine reduce requirement of Thiopentone and inhalational anaesthetic agents, conducted a study to assess the requirement of Propofol after Dexmedetomidine in maintaining adequate depth of anaesthesia with stable haemodynamics. 70 adult patients of American Society of Anaesthesiologists (ASA) Grade I and II aged 20-60 years undergoing elective spinal surgeries under general anaesthesia were included in this study. Patient to a placebo group (Group P, n=35) or Dexmedetomidine group (Group D, n=35). Fifteen minutes before induction of anaesthesia, patients of both groups received identical premedication of injection Glycopyrolate 0.2 mg intravenous (I.V.). At the same time, infusion of the study or control solution was started for patients of Group D or Group P respectively.

Injection Fentanyl 2 mcg/kg body weight was given I.V. 3 min before induction. Induction of anaesthesia was started in all patients by injection Propofol, slow I.V. until loss of response to verbal command. Injection Fentanyl 2 mcg/kg body weight was given I.V. 3 min before induction. Haemodynamics were monitored at regular interval and depth of anaesthesia monitored by BIS monitoring. In patients of Group D, mean requirement of Propofol for induction and maintenance of anaesthesia were 48.08% and 61.87% lesser respectively, than the mean requirement in patients of Group P. they concluded that infusion of Dexmedetomidine in peri-operative period significantly reduced the requirement of Propofol for induction and maintenance of adequate depth of anaesthesia with stable haemodynamic parameters [38].

Soumya Jayram et al in 2013 conducted a study on 60 patients posted for lower abdominal and lower limb surgery to compare the effect of Dexmedetomidine combined with Propofol versus Fentanyl combined with Propofol for laryngeal mask airway insertion. 30 seconds after the study drug was administered (Fentanyl 1mcg/kg in group F and Dexmedetomidine 1 mcg/kg in group D); both the groups were induced with Inj. Propofol 2.0 mg/kg. 90 sec after induction, jaw relaxation assessed and LMA of appropriate size was inserted. After failed attempts incremental dose of Propofol 0.5 mg/kg given and 2^{nd} attempt made, maximum three attempts were done. Insertion conditions were assessed by jaw relaxation, coughing, movements, number of attempts required and additional doses of Propofol given. At the end of study they concluded that insertion conditions were similar and comparable in both the groups but Dexmedetomidine - Propofol group had more stable haemodynamic conditions and there

was less respiratory depression. Thus Dexmedetomidine can be used as potential alternative to Fentanyl that can be used as an adjuvant to Propofol induction [39].

Mrunalini Parasa 2014 did a study in 60 ASA 1 and 2 patients scheduled for elective surgical procedures under general anaesthesia. Those 60 patients were assigned in two groups of 30 patients each, of them one is assigned as receiving Propofol and other one is for thiopental as an induction agent. At the end of their study they concluded that Propofol is an ideal induction agent giving better condition for LMA insertion than Thiopentone [40].

Various studies have conducted and Propofol was considered as near ideal induction agent for insertion of LMA. But it is associated with few side effects as pain on injection, myoclonus, hypotension, apnoea and rarely anaphylactic reaction. **Dr.Nirmala B. C.** Carried out a study published in 2014 to compare the ease of insertion of laryngeal mask airway with Thiopentone sodium and Propofol. At the end of study conclusion was made as the ease of insertion was significantly greater in group of patients induced with Propofol compared to induction with Thiopentone and Fentanyl. However there was no difference in jaw relaxation, coughing, limb movement, laryngospasm between two groups. 10 % cases induced with Thiopentone and Fentanyl had swallowing/gagging [41].

Ravipati et al conducted a study to assess effects of Dexmedetomidine on requirement of Propofol, Ketamine and intraoperative haemodynamic variations during burn debridement and dressing, which was published in 2014. Sixty adult patients posted for elective debridement and dressing were included in the study. Thirty patients received Dexmedetomidine intramuscular (IM) 1 mcg/kg, 1 h before shifting to the operation

theatre while the other thirty did not. Anaesthesia was induced with Propofol and Ketamine followed by adjusted infusion to achieve a Ramsay Sedation Scale score (RSS) of six in all patients. Intraoperatively haemodynamic parameters were recorded at regular intervals. In operating room patients were pre-medicated with Inj. Glycopyrolate, Inj. Ramesetron and Inj. Fentanyl. Then all the patients were administered Inj. Ketamine 0.5 mg/kg and Inj. Propofol 1 mg/kg. Then infusion of Propofol 100 mcg/kg/hr and Ketamine 1mg/kg/hr was started to achieve Ramsey sedation score of 6, after that LMA was inserted. They concluded that Dexmedetomidine (1 mcg/kg IM dose) is a good anaesthetic adjuvant that decreases the requirement of Propofol and Ketamine during burns debridement and dressings, attenuates sympathoadrenal response, maintains stable intraoperative haemodynamics and adequate duration of analgesia, and also has an excellent recovery profile [42].

Pain relief remains the most fundamental and consequential aspect of surgery for patients throughout period. Dexmedetomidine has created interest in alpha-2 adrenoceptor agonist in the management of pain. It's well documented benefits include anxiolysis, analgesia, sedation and sympatholysis, thus rendering this especially suitable for anaesthesia and intra operative period. As more selective and specific for alpha-2 adrenoceptor agonist it gives more sedation and analgesia than Clonidine. In reference to this **Suchit Khanduja et al 2014**, conducted a study in total of 60 patients posted for laparoscopic Cholecystectomy under general anaesthesia to assess the requirement of Thiopentone and Pentazocine. They gave Inj. Dexmedetomidine 0.5 m cg/kg/hr followed by 0.6 mcg/kg/hr 30 min before induction to one group and other group received equivolume of normal saline as placebo. Then both groups received Pentazocine 0.3

mg/kg and were induced with Inj. Thiopentone 2 mg/kg in bolus which was supplemented with 25 mg boluses intravenous every 15 sec. till loss of eyelid reflex. Thus induction dose of Thiopentone was recorded. And then patients were intubated after administration of Succinylcholine 1.5 mg/kg. Results were obtained after statistical analysis. They concluded that an infusion of Dexmedetomidine at 0.5 mcg/kg/hr 30 min before induction and then 0.6 mcg/kg/hr until the end of surgery reduced the dose requirements of Thiopentone and Pentazocine, also reduced post operative pain and led to better recovery of patients undergoing laparoscopic Cholecystectomy [6].

Dr. surabhi A. Lande et al published their study Journal of evolution of medical and dental sciences 2014, in this study they compared the insertion conditions in two groups posted for elective surgical procedures after Propofol induction. Both the groups were differing in use of the co-induction agents used with Propofol, one group used Dexmedetomidine and other group used Fentanyl. The objectives were to assess the ease of insertion of laryngeal mask airway. In this prospective randomized double blinded study 60 patients were included and divided in two groups of 30 patients each, one group is named as DP receiving Dexmedetomidine and other one is FP receiving Fentanyl before Propofol induction at 2.5 mg/kg. Both the drugs were given over 10 min by infusion in a dose of 1 mcg/kg. 90 sec after induction first attempt of LMA insertion was made. Unsuccessful attempt was followed by incremental dose of Propofol 0.5 mg/kg and then next attempt was attempted. Maximum three attempts were tried. Successful insertion was confirmed by end tidal CO_2 waveform, five point auscultations. Patients were monitored for haemodynamic responses at regular interval in both the groups. Insertion conditions were assessed by presence of jaw relaxation and coughing during

insertion. The pressor responses during insertion of LMA were assessed by heart rate, systolic BP, Diastolic BP and Mean BP. At the end of the study they found that Dexmedetomidine gives better insertion conditions and better attenuation of pressor response to LMA insertion compared to Fentanyl in given doses and Dexmedetomidine can be used with an advantage for LMA insertion for short surgical procedures [17].

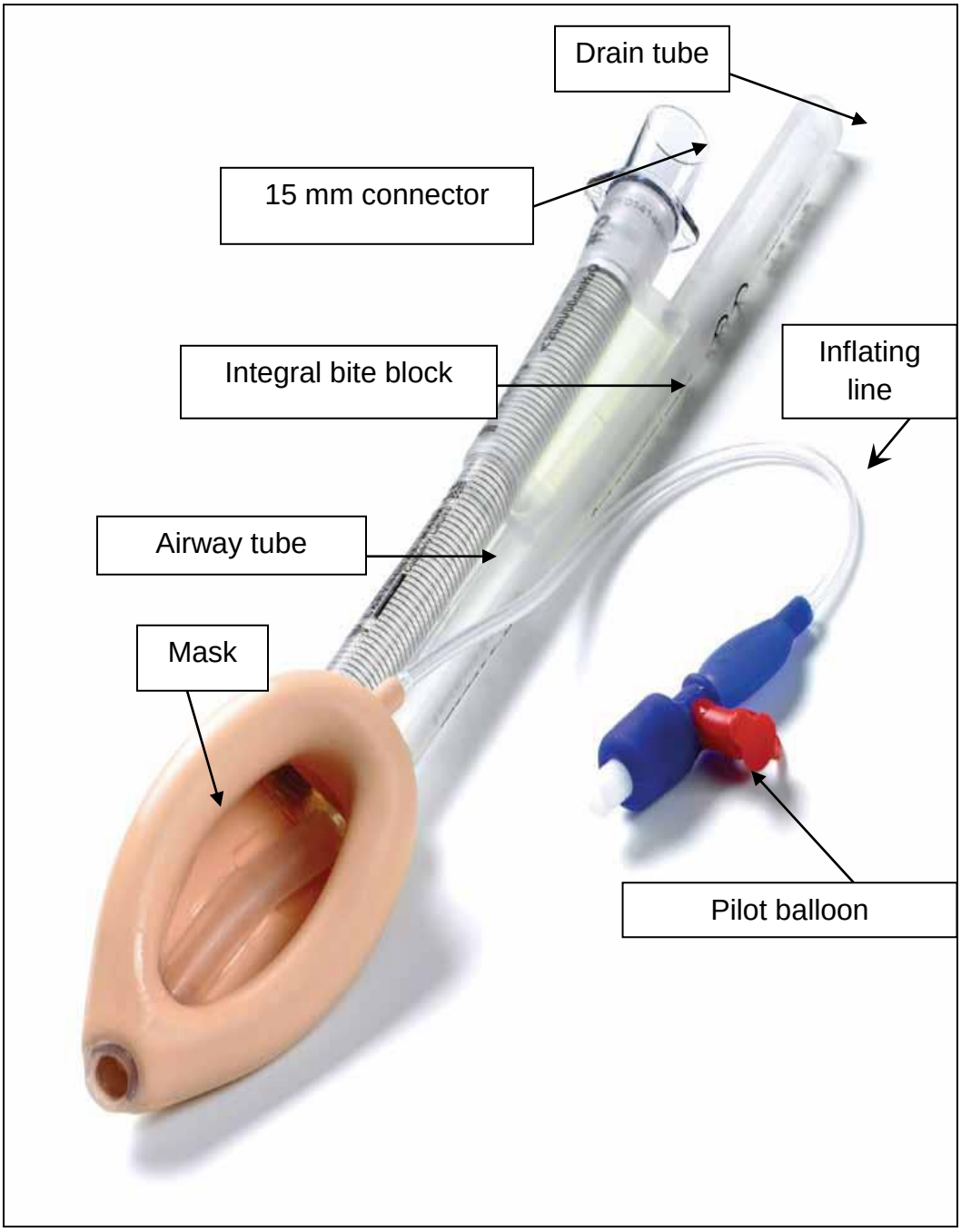
Kwak HJ et al 2014 conducted a study to find out the median effective dose of Dexmedetomidine for laryngeal mask airway with Propofol 2.0 mg/kg. They included 22 patients between 18 – 60 years posted for minor orthopaedic and gynaecological procedures. The modified Dixon's up-and-down method was used to determine the bolus dose of Dexmedetomidine, starting from 0.5 mcg/kg (step size; 0.1 mcg/kg). After a predetermined bolus of Dexmedetomidine patients were induced with Propofol 2.0, g/kg. 90 seconds after LMA was inserted and response was categorized as success or failure. They concluded that the single dose of Dexmedetomidine for successful LMA insertion to be feasible in 50% of patients was 0.55 mcg/kg during anaesthesia induction with Propofol 2 mg/kg [43].

ASB Tan and CY Wang conducted a study to measure optimal dose of Fentanyl for the insertion of classic laryngeal mask airway in non-paralyzed patients induced with Propofol 2.5 mg/kg. Seventy-five ASA I or II patients were randomly assigned to five groups of Fentanyl dosage: 0 mcg/kg (placebo), 0.5 mcg/kg, 1.0 mcg/kg, 1.5 mcg/kg and 2.0 mcg/kg. Anaesthesia was induced by first injecting the study drug over 10 seconds. Three minutes after the study drug was injected, Propofol (2.5 mg/kg) was injected over 10 seconds. The Classic™ Laryngeal Mask Airway was inserted four minutes and 30 seconds after injection of the study drug. Insertion conditions were evaluated. The

incidence of prolonged apnoea increased as Fentanyl dose increased. They recommended 1.0 mcg/kg as the optimal dose of Fentanyl when used in addition to Propofol 2.5 mg/kg for the insertion of the Classic Laryngeal Mask Airway [44].

PROSEAL LARYNGEAL MASK AIRWAY (PLMA)

LMA is an innovative supraglottic airway device. PLMA is an advanced form of LMA that can be used for the same indications as the Classic LMA (cLMA). PLMA was introduced in 2000. PLMA is designed to provide additional benefits over the cLMA.



ADVANTAGES [45]

- A softer cuff material, deeper mask bowl and special cuff shape allows a higher seal than the cLMA for a given intracuff pressure with the adult sizes.
- The revised cuff arrangement allows for a higher seal pressure than the cLMA.
- The drain tube opening at the upper oesophageal opening permits the drainage of the gastric secretions and allows access to the alimentary tract.
- The double tube arrangement reduces the likelihood of mask rotation; the revised cuff profile, together with flexible tubes result in the device being more securely anchored in place.

KEY COMPONENTS

Mask

The mask is designed to conform to the contours of the hypopharynx, with its lumen facing the laryngeal opening. The mask has a main cuff that seals around the laryngeal opening and the larger sizes also have a rear cuff which helps to increase the seal.

Inflating line

Attached to the mask is an inflation line terminating in a pilot balloon and valve for mask inflation and deflation. A red plug is also fitted to the valve assembly to allow the residual air in the mask to be vented during autoclaving.

Drain tube

The drain tube passes lateral to the airway tube and traverses the floor of the mask and opening at the mask opposite the upper oesophageal sphincter.

Airway tube

The airway tube is reinforced to prevent collapse and terminates with a 15 mm connector.

Introducer

A malleable introducer tool is also available in adult and paediatric sizes to aid insertion if it is desirable to avoid placing a finger in the patient's mouth. It is supplied in the recommended curvature for immediate use, but may be bent to any desired shape.

INDICATIONS [46]

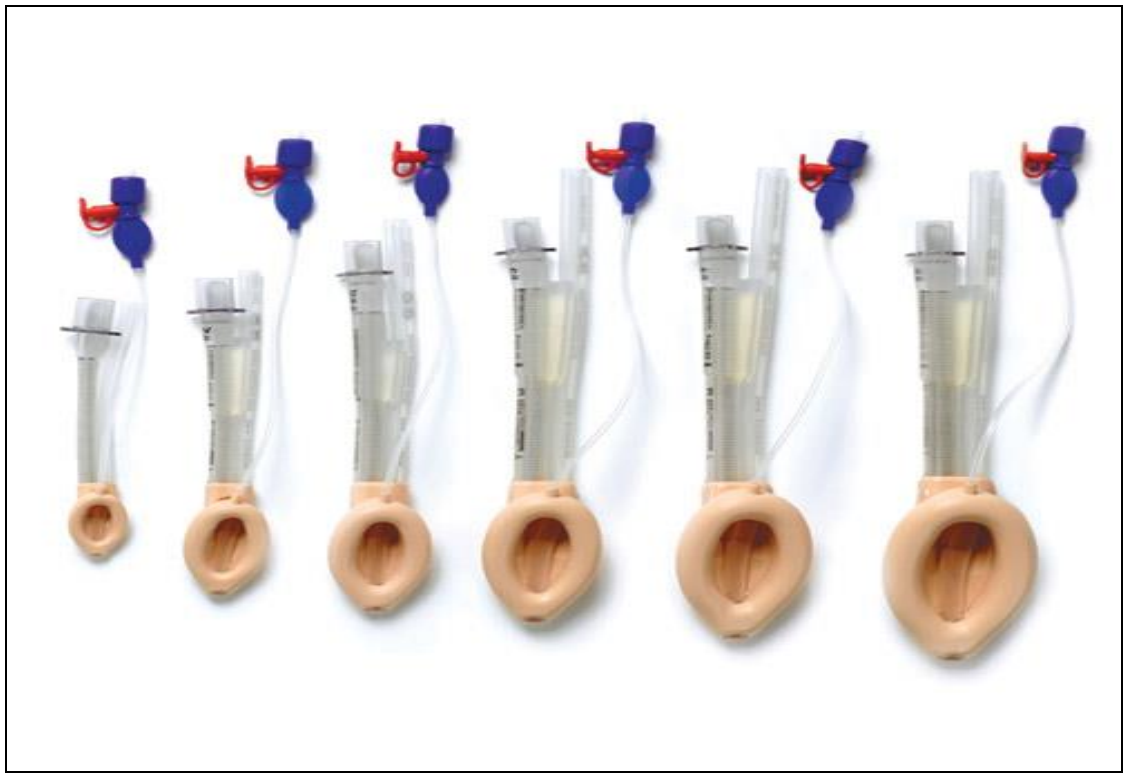
- The PLMA can be used for both spontaneous and controlled ventilation, but is more suited for controlled ventilation [47, 48].
- The sealing pressure is higher than that with the cLMA in adult and paediatric patients, making it a better choice for situations where higher airway pressures are required and better airway protection is desirable as in laparoscopic surgeries [20].
- It is used for surgical procedures in which intraoperative gastric drainage or decompression is needed [20, 49, 50].
- It may be easier to place the PLMA than the cLMA during manual in line stabilization [51].

- It has been used in cases of known difficult airway and has been successfully used after failure with cLMA [52, 53].
- The PLMA may be useful in cases where it is important to avoid airway trauma, as it exerts lower pressure against the pharyngeal mucosa than the cLMA [49].

LIMITATIONS [45, 46]

- Patients who are not fasting and the patients whose starvation cannot be confirmed.
- Patients who are morbidly obese, more than 14 weeks pregnant or those with multiple or massive injury, acute abdominal or thoracic injury, any condition associated with delayed gastric emptying or using opiate medication prior to fasting.
- Patients with fixed decreased pulmonary compliance.
- Patients where the peak airway inspiratory pressures are anticipated to exceed 30 cm of H_2O.
- PLMA is less suitable as an intubation device than the cLMA because of the narrower airway tube.
- It requires a greater depth of anaesthesia for insertion than does the cLMA.
- PLMA has a shorter life span than the cLMA [54].

VARIOUS SIZES OF PLMA



PPROPRIATE SIZES FOR USE: [45]

Proseal LMA size	Patient weight	Maximum inflation volume	NG tube size
1	0 – 5 kg	4ml	8
1.5	5 – 10 kg	7ml	10
2	10 – 20 kg	10ml	10
2.5	20 – 30 kg	14ml	14
3	30 – 50 kg	20ml	16
4	50 – 70 kg	30ml	16
5	70 – 100 kg	40ml	18

PROSEAL LMA WITH AN INTRODUCER

INSERTION TECHNIQUES [46]

It is recommended that the PLMA cuff be deflated into a wedge shape, as with the cLMA. The patient should be in the “sniffing position”.

Introducer Technique

The tip of the metal introducer is inserted into the strap at the top of the cuff. The airway and drainage tubes are folded around the introducer blade and into matching slots on either side of the introducer. Lubricant should be placed on the posterior tip. The tip is then pressed against the hard palate and manoeuvred to spread the lubricant along the hard palate. The cuff is then slid inward, keeping pressure against the palate.

As the PLMA is inserted, the introducer is kept close to the chin. The introducer is swung inward in a smooth circular movement. The jaw can be pulled downward by an assistant or pushed downward with the middle finger until the cuff has passed the teeth, but the jaw should not be held widely open, because this may cause the tongue and epiglottis to drop downward, blocking the mask's passage. The PLMA is advanced until resistance is felt. The non dominant hand should be used to stabilize the airway tube as the introducer is removed by following the curvature backward out of the mouth, taking care to avoid damage to the teeth. The bite block portion should be at the level of the incisors.

Insertion in patients with a stereotactic frame or neck collar is probably best performed without the introducer.

Digital Method

The digital method for insertion is similar to the introducer method except that the tip of the index finger is placed at the junction of the cuff and the two tubes. As the index finger passes into the mouth, the finger joint is extended and the PLMA is pressed backward towards the other hand that exerts counter pressure to maintain the sniffing position. Depending on patient and user finger size, the finger may need to be inserted to its fullest extent before resistance is encountered. The non dominant hand should be used to stabilize the LMA as the finger is withdrawn. The thumb may be used to aid insertion when it is difficult to get access to the patient from behind.

After the Proseal LMA has been inserted, the cuff should be inflated with enough air to achieve an intracuff pressure of up to 60 cm H_2O. During insertion and cuff inflation, the front of the neck should be observed to see if the cricoid cartilage moves forward, indicating that the mask has correctly passed behind it. The cuff volume required for the PLMA to form an effective seal with the respiratory tract is lower than for the cLMA. In fact, an adequate seal can be obtained in most patients with no air in the cuff; however, the cuff should be inflated with at least 25% of the maximum recommended volume to ensure an effective seal with the gastrointestinal tract.

Insertion Problems [46]

Several malpositions for the Proseal LMA have been described, including insufficient depth, the tip inserted into the glottis, the tip folded backward, and severe epiglottic downfolding.

If the Proseal LMA is inserted to an insufficient depth, there will be a poor seal. If advancing the Proseal LMA does not correct the problem, it should be removed and reinserted.

Cases of aspiration have been noted with malpositions.

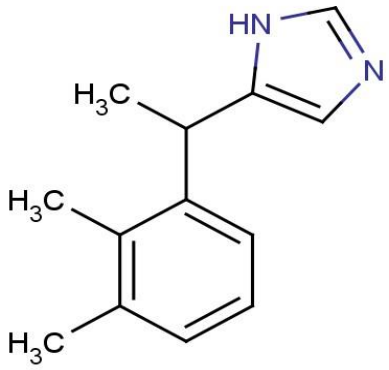
PHARMACOLOGY

DEXMEDETOMEDINE

INTRODUCTION:

Dexmedetomidine is a potent, highly selective and specific α_2-adrenoreceptor agonist that has both sedative and analgesic effects. The prototype of α_2-adrenoreceptor agonist Clonidine was initially developed in 1960s as a nasal decongestant for its locally acting α_2-adrenergic vasoconstrictor action, but later in 1966 it was introduced into the market as a potent antihypertensive drug [55]. Nowadays the therapeutic use of this class of drugs has shifted to various other clinical indications including anxiolysis, analgesia, and sedation that render them suitable as adjuncts in anaesthesia. Dextmedetomidine was approved in the USA in 1999 for sedation and analgesia in the intensive care unit. Compared with Clonidine, Dexmedetomidine is about eight times more specific for α_2-adrenoreceptor. These unique properties of Dexmedetomidine make it a α_2-adrenoreceptor agonist agent with sedative and anxiolytic effects. The elimination half-life of Dexmedetomidine is approximately 2 hours with a rapid distribution half-life being approximately 6 min [56]. It has a rapid onset of action, it acts with in 5min and peak action is achieved by 15 min. It undergoes biotransformation in the liver, and the kidney excretes 95% of its metabolites. The short half-life of Dexmedetomidine makes it particularly suitable for intravenous infusion. Although Dexmedetomidine is approved for sedation/analgesia in an intensive care setting, in the last years it has emerged as an effective therapeutic drug in a wide range of anaesthetic management.

CHEMICAL STRUCTURE:



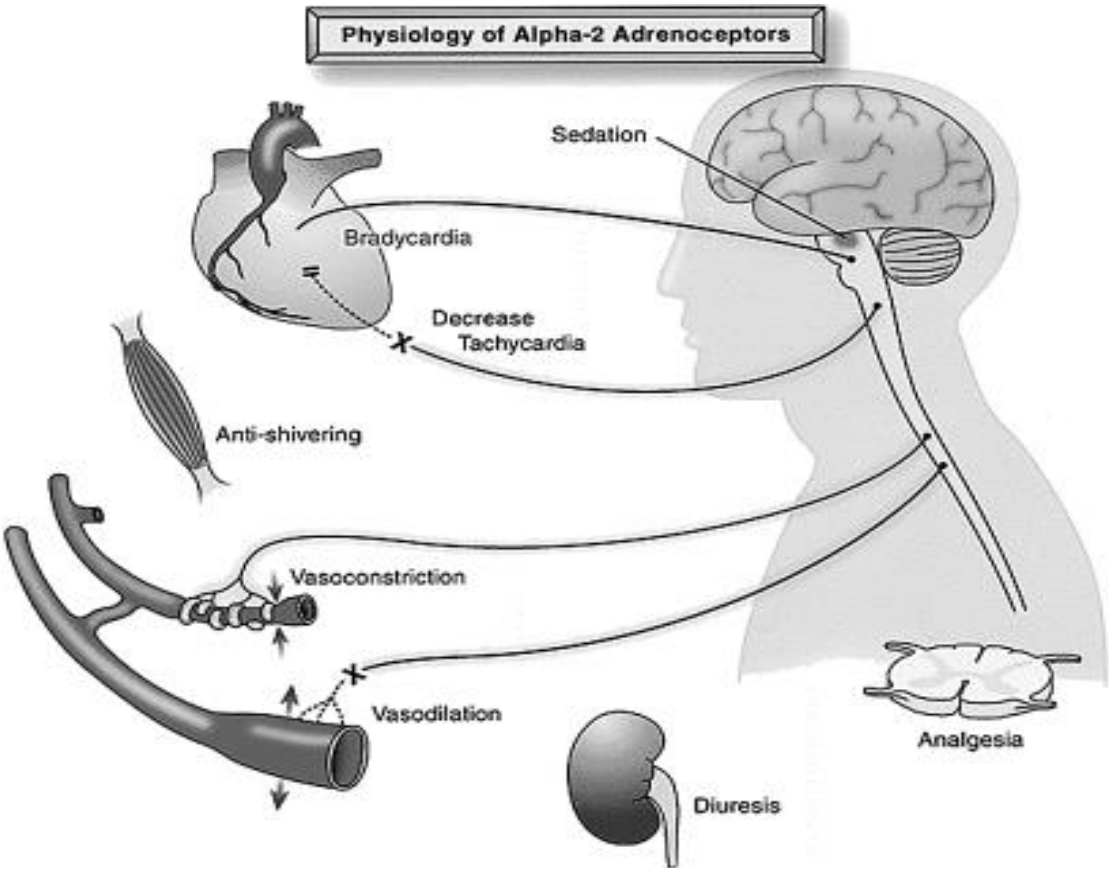
Molecular formula: $C_{13}H_{16}N_2$

Molecular weight: 200.13 gm/mol

IUPAC name: 5-[1-(2,3-dimethylphenyl)ethyl]-1H-imidazole

PHYSIOLOGY OF ALPHA RECEPTORS:

α_2-adrenoreceptor agonists act at presyanaptic and postsynaptic adrenoceptors and their pharmacology is complex. The human α_2-adrenoreceptors can be classified into α_{2A}, α_{2B} and α_{2C} -adrenoreceptor subtypes. These receptor subtypes are distributed ubiquitously and each may be responsible for a specific action of α_2-agonists [57] The predominant α_2-adrenoreceptor agonist subtype mediating sedative and antinociceptive actions is the α_{2A}-adrenoceptor, whereas stimulation of α_{2B}-adrenoreceptor mediates the vasoconstrictive cardiovascular effect, which causes the initial hypertension observed after the administration of α_2–adrenoreceptor agonists [58]. The α_{2C}-adrenoreceptors subtype has been shown to modulate dopaminergic neurotransmission, hypothermia and a variety of behavioural responses.



MECHANISM OF ACTION:

The hypnotic effect of Dexmedetomidine is mediated by the hyperpolarisation of noradrenergic neurons located in the locus ceruleus and spinal cord which is the principal site for analgesic action, both acting through $\alpha_{2A.}$ Dexmedetomidine acts through a G coupled protein receptor that produces an inhibition of adenyl cyclase and these results in decreased formation of cyclic AMP (cAMP) that is an important regulator of many cellular functions acting in various intracellular subsystems like the control of phosphorilation state of regulatory proteins. Other effects of α_2-drenoreceptor agonists include activation of potassium ion channels causing efflux of potassium and an inhibition of calcium entry into calcium channels in neuronal cell [59]. These effects lead to change in membrane ion conductance and produce α_2-adrenoreceptor agonist

hyperpolarisation of the membrane which suppresses neuronal activity. The main effect is an inhibition of noradrenaline release causing a reduction of excitation, especially in locus ceruleus. The locus ceruleus is α_2-adrenoreceptor agonist small neuronal nucleus located bilaterally in the upper brainstem and is the α_2-adrenoreceptor agonist major site of noradrenergic innervations in the brain [60]. The locus ceruleus has also been implicated as α_2-adrenoreceptor agonist key modulator for α_2-adrenoreceptor agonist variety of important brain functions, including arousal, sleep, anxiety and drug withdrawal associated with CNS depressant, like opioids.

PHARMACOKINETICS:

ABSORPTION AND DISTRIBUTION:

Dexmedetomidine exhibits linear pharmacokinetics in the recommended dose range of 0.2 – 0.7 mcg/kg/hr administered as intravenous infusion over 24 hrs. The distribution phase is rapid, with half life of distribution of approximately 6 minutes and elimination half life of 2 hours. The steady state of volume of distribution is 118 L. The average protein binding is 94 % and is constant across different plasma concentrations and also similar in males and females. It has negligible protein binding displacement by drugs commonly used during anaesthesia and in ICU like Fentanyl, Ketorolac, Theophylline, Digoxin and Lidocaine [60]. Context sensitive half life ranges from 4 mins after a 10 min infusion to 250 mins after 8 hour infusion. Oral bioavailability is poor because of excess first pass metabolism. However bioavailability of sublingually administered Dexmedetomidine is high (84%), offering a potential role in paediatric sedation and premedication.

METABOLISM AND EXCRETION:

Dexmedetomidine undergoes complete biotransformation through conjugation (41%), N-methylation (21%), or hydroxylation followed by conjugation to inactive metabolites. Metabolites are excreted in urine (95%) and faeces (4%). Dexmedetomidine has profound effects on cardiovascular variables and may alter its own pharmacokinetics. With large doses, there is marked vasoconstriction, which probably reduces the drug's volumes of distribution. Dose adjustment is required in patients with hepatic failure because of low rate of metabolism.

PHARMACODYNAMICS:

CARDIOVASCULAR EFFECTS:

The haemodynamic effects of Dexmedetomidine result from peripheral and central mechanism.α_2-adrenoreceptor agonists show a biphasic, dose dependent, blood pressure effect. At low doses the dominant action of α_2-adrenoreceptor agonist activation is a reduction in sympathetic tone, mediated by a reduction of norepinephrine release at the neuroeffector junction, and a inhibition of neurotransmission in sympathetic nerves. The net effect of Dexmedetomidine action is a significant reduction in circulating catecholamines with a slight decrease in blood pressure and a modest reduction in heart rate [61]. When Dexmedetomidine is administered as a continuous infusion, is associated with an expected and stable haemodynamics response. Significant hypotension is usually only observed in patients with pre-existing hypovolemia or vasoconstriction. The bradycardia frequently seen after the administration of Dexmedetomidine may be due to the central sympatholytic action and partly by baroreceptor reflex and enhanced vagal

activity. This effect is frequently observed in younger patients with high levels of vagal tone. At higher doses of Dexmedetomidine produce a hypertensive action caused by the activation of α_{2B}-adrenoceptors located on vascular smooth muscle cells. This effect prescribes the rapid intravenous injection of Dexmedetomidine.

RESPIRATORY SYSTEM EFFECTS:

The α_2-adrenoreceptor agonists have minimal effects on ventilation. Although Dexmedetomidine produces sedative, analgesic and anxiolytic effects, unlike other sedatives, it provides respiratory stability and does not cause ventilator depression. This was shown in healthy volunteers in whom even very high doses of Dexmedetomidine did not compromise respiratory function. Absence of respiratory depression was also observed in patients sedated with Dexmedetomidine, which was administered at infusion rates 10 to 15 times higher than maximally recommended. It was also demonstrated that combination of α_2-adrenoreceptor agonist with opioids does not lead to further ventilator depression [62].

CENTRAL NERVOUS SYSTEM EFFECTS:

Dexmedetomidine, like other α_2-adrenoreceptor agonists, provides sedation, anxiolysis and analgesia. The sedation produced by α_2-adrenoreceptor agonists does not depend primarily on activation of the α_2-aminobutyric acid (GABA) receptors like that produced by traditional sedatives such as Propofol or benzodiazepines. The primary site of action of α_2-adrenoreceptor agonist is the locus ceruleus and not the cerebral cortex, as would be the case with GABA-mimetic drugs. This should be the reason why this class of drugs produces a different type of sedation compared with benzodiazepines and Propofol.

Sedation induced by Dexmedetomidine has unique properties, it produces an unusually cooperative form of sedation in which the patient is calmly and easily aroused from sleep to wakefulness to allow task performance and excellent communication and cooperation while intubated and ventilated and then quickly back to sleep when not stimulated. The unusual subcortical form of Dexmedetomidine induced sedation is characterized by an easy and quick arousal, resembling natural sleep. With increasing doses of Dexmedetomidine, profound anaesthetic actions have been demonstrated, and this advocates that Dexmedetomidine could be used as total intravenous agent. The neuroprotective properties of Dexmedetomidine have been demonstrated in various animal models of cerebral ischemia. There are recent experimental data suggesting that in addition to α_2-adrenoreceptor agonists, the neuroprotective effect of Dexmedetomidine may include other pathways in the brain, independent of α_2-adrenoreceptor agonists and most probably involve 1- imidazoline receptors in the brainstem and hippocampus.

ANALGESIA:

Dexmedetomidine has been demonstrated to have significant analgesic effects and consistently reduce opioid requirements [63]. It is believed that the spinal cord is probably the major site of analgesic action, where the activation of α_{2c}-adrenoreceptor agonist subtype seems to increase the analgesic action of opioids in lowering the transmission of nociceptive signals to brain centre. Dexmedetomidine also inhibits the release of substance P from the dorsal horn of the spinal cord, leading to primary analgesic effects.

RENAL SYSTEM EFFECTS:

Stimulation of α_2-adrenoreceptors in the kidneys results in diuresis and natriuresis possibly through an ability to reduce efferent sympathetic outflow of the renal nerve. In addition Dexmedetomidine has shown to decrease the secretion of vasopressin and to antagonize its effect on renal tubules. α_2-adrenoreceptor agonists are also thought to increase the release of atrial natriuretic peptide resulting in natriuresis.

ENDOCRINE SYSTEM EFFECTS:

Action of α_2-adrenoreceptor agonists on endocrine system are mainly related to their action on sympathetic outflow and the decrease of catecholamines, this can attenuate the responses to stress by inhibiting the secretion of adrenocorticotropic hormone (ACTH) and cortisol. In addition stimulation of α_2-adrenoreceptor agonists located on α cells of the islet of Langerhans can temporally cause direct inhibition of insulin release with concomitant detectable clinical hyperglycaemia.

CLINICAL APPLICATION OF DEXMEDETOMIDINE:

1. PREMEDICATION:

Dexmedetomidine is used as an adjuvant for premedication especially in patients susceptible to preoperative and perioperative stress because of its sedative, anxiolytic, analgesic and stable hemodynamic profile. Dexmedetomidine decreases oxygen consumption in intraoperative period (up to 8%) and postoperative period (up to17%) [64]. Premedication dose is 0.33 to 0.67 mcg/kg I.V. given 15 mins before surgery.

2. PERIOPERATIVE USE:

Dexmedetomidine may be a useful adjuvant during general anaesthesia to employ its sedative, hypnotic, analgesic and sympatholytic properties for the benefit of surgical patients by promoting hemodynamic stability and decreasing the doses of anaesthetics and analgesics.

3. LOCOREGIONAL ANAESTHESIA:

Highly liphophilic nature of Dexmedetomidine allows rapid absorption into cerebrospinal fluid and binding to α_2-adrenoreceptor of spinal cord for its analgesic action. It prolongs both the duration of sensory and motor blockade induced by local anaesthetics irrespective of routes of administration (Epidural, caudal, spinal). It enhances both central and peripheral neural blockade by local anaesthetics.

4. SEDATION IN ICU:

Dexmedetomidine has become popular sedative agent in the ICU because of its ability to produce cooperative sedation i.e. patient remain awake, calm and able to communicate, their needs. It does not interfere with respiratory drive or produce any agitation; hence fascinating early weaning from ventilator and thus reducing overall stay of ICU. Dexmedetomidine is currently approved by FDA for use in ICU for not more than 24 hrs. It has both sedative and analgesic sparing effects, reduced delirium and agitation, minimal respiratory depression and cardiovascular stability.

5. PROCEDURAL SEDATION

Dexmedetomidine is an attractive agent for short term procedural sedation. It has been safely used in transoesophageal echocardiography, colonoscopy, awake carotid endarterectomy, shockwave lithotripsy, vitreoretinal surgery, elective awake fiberoptic

intubation, paediatric patients undergoing tonsillectomy and paediatric MRI. The usual dose of Dexmedetomidine for procedural sedation is 1 mcg/ kg, followed by an infusion of 0.2 mcg/kg/hr. It's onset of action is less than 5 minutes and the peak effect occur within 15 minutes. As the pharmacologic effects of Dexmedetomidine can be reversed by the α_2-adrenoreceptor antagonist Atipamezole, Dexmedetomidine provides a titratable form of hypnotic sedation that can be readily reversed.

6. CONTROLLED HYPOTENSION:

Dexmedetomidine is an effective and safe agent for controlled hypotension mediated by its central and peripheral sympatholytic action. It's easy administration, predictability with anaesthetic agents, and lack of toxic side effect while maintaining adequate perfusion of the vital organs makes it a near ideal hypotensive agent. Spinal fusion surgery for idiopathic scoliosis, septoplasty and tympanoplasty operations and maxillofacial surgery have been safely done with Dexmedetomidine controlled hypotension.

7. ANALGESIA:

Dexmedetomidine activates α_2-adrenoreceptor in the spinal cord reducing transmission of nociceptive signals like substance P. It has significant opioid sparing effect and is useful in intractable neuropathic pain.

8. CARDIAC SURGERY:

Dexmedetomidine in addition to blunting the haemodynamics response to endotracheal intubation also reduces the extent of myocardial ischemia during cardiac surgery. Dexmedetomidine has been successfully used to manage patients with

pulmonary hypertension undergoing mitral valve replacement, with reduction in pulmonary vascular resistance, pulmonary artery pressure, and pulmonary capillary wedge pressures.

9. NEUROSURGERY:

Dexmedetomidine provides stable cerebral haemodynamics without sudden increase in ICP during intubation, extubation, and head pin insertion. It attenuates neurocognitive impairment (delirium and agitation) allowing immediate postoperative neurological evaluation. It exerts its neuroprotective effects through several mechanisms which make the usage of this drug a promising tool during cerebral ischemia. It does not interfere with neurological monitoring and has an upcoming role in "functional" neurosurgery. This includes awake craniotomy for the resection of tumours or epileptic foci in eloquent areas, and the implantation of deep brain stimulators for Parkinson's disease.

10. OBESITY:

Dexmedetomidine does not cause respiratory depression and has been infused at a dose of 0.7 mcg/kg intraoperatively to avoid respiratory depression due to narcotic usage in a morbidly obese patient [65].

11. OBSTRETICS:

Dexmedetomidine has been successfully used as an adjunct to unsatisfactory analgesia by systemic opioids in labouring parturients who could not benefit from epidural analgesia. It provides maternal hemodynamic stability, anxiolytic, and stimulation of uterine contractions. It is retained in placental tissue and passes less

readily into the fetal circulation than Clonidine because of high lipophilicity and thereby has less susceptibility to cause fetal bradycardia.

12. PAEDIATRICS:

It is currently being used off label as an adjunctive agent in paediatric patients for sedation and analgesia in the critical care unit and for sedation during non-invasive procedures in radiology like computed tomography and magnetic resonance imaging.

13. OTHER USES:

The literature suggests other potential uses for Dexmedetomidine, for example, Dexmedetomidine has been used successfully in the treatment of withdrawal from benzodiazepines, opioids, alcohol, and recreational drugs.

- As an adjunct in oto-rhino-laryngology anaesthesia for middle ear surgery and rhinoplasty.
- As an adjunct in the repair of aortic aneurysms.
- Management of tetanus in ICU.
- As an antishivering agent.
- Dexmedetomidine is effective in preventing ethanol induced neurodegeneration.

ADVERSE EFFECTS:

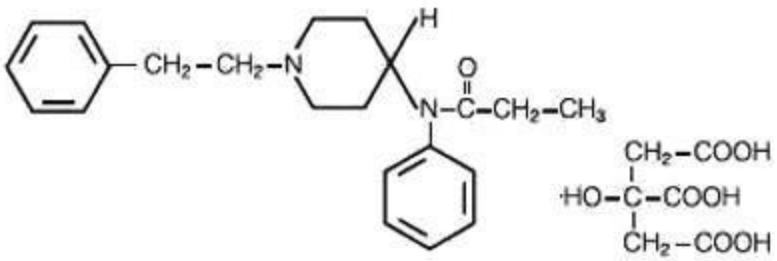
The various reported side effects are hypotension, hypertension, nausea, vomiting, dry mouth, bradycardia, atrial fibrillation, pyrexia, chills, pleural effusion, atelectasis, pulmonary oedema, hyperglycaemia, hypocalcaemia, acidosis, etc. Rapid administration of Dexmedetomidine infusion (Loading dose of 1 mcg/kg/hr if given in less than 10

minutes) may cause transient hypertension mediated by peripheral α_2-adrenoreceptor vasoconstriction. But hypotension and bradycardia may occur with ongoing therapy mediated by central α_{2A}-adrenoreceptor, causing decreased release of noradrenaline from the sympathetic nervous system. Long-term use of Dexmedetomidine leads to super sensitization and up regulation of receptors, so with abrupt discontinuation, a withdrawal syndrome of nervousness, agitation, headaches, and hypertensive crisis can occur. Dexmedetomidine is not recommended in patients with advanced heart block and ventricular dysfunction. FDA has classified it as a category C pregnancy risk, so the drug should be used with extreme caution in women who are pregnant.

FENTANYL

Fentanyl is a phenyl piperidine derivative synthetic opioid agonist that is structurally related to meperidine.

CHEMICAL FORMULA:



N-(1-Phenethyl-4-piperidyl) propionanilide citrate (1:1)

MECHANISM OF ACTION:

In 1973, based on radioligand binding assays, three types of opioid receptors were postulated. They were named μ for the morphine type, κ for the ketocyclazocine type, and σ for the SKF10047 (*N*-allylnormetazocine) type. Pain control by opioids needs to be considered in the context of brain circuits modulating analgesia and the functions of the various types of receptors in these circuits [66]. It has been well established that the analgesic effects of opioids arise from their ability to inhibit directly the ascending transmission of nociceptive information from the dorsal horn of the spinal cord and to activate the pain control circuits that descend from the midbrain, via the rostral ventromedial medulla, to the dorsal horn of the spinal cord. Fentanyl is a strong μ and κ receptor agonist and mild stimulant of σ receptor and is 100 times more potent than

morphine as an analgesic. The μ-receptor produces analgesia within descending pain control circuits, at least in part by the removal of GABAergic (transmitting or secreting γ-aminobutyric acid) inhibition of RVM-projecting neurons in the PAG and spinally projecting neurons in the RVM [66]. The distribution of opioid receptors in descending pain control circuits indicates substantial overlap between μ and κ-receptors. Interactions between the κ-receptor and the μ-receptor may be important for modulating nociceptive transmission from higher nociceptive centres, as well as in the spinal cord dorsal horn. The actions of μ-receptor agonists are invariably analgesic, whereas those of κ-receptor agonists can be either analgesic or antianalgesic [67].

PHYSICOCHEMICAL PROPERTIES:

PKa	:	8.4
Percentage nonionised at pH 7.4	:	8.5
Protein binding capacity	:	84 %
Clearance (ml/min)	:	1530
Volume of Distribution (Litres)	:	335
Partition Coefficient	:	955
Elimination ½ time (hrs)	:	3.1-6.6
Context sensitivity t ½, 4 hr infusion	:	260 min
Effect site equilibration time	:	6.8 min

PHARMACOKINETICS:

ABSORPTION: Fentanyl is 800 times more lipid soluble than morphine. Hence, it is rapidly taken up by spinal tissues and cephalad movement of drug in the CSF is limited.

DISTRIBUTION: The volume of distribution for Fentanyl is 335 litres**.** It accumulates in skeletal muscle and fat and is released slowly into the blood. The lungs also serve as a large, inactive storage site, with an estimated 75 % of the initial Fentanyl dose undergoing first pass pulmonary uptake.

METABOLISM AND ELIMINATION: Fentanyl is primarily transformed in the liver by N- demethylation, producing norfentanyl, which may be the principal metabolite in humans. Norfentanyl has lesser analgesic potency than Fentanyl.

Approximately 75% of an intravenous dose is excreted in the urine, mostly as metabolites with less than 10% representing the unchanged drug. Fentanyl has an elimination half-time of 3.1 to 6.6 hrs.

It crosses the placental barrier and small amounts have been detected in breast milk.

PHARMACODYNAMICS:

CARDIOVASCULAR SYSTEM:

Preserves the cardiac stability and has no major side effects at therapeutic dosages. However, it can cause bradycardia and may lead to occasional decreases in blood pressure and cardiac output.

RESPIRATORY SYSTEM:

Fentanyl, like other opioid agonists, causes a dose related respiratory depression. Its action on the respiratory centre in the brainstem may decrease the respiratory rate, the tidal volume, the minute ventilation and the ventilatory response to carbon dioxide. However this depression is less pronounced and of shorter duration as compared with meperidine and morphine.

GASTROINTESTINAL SYSTEM:

Fentanyl may produce nausea vomiting at analgesic doses, by stimulating the chemoreceptor trigger zone. It is not known to affect the gastrointestinal transit time. .

CENTRAL NERVOUS SYSTEM:

1) Seizure activity may be uncommonly seen with high doses of Fentanyl.

2) It elevates the intra cranial tension especially if respiration is depressed.

3) It stimulates the vagal centre more than morphine does; producing bradycardia and sweating, its action being blocked by atropine.

4) It crosses the blood brain barrier and can cause psychic and physical dependence.

5) A state called the wooden chest syndrome marked by the presence of smooth and skeletal muscle rigidity may be produced and may require administration of muscle relaxants.

SIDE EFFECTS:

PRURITUS: Most common side effect after neuraxial use. It occurs within few hours of injection and may precede the onset of analgesia. Pruritis occurs likely due to cephalad movement of opioid in CSF which causes subsequent interaction with opioid receptors in the trigeminal nucleus. Paradoxically, antihistamines may be effective in the treatment of pruritis, like due to sedative effect.

URINARY RETENTION: it occurs after neuraxial administration more commonly than intravenous and intramuscular administration of equivalent doses. Interaction with sacral opioid receptors promotes inhibition of parasympathetic nervous system outflow that causes detrusor muscle relaxation and increases maximal bladder capacity.

DEPRESSION OF VENTILATION: It is the most serious complication and incidence is almost similar with neuraxial, intravenous or intramuscular administration. Most reliable clinical sign of ventilation depression is depressed level of consciousness, possibly because of hypercarbia.

SEDATION: Sedation after use of opioid is dose dependent.

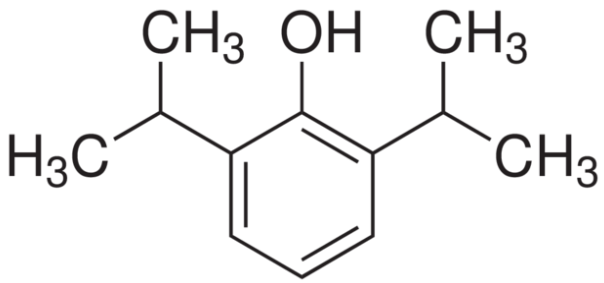
OTHER: Other side effects are central nervous system excitation, viral reactivation, and neonatal morbidity, delayed gastric emptying and decreased body temperature.

PROPOFOL:

INTRODUCTION:

It is the most frequently used intravenous anesthetic today. The first clinical trial by Kay and Rolly in 1977, confirmed the potential of Propofol as an anaesthetic to induce anaesthesia. Propofol is insoluble in water and initially prepared in cremophor EL, but due to anaphylactic reaction it's reformulated in an emulsion.

CHEMICAL STRUCTURE:



PHYSIOCHEMICAL PROPERTIES:

Propofol is an alkyl phenol derivative having hypnotic properties in animals. Alkyl phenols are oils at room temperature and insoluble in aqueous solution, but they are highly lipid soluble. The Propofol composition consist of 1% Propofol, 10 % soyabean oil, 2.25 % glycerol and 1.2 % purified egg phosphatide. As an emulsion, disodium edentate 0.005 % added to the solution as retardant of bacterial growth. Due to the chances of bacterial growth, it should not be used more than 6 hours of opening the vial / ampoule and should be kept sterile. It appears as slightly viscous, milky white substance with a pH of 7.0. For dilution of Propofol 5 % dextrose in water is used as diluents, dilution may change the pharmacologic properties slightly.

The diluted concentration of Propofol should not be less than 2 mg/ml to preserve the emulsion base. In diluted form it has been shown to be more stable when in contact with glass than with plastic. Propofol has been shown to be compatible with the following intravenous fluids: 5% Dextrose Injection USP, Lactated Ringers Injection USP, Lactated Ringers and 5% Dextrose Injection, 5% Dextrose and 0.45% Sodium Chloride Injection USP, 5% Dextrose and 0.2% Sodium Chloride Injection USP.

To avoid pain during injection it can be added with Inj. Lidocaine, but it should be not more than 20 mg/ 200 ml of Propofol. Addition of Lidocaine may pose the risk of coalescence of oil droplets which may pose the risk of pulmonary embolism.

METABOLISM:

Propofol is rapidly metabolized in the liver by conjugation to glucuronide and sulfate to produce water-soluble compounds, which are excreted by the kidneys. Only 1 % is excreted unchanged in urine and 2 % in feces. Propofol clearance exceeds the hepatic blood flow thus there are extra hepatic and extra renal routes of excretions are present. Lungs also play an important role on extra hepatic metabolism and responsible for 30 % of the uptake and first-pass metabolism after a bolus dose. Propofol itself causes a dose dependent inhibition of cytochrome P-450 enzyme system. Propofol may also be oxidized by liver cytochrome to 4-hydroxypropofol (active component with 1/3rd activity), which is then glucuronidated or sulphated into inactive compounds.

MECHANISM OF ACTION:

Ultra short-acting anaesthetics depress the central nervous system (CNS) to produce hypnosis and anaesthesia without analgesia:

1. SITE OF ACTION: $GABA_A$: BZD: Chloride receptor complex in CNS Binding of Propofol to $GABA_A$ receptor causes prolongation of action of GABA and increased duration of opening of chloride channel resulting in hyperpolarisation of postsynaptic cell membrane and functional inhibition of postsynaptic neurons.

2. It causes wide spread inhibition of NMDA (N- methyl- D Aspartate) receptor through sodium channel gating.

3. Propofol increases dopamine concentration in the nucleus acumens (phenomenon associated with drug abuse and pleasure seeking behaviour) resulting in a sense of well being in a patient.

4. It also decreases serotonin levels in the area postrema through action on GABA receptors resulting in its anti emetic effect.

5. Depresses spinal cord activity (anti pruritic effect)

PHARMACOKINETICS:

Molecular weight— 178.

pKa — 11.

The octanol / water partition coefficient for Propofol is 6761:1 at a pH of 6-8.5

Absorption: Only Intravenous

Volume of distribution at steady state (Vd):3.5- 4.5 L/kg

Protein binding: — 95%–98%

DISTRIBUTION: Three compartment phase linear model after intravenous injection

Following an I.V. bolus dose, the highly lipid soluble Propofol rapidly equilibrates between the plasma and the brain, accounting for the rapid onset of anaesthesia (one-arm-to-brain circulation time).

- Phase 1/very rapid distribution: (half life 1- 8 minutes): Then the drug is rapidly distributed to other highly perfused organs like kidneys, heart, lungs and liver. Awakening from a single bolus dose is rapid due to a very short initial distribution half-life (2–8 min) and rapid clearance. Plasma level of Propofol decreases.
- Phase 2/slow distribution: (half life 30- 60 minutes) Drugs are rapidly redistributed from the brain / other highly perfused area to other body tissues first to muscle, and then slowly to fat.
- Phase 3/ terminal elimination: (half-life from 4 to 24 h) Depending on the study conditions using bolus or infusion dosing, drug is slowly released from deep compartment with limited perfusion (fat) to plasma, and it is metabolized. Blood level of Propofol required during surgery is 2- 5 mcg/ml, while patient becomes awake at plasma level less than 1.5 mcg/ml. Because required decrease in concentration for awakening after anaesthesia or sedation is less than 50%, recovery from Propofol remain rapid even after prolonged infusions.

The context sensitive half time for Propofol for infusion of up to 8 hours is less than 40 minutes. But, longer duration of infusion may result in accumulation of drug in fat stores, and longer time may be required for elimination.

PHARMACODYNAMICS:

CENTRAL NERVOUS SYSTEM EFFECTS:

Hypnotic action of Propofol is mostly mediated by enhancing GABA induced chloride current through beta subunit binding on hippocampus. Alpha and gamma subunits also modulate effects on GABA receptors. The α_2-adrenoreceptor system also seems to play an indirect role in the sedative effects of Propofol. Propofol results in widespread inhibition of the *N*-methyl-d-Aspartate (NMDA) subtype of glutamate receptor through modulation of sodium channel gating. Studies have shown that Propofol has a direct depressant effect on neurons of the spinal cord.

CARDIOVASCULAR SYSTEM EFFECTS:

Myocardial depression caused by Propofol is dose dependent. Propofol causes 25-40% decrease in SBP. Similar changes in Mean BP and DBP due to direct vasodilatation. Propofol blocks / reset Baroreceptor, so there is little (no) compensatory tachycardia due to decrease in MBP. Propofol attenuates heart rate response to atropine. Propofol causes decrease in cardiac output which is, more significant in hypovolemic patients, cardiac disease, on beta blockers, hypertensive patients on treatment.

RESPIRATORY SYSTEM EFFECTS:

Propofol causes dose dependent respiratory depression, first it results in reduction in tidal volume associated with tachypnoea which is then followed by apnoea. Apnoea occurs in 25- 30% of patients depending on dose. Duration of apnoea depends upon dose, concomitant drugs like opioids, benzodiazepines and may be more than 30 seconds.

Decreased sensitivity of respiratory center to increase in carbon dioxide and hypoxia via carotid body chemoreceptors. Laryngeal reflexes and cough reflexes are depressed by Propofol. Propofol has bronchodilator effect through direct action on muscarinic receptors. Propofol also attenuates the magnitude of hypoxic pulmonary vasoconstriction.

RENAL SYSTEM EFFECTS:

Propofol causes constriction of splanchnic and renal blood vessels which leads to decrease in renal blood flow and glomerular flow rate. Prolonged infusion of Propofol results in green urine due to phenols in urine, cloudy urine due to increased uric acid in urine (crystallization of uric acid at low pH and temperature). Presence of these does not affect renal function.

GASTRO-INTESTINAL SYSTEM EFFECTS:

Hepatic blood flow is decreased.

OTHER:

Minimal muscle relaxation is required though good intubating condition may be obtained with Propofol use alone.

Decrease in IOP (intra ocular pressure, 30- 40%) is more than Thiopentone, so more useful in blunting increase in IOP due to Succinylcholine or laryngoscopy.

Propofol have no effect on uterine muscle tone. Crosses placenta (equilibrium between mother and fetus within 2- 3 minutes) and causes neonatal depression.

Propofol after single dose does depress cortisol synthesis or alter the normal response to ACTH.

It has antioxidant properties like vitamin E.

It has anti pruritic effect.

It does not alter coagulation.

CLINICAL APPLICATION OF PROPOFOL:

1. INDUCTION OF ANAESTHESIA:

a. It is the most commonly used IV induction agent, has replaced Thiopentone for this purpose

b. Dose: 1- 2.5 mg/kg IV dose reduced with increasing age.

c. Blood level: 2- 6 mcg/ml.

2. MAINTENANCE OF ANAESTHESIA:

a. A bolus of 10- 40 mg repeated every few minutes.

b. Continuous infusion at a rate of 50 - 150 (100- 300) mcg/kg/min IV combined with N_2O or opiate.

c. Preferred anaesthetic drug for TIVA (Total Intravenous Anaesthesia) technique in conjugation with short acting opioids.

3. SEDATION:

a. For short surgical procedure or ICU sedation / conscious sedation.

b. Dose at a rate of 25-75 mcg/kg/min I.V.

c. Preferred drug in Day care surgery sedation.

4. ANTIEMETIC EFFECT:

a. 10 - 20 mg IV, can be repeated every 5- 10 minutes or start infusion of 10 mcg/kg/minute.

5. ANTIPRURITIC EFFECT:

a. Propofol 10 mg IV is effective in the treatment of pruritis associated with neuraxial opioids or cholelithiasis.

b. Mechanism of antipruritic effect is due to depression of spinal cord activity.

6. ANTICONVULSANT ACTIVITY:

a. It has anti epileptic activity due to GABA mediated pre- and post- synaptic inhibition of chloride ion channels.

b. At a dose of > 1 mg/kg body weight decreases seizure duration.

7. ATTENUATION OF BRONCHOSPASM:

a. Propofol acts as bronchodilator.

b. It's preservative sodium metabisulfite may produce bronchoconstriction in asthmatics.

8. ANTI- OXIDANT:

a. Beneficial in acute lung injury.

ADVERSE EFFECTS / PRECAUTIONS:

LOCAL:

1. Pain on injection: Attention should be paid to minimize pain on administration of Propofol.

a. Transient local pain can be minimized if the larger veins of the forearm or antecubital fossa are used.

b. Pain during intravenous injection may also be reduced by prior injection of I.V. Lidocaine (1 ml of a 1% solution). Adding Lignocaine with Propofol may cause instability of emulsion and reduced drug potency. Therefore, it is recommended that Lidocaine be administered prior to Propofol administration or it should be added to Propofol immediately before administration and in quantities not exceeding 20 mg Lidocaine / 200 mg Propofol.

c. Prior administration of potent short acting opioids.

d. Other drugs tried with different efficacy: NSAIDs, Ketamine, Esmolol / Metoprolol, Magnesium, Clonidine / Ephedrine combination, Dexamethasone, Metoclopromide.

2. Phlebitis or thrombosis have been reported rarely (<1%).

3. Intra-arterial injection in animals did not induce local tissue effects or vascular complications.

4. Intentional injection into subcutaneous or perivascular tissues of animals caused minimal tissue reaction.

SYSTEMIC:

1. Clinical features of anaphylaxis, including angioedema, bronchospasm, erythema, and hypotension, occur rarely due to allergy to components of emulsion or due to phenyl nucleus and diisopropyl side chain of Propofol.

2. CNS: Perioperative myoclonus, hallucination, sexual fantasies, convulsions and opisthotonos have been reported.

3. CVS: hypotension, bradycardia, asystole (no vagolytic activity). Paediatric patients are susceptible to this effect, particularly when Fentanyl is given concomitantly. The intravenous administration of anticholinergic agents (e.g., atropine or Glycopyrolate) should be considered to modify potential increases in vagal tone due to concomitant agents (e.g., Succinylcholine) or surgical stimuli.

4. Respiratory system: Apnoea

5. GIT: Rarely, cases of unexplained postoperative pancreatitis (requiring hospital admission) have been reported after anaesthesia in which Propofol was one of the induction agents used. Due to a variety of confounding factors in these cases, including concomitant medications, a causal relationship to Propofol is unclear.

6. 1 ml of Propofol contains approximately 0.1 g of fat (1.1 kcal).

7. Abuse Potentials

8. Bacterial growth:

a. Intralipid that acts as solvent for Propofol is excellent medium for bacterial growth.

b. Support growth of E. coli, pseudomonas aeruginosa and other bacteria, so may cause sepsis.

c. Some preparation contains anti- bacterial or bacteriostatic components.

9. Propofol Infusion Syndrome:

a. A rare but lethal complication of Propofol infusion at dose more than 4 mg/kg/hr or more for 48 hours or longer.

b. Initially described in children, but later on also found in critically ill patients.

c. Presentation: acute refractory bradycardia leading to asystole, in the presence of one or more of following: metabolic acidosis (base deficit > 10mmol/L), rhabdomyolysis, hyperlipidemia and enlarged or fatty liver.

d. Other features may include: cardiomyopathy with acute cardiac failure, skeletal myopathy, hyperkalemia, hepatomegaly, and lipidemia.

e. Major risk factors: poor oxygen delivery, sepsis, serious cerebral injury and high Propofol dose.

f. Basic Pathology: mitochondrial toxicity / defect, impaired tissue oxygenation, carbohydrate deficiency.

MATERIAL AND METHODOLOGY

After institutional ethics committee approval, this study was conducted on 94 ASA I and II patients satisfying inclusion criteria, aged 18 – 60 years of either sex scheduled for short surgical procedures under general anaesthesia. It was randomised prospective study.

They were divided into two groups using randomisation in a group of 47 patients each by a blinder by chit block method (block of 6). And they were named as group D, who received Dexmedetomidine with Propofol and group F, who received Fentanyl with Propofol. A complete pre-operative assessment was done and checked out for patient's fitness. Patients were assessed for all inclusion and exclusion criteria.

Inclusion criteria:

- ASA Class I & II
- Age 18-50 years.
- Obesity BMI<30wt/m2
- Mouth opening > 2.5cm
- Mallampatti grade 1 and 2
- GA with short surgical procedure

Exclusion criteria:

- Anticipated difficult airway
- Patient undergoing oral and neck surgeries
- Heart rate < 50bpm
- Blood pressure < 90/60mm of Hg

- Allergic to propofol or dexmeditomedine or fentanyl
- Pregnant female
- Known case of asthama , reactive airway , URTI
- Edentulous and patients with dentures

After thorough assessment the procedure was explained to patients. Written informed consent was taken. Then patient was taken on the OT table and monitors were attached. Intra-venous (I.V.) cannula was secured and I.V. Ringers lactate fluid 4 ml/kg/hr infused. Heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure, saturation and respiratory rate noted for baseline characteristics.

Patients were pre-medicated with Inj. Glycopyrolate 0.004 mg/kg I.V. Oxygen was delivered to patient through Hudson's mask at the rate of 6 L/min.

Among the two groups created, group D, Inj. Dexmedetomidine was calculated according to 1 mcg/kg dose based on body weight and diluted in normal saline upto 10ml by an anaesthesiology resident. This single bolus dose was given to the patient intravenously over 10 min. by an infusion pump. Similarly for other group, group F, Inj. Fentanyl was calculated according to 1 mcg/kg and diluted in normal saline upto 10ml by an anaesthesiology resident. This single bolus dose was given to the patient intravenously over 10 min. by an infusion pump.

Inj. Midazolam 0.02 mg/kg was given over 4 min. intravenously in either group.

Parameters like heart rate, blood pressure (systolic, diastolic and mean), saturation and respiratory rate was noted after giving premedication.

After 5 min of completion of either Dexmedetomidine or Fentanyl infusion patient was induced with Inj. Propofol 2.5 mg/kg till loss of eyelash reflexes or loss of

consciousness. Patients head was placed in sniffing morning air position.Ninety seconds after the administration of Propofol, investigator who had experience of at least 25 PLMA insertions, inserted a PLMA of appropriate size using the Introducer technique after lubricating the deflated cuff with water based jelly, then the cuff was inflated and adequacy of ventilation was checked, Then the device was fixed and secured and connected to breathing circuit. Following successful insertion of the LMA, its position was assessed by observing chest expansion and capnography during spontaneous or assisted breathing.

The blinded investigator graded the PLMA insertion conditions according to mouth opening, swallowing, gagging or coughing, head or limb movements, lacrimation, laryngospasm and ease of PLMA insertion. Mal-positioned PLMAs were removed. If the first attempt at PLMA insertion was unsuccessful or the PLMA was mal-positioned, we gave a further dose of Propofol 0.5 mg/kg and made another attempt at PLMA insertion 1 min later. Time taken for insertion of PLMA was defined as after induction since taking up PLMA till successful insertion and attaching breathing circuit to anaesthesia machine and confirming the correct positioning.

Laryngospasm was defined as the presence of stridor or other evidence of upper airway obstruction, which was relieved by deepening of anaesthesia. Apnoea was defined as the absence of spontaneous breathing for more than 30 s, and the duration of apnoea following PLMA insertion was recorded. In apnoeic patients, breathing was assisted manually to maintain an arterial oxygen saturation > 95%, until the return of spontaneous breathing. Following successful insertion and correct positioning of the PLMA, anaesthesia was maintained with 1.5% isoflurane, 50% Nitrous oxide in Oxygen.

Analgesia in the form of Inj.pentazocine 0.5 mg/kg was given before surgical incision in either group.

The device insertion was abandoned after 3 unsuccessful attempts. In case of failure patient was withdrawn from the study and muscle relaxant was given and intubated with endotracheal tube.

For any bradycardia less than 45 bpm, Inj. Atropine 0.01 mg/kg was given. If there was only fall in blood pressure, it was treated with administration of fluids.

At the end of 1 min. of PLMA insertion all the parameters were noted again, then the parameters were noted at the interval of 3 min., 5 min., 10 min., 15 min. and 20min. Device was removed when patient was able to open mouth on command.

Then the patient was inspected for any injury to lip, teeth and tongue. The device was inspected for any blood stains.

Parameters assessed for insertion condition was-

- Dose of Propofol - Total:- _____ Increments:-_____
- Time required for insertion of Pro-seal LMA: _____
- Presence of apnoea- Yes / No
- No. of attempts required for insertion of Pro-seal LMA: _____
- Ease of insertion: jaw relaxation according to **Young's criteria**-

  Absolutely relaxed muscle tone - 1
  Moderately relaxed muscle tone - 2
  Poorly relaxed muscle tone - 3

- Coughing and gagging – Grade I (nil), Grade II (mild), Grade III (severe)
- Laryngospasm - Grade I (nil), Grade II (mild), Grade III (severe)
- Limb and head movements - Grade I (nil), Grade II (mild), Grade III (severe)

- Overall insertion conditions by **Modified scheme of Lund and Stovener**, as-

  1.Excellent: No gagging or coughing, no patient movement or laryngospasm.

  2. Good: mild to moderate gagging, coughing, or patient movement with no laryngospasm

  3.Poor: moderate to severe gagging, coughing, or patient movement with no laryngospasm

  4.Unacceptable: severe gagging, coughing, or patient movement or laryngospasm.

Throughout the surgical procedure parameters noted was-

- ❖ Heart rate:
- ❖ Blood pressure: (SBP)(DBP)
- ❖ Respiratory rate :
- ❖ SpO2:
- ❖ ECG:

All above parameters was checked at intervals as baseline, before induction, after induction, after PLMA insertion, after 1, 3, 5, 10, 15 and 20min.

STATISTICAL ANALYSIS

Mean and standard deviation for all the values were calculated and compared between two groups, group D-P and group F-P. For analysis of demographic data either Unpaired – t test or Fisher's exact test were used. Ordinal categorical data such as PLMA insertion conditions and number of attempts were analyzed with either Fisher's exact test or Chi Square test and the haemodynamic parameters were analyzed by using either unpaired T test or Mann Whitney test.

A p value < 0.05 was accepted as statistically significant.

OBSERVATION AND RESULTS

This prospective randomized study was carried out on 94 adult patients belonging to ASA I and II undergoing short surgical procedure under general anaesthesia. The patients were randomly divided into two groups of 47 each. Patients in group D-P, received Inj. Dexmedetomidine 1 mcg/kg and patients in group F-P received Inj. Fentanyl 1 mcg/kg bolus before induction with Inj. Propofol. Then insertion conditions for PLMA were assessed with reference to demographic and statistical data.

Table 1: Age

Parameter	DP		FP		p value
	Mean	SD	Mean	SD	
AGE(YR)	30.3	9.6	30.8	7.3	0.790

Table 2: Weight

COMPARISON OF MEAN WEIGHT BETWEEN STUDY GROUPS

Parameter	DP		FP		p value
	Mean	SD	Mean	SD	
WEIGHT	56.9	8.2	58.8	5.5	0.203

FIGURE 1: COMPARISON OF MEAN AGE BETWEEN STUDY GROUPS

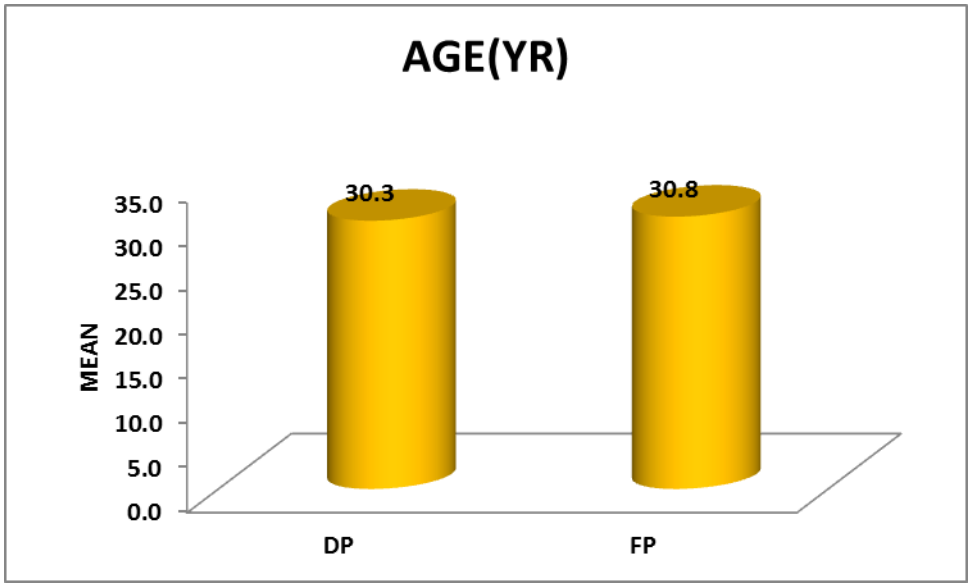
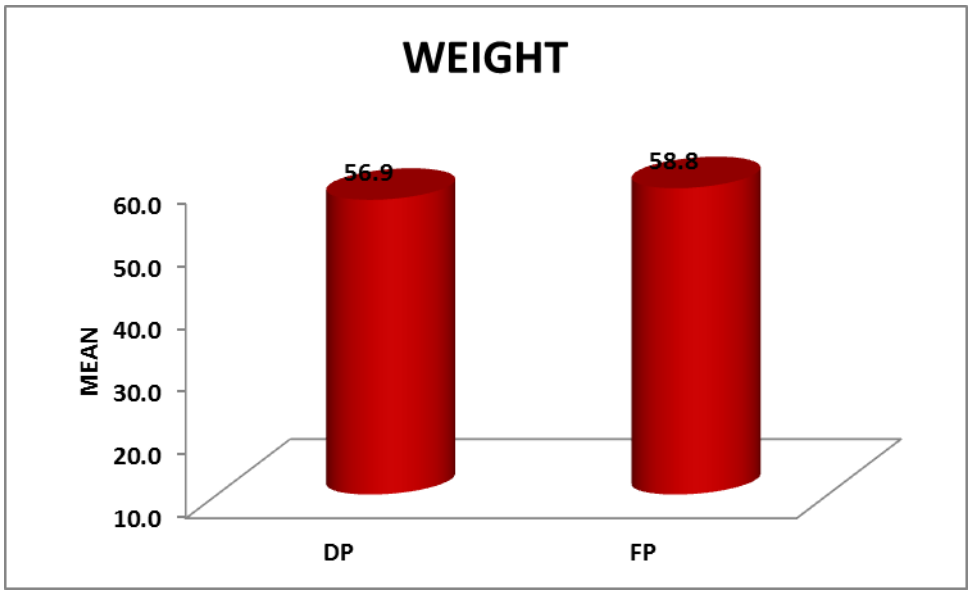


FIGURE 2: COMPARISON OF MEAN WEIGHT BETWEEN STUDY GROUP



P > 0.05 is statistically not significant and the groups are comparable.

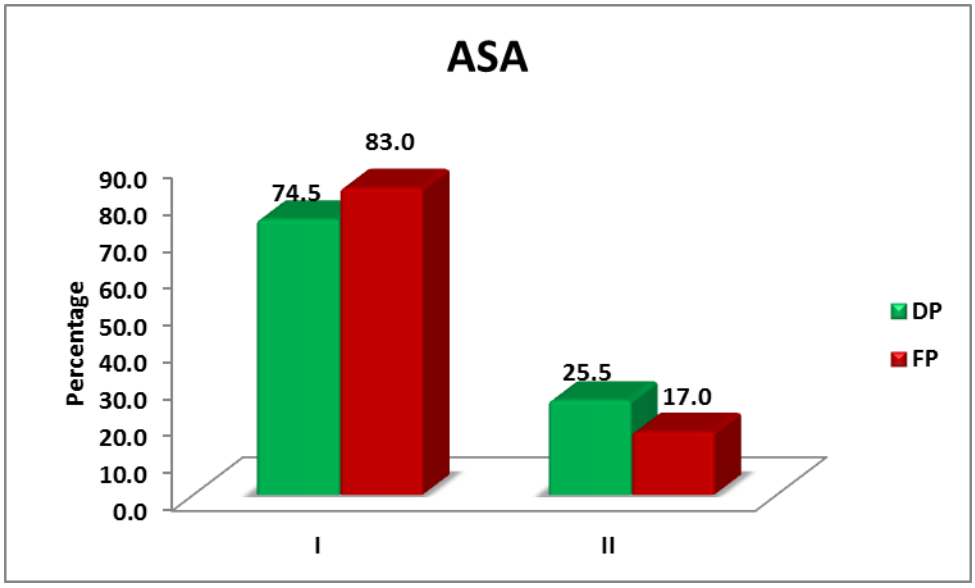
With reference to demographic data Age (p=0.790) and weight (p = 0.203) both the groups were comparable and there was no statistically significant difference in both the groups.

Table 3: ASA STATUS

DISTRIBUTION OF CASES ACCORDING TO ASA BETWEEN STUDY GROUPS

ASA	DP		FP		p value
	N	%	N	%	
I	35	74.5	39	83.0	0.313
II	12	25.5	8	17.0	
Total	47	100.0	47	100.0	

FIGURE 3 : DISTRIBUTION OF CASES ACCORDING TO ASA BETWEEN STUDY GROUPS



p > 0.05 is statistically not significant and the groups are comparable.

ASA physical status of the patients selected in this study were comparable (p = 0.313) and there is no statistically significant difference in both the groups.

Table 4 : MPC

DISTRIBUTION OF CASES ACCORDING TO MPC BETWEEN STUDY GROUPS

MPC	DP		FP		p value
	N	%	N	%	
I	30	63.8	38	80.9	0.065
II	17	36.2	9	19.1	
Total	47	100.0	47	100.0	

FIGURE 4 : DISTRIBUTION OF CASES ACCORDING TO MPC BETWEEN STUDY GROUPS

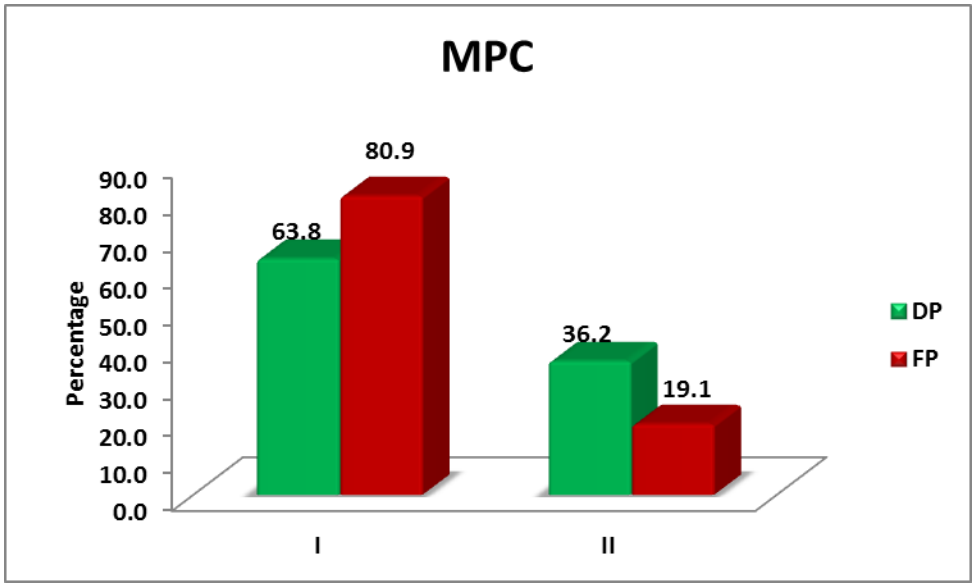


Table 4 and figure 4 shows the comparison of Mallampatti class between group D-P and group F-P. Both the groups were comparable with p value 0.065 calculated by Fisher's exact test.

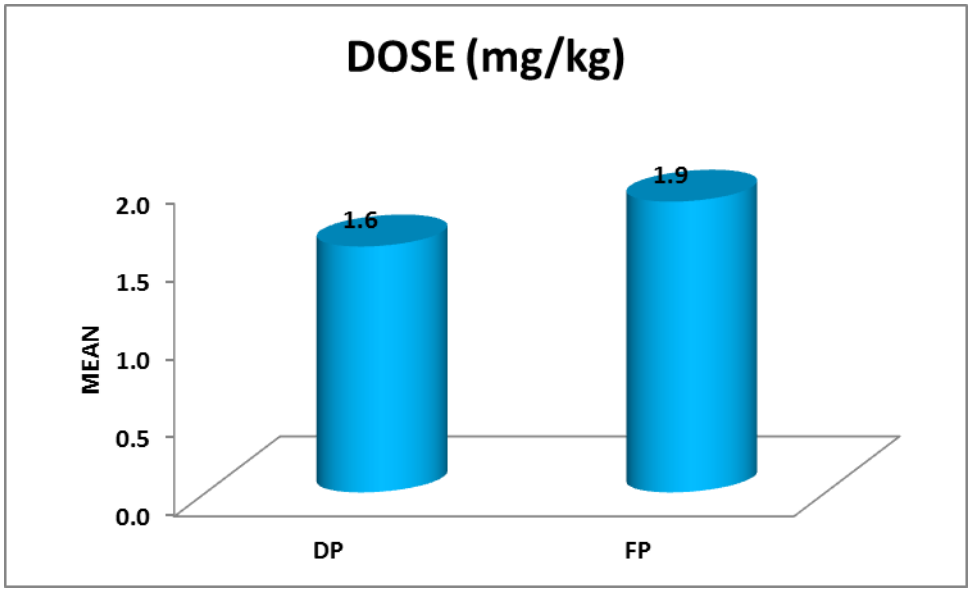
Table 5: MEAN DOSE OF PROPOFOL

COMPARISON OF MEAN DOSE OF PROPOFOL PER KG BODY WEIGHT(mg/kg)

Parameter	DP		FP		p value
	Mean	SD	Mean	SD	
DOSE **(mg/kg**	1.6	0.3	1.9	0.3	<0.001*

Note: *means significant at 5% level of significance (p<0.05)

FIGURE5: COMPARISON OF MEAN DOSE OF PROPOFOL PER KG BODY WEIGHT (mg/kg)



Here in table 5 and figure 5, it shows the dose of Propofol required per kg body weight, in group D-P 1.6 mg/kg and in group F-P its 1.9 mg/kg to insert PLMA. According to Mann Whitney test p value <0.0001. The induction dose in the F-P group is significantly higher than in the D-P group

Table 6: MEAN INDUCTION DOSE OF PROPOFOL

TABLE 6: COMPARISON OF MEAN INDUCTION DOSE OF PROPOFOL BETWEEN STUDY GROUPS

Parameter	DP		FP		p value
	Mean	SD	Mean	SD	
INDUCTION DOSE OF PROPOFOL (mg)	94.8	28.3	110.7	25.0	0.005*

Note: *means significant at 5% level of significance (p<0.05)

FIGURE 6: COMPARISON OF MEAN INDUCTION DOSE OF PROPOFOL BETWEEN STUDY GROUPS

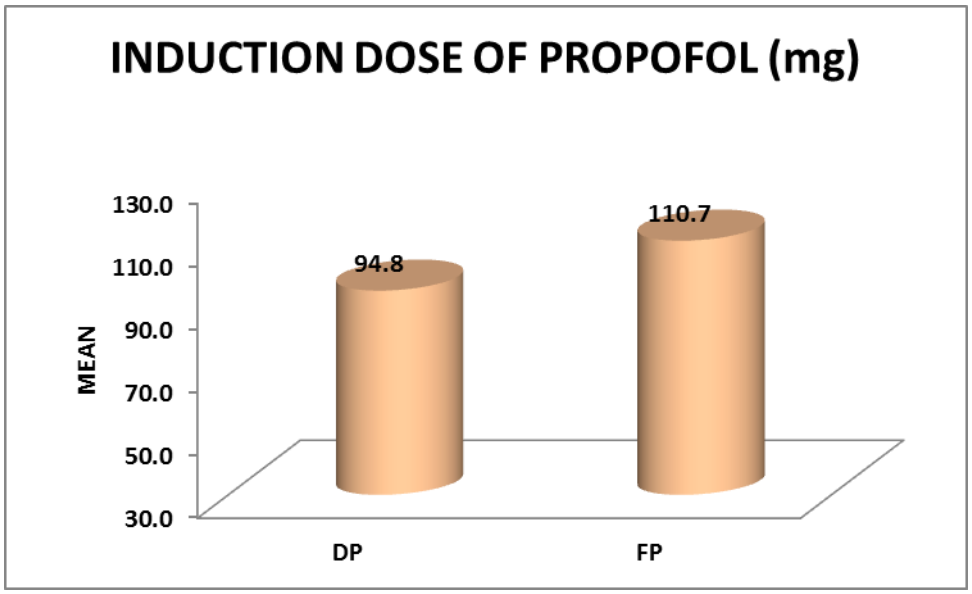


Table 6 and figure 6 shows comparison of induction dose of Propofol required for insertion of PLMA after the study drug has been infused. Group D-P required 94.8 mg and group F-P required 110.7 mg of Inj. Propofol for induction. According to Mann Whitney test this data is statistically highly significant (p value 0.0051). Group F-P required induction dose of Propofol significantly higher than group D-P.

Table 7: MEAN TOTAL DOSE OF PROPOFOL (mg) BETWEEN STUDY GROUPS

TABLE 7: COMPARISON OF MEAN TOTAL DOSE OF PROPOFOL (mg) BETWEEN STUDY GROUPS

Parameter	DP		FP		p value
	Mean	SD	Mean	SD	
DOSE OF PROPOFOL	98.7	34.7	115.7	30.1	0.013*

Note: *means significant at 5% level of significance (p<0.05)

FIGURE 7 : COMPARISON OF MEAN TOTAL DOSE OF PROPOFOL(mg) BETWEEN STUDY GROUPS

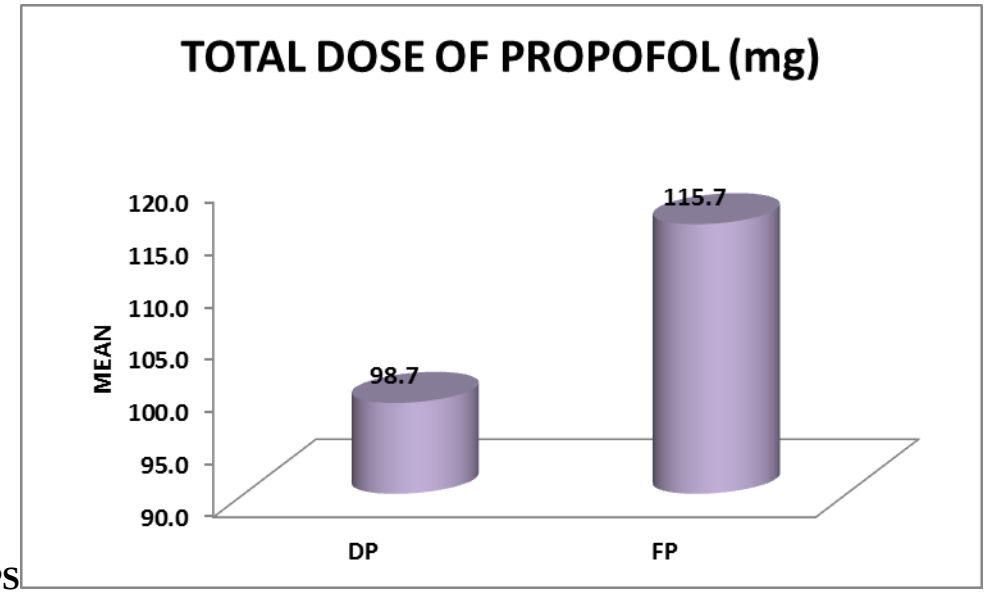


Table 7 and figure 7 shows total dose of Inj. Propofol required after considering the repeated attempts in group D-P is 98.7 and in group F-P is 115.7. Statistically the total dose of Propofol in the F-P group is significantly higher than in the D-P group calculated by unpaired T test.

Table 8: ATTEMPTS

TABLE 8: DISTRIBUTION OF CASES ACCORDING TO ATTEMPTS BETWEEN STUDY GROUPS

ATTEMPTS	DP		FP		p value
	N	%	N	%	
1	41	87.2	37	78.7	0.272
2	6	12.8	10	21.3	
Total	47	100.0	47	100.0	

FIGURE 8: DISTRIBUTION OF CASES ACCORDING TO ATTEMPTS BETWEEN STUDY GROUPS

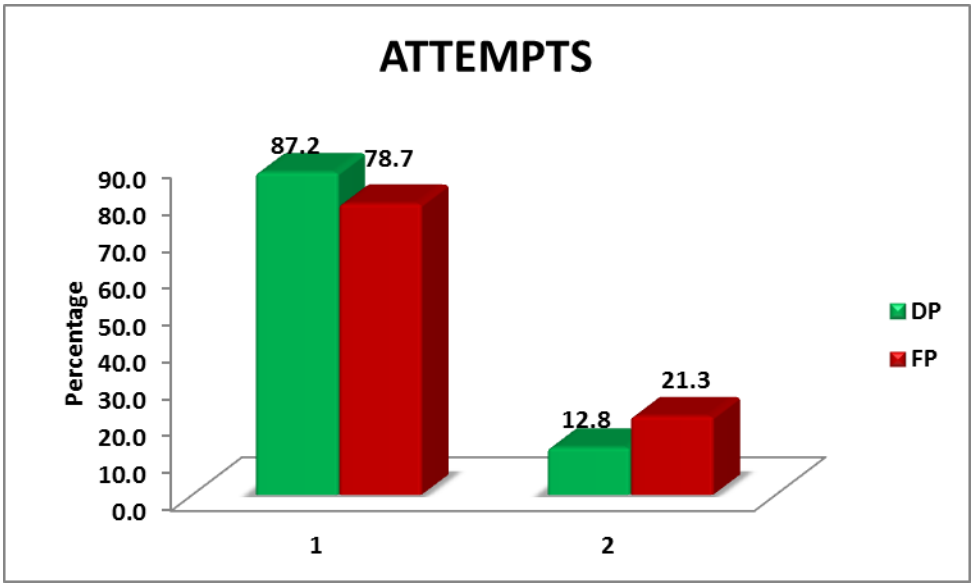


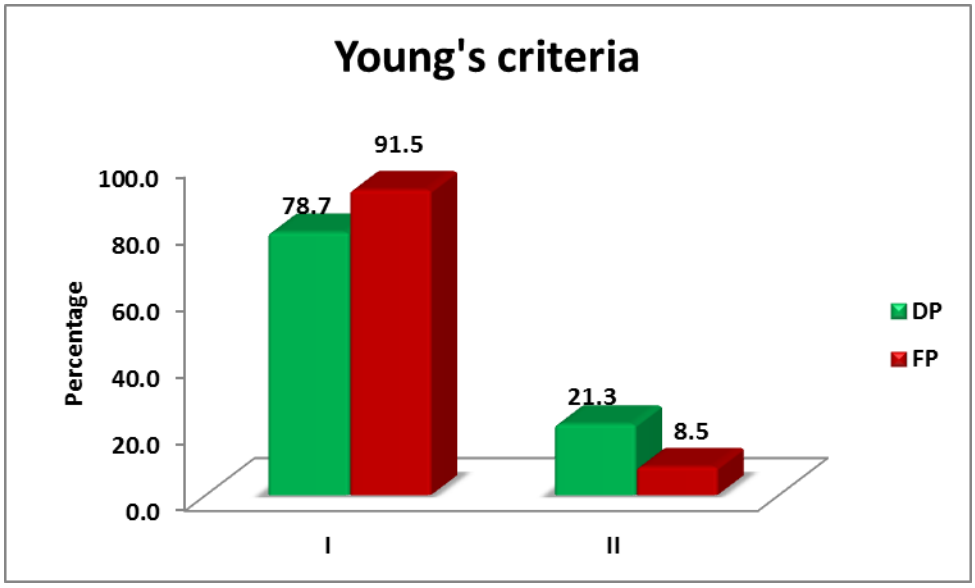
Table 8 and figure 8 shows comparison of number of attempts required for PLMA insertion after patient being induced with Inj. Propofol. In group D-P 6 patients required second attempt while in group F-P 10 patients required second attempt. Statistically on Fisher's exact test these two groups were comparable.

Table 9: Young's criteria of jaw relaxation

TABLE 9 : DISTRIBUTION OF CASES ACCORDING TO YOUNG'S CRITERIA BETWEEN STUDY GROUPS

Young's criteria	DP		FP		p value
	N	%	N	%	
I	37	78.7	43	91.5	0.082
II	10	21.3	4	8.5	
Total	47	100.0	47	100.0	

FIGURE 9: DISTRIBUTION OF CASES ACCORDING TO YOUNG'S CRITERIA BETWEEN STUDY GROUPS



Insertion conditions were assessed with Young's criteria based on jaw relaxation.

Table 9 and figure 9 shows 10 patients out of 47 in group D-P and 4 patients in group F-P experienced grade II of jaw relaxation according to Young's criteria. Group F-P patients experience better jaw relaxation.

Table 10: Coughing and Gagging

TABLE10: DISTRIBUTION OF CASES ACCORDING TO COUGHING, GAGGING BETWEEN STUDY GROUPS

Coughing, gagging	DP		FP		p value
	N	%	N	%	
Mild	0	0.0	6	12.8	0.011*
Nil	47	100.0	41	87.2	
Total	47	100.0	47	100.0	

Note: *means significant at 5% level of significance (p<0.05)

FIGURE: DISTRIBUTION OF CASES ACCORDING TO COUGHING, GAGGING BETWEEN STUDY GROUPS

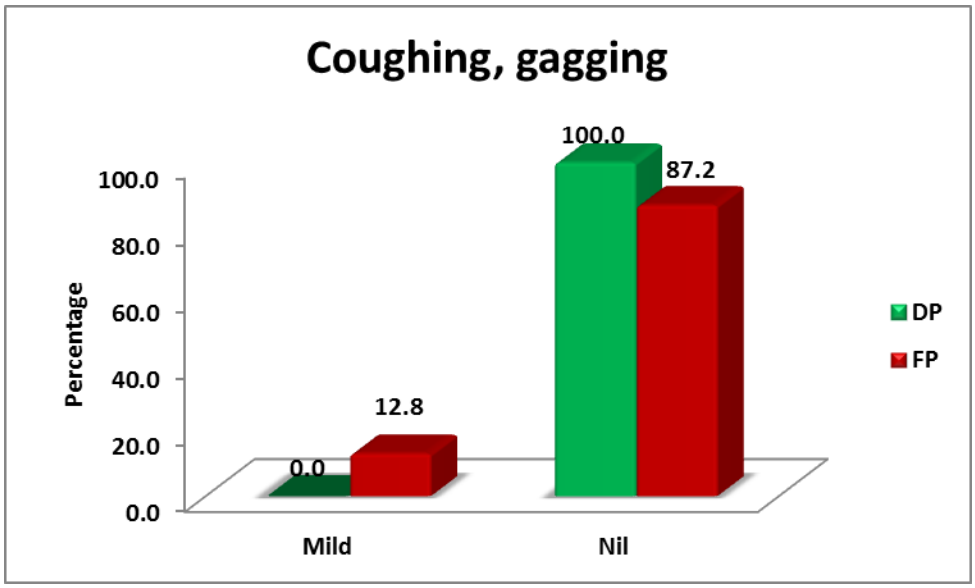


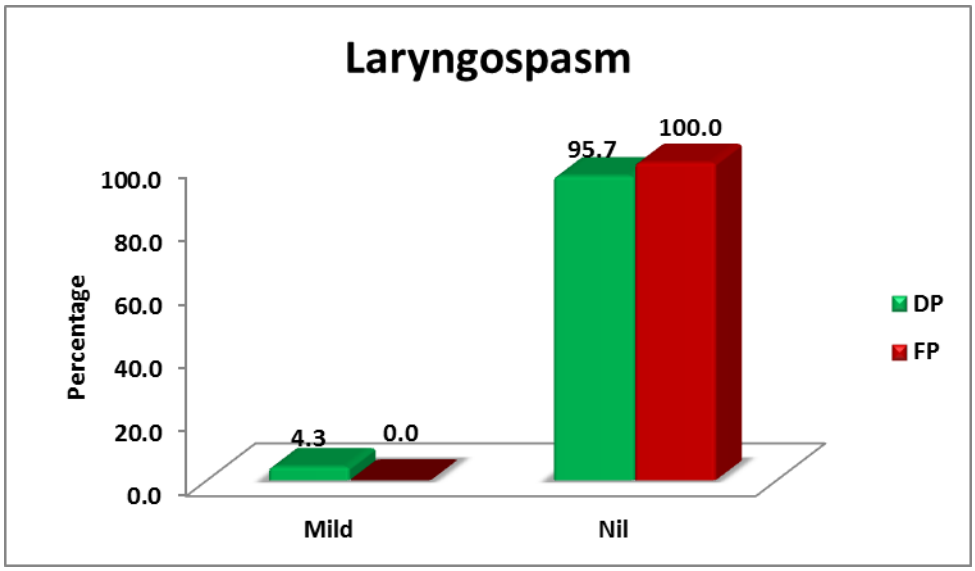
Table 10 and figure 10 shows comparison of evidence of coughing and gagging in group D-P and group F-P. In group D-P no patient had coughing and gagging, while 6 patients in group F-P had mild coughing.

Table 11: Laryngospasm

TABLE11: DISTRIBUTION OF CASES ACCORDING TO LARYNGOSPASM BETWEEN STUDY GROUPS

Laryngospasm	DP		FP		p value
	N	%	N	%	
Mild	2	4.3	0	0.0	0.153
Nil	45	95.7	47	100.0	
Total	47	100.0	47	100.0	

FIGURE11: DISTRIBUTION OF CASES ACCORDING TO LARYNGOSPASM BETWEEN STUDY GROUPS



Graph 14

Table 11 and figure 11 shows 2 patients in group D-P had episode of laryngospasm out of 47 patients, while group F-P had no such event.

Table 12: Limb and head movements

TABLE12: DISTRIBUTION OF CASES ACCORDING TO LIMB AND HEAD MOVEMENT BETWEEN STUDY GROUPS

Limb and head movement	DP		FP		p value
	N	%	N	%	
Mild	4	8.5	11	23.4	0.049*
Nil	43	91.5	36	76.6	
Total	47	100.0	47	100.0	

Note: *means significant at 5% level of significance (p<0.05)

FIGURE12: DISTRIBUTION OF CASES ACCORDING TO LIMB AND HEAD MOVEMENT BETWEEN STUDY GROUPS

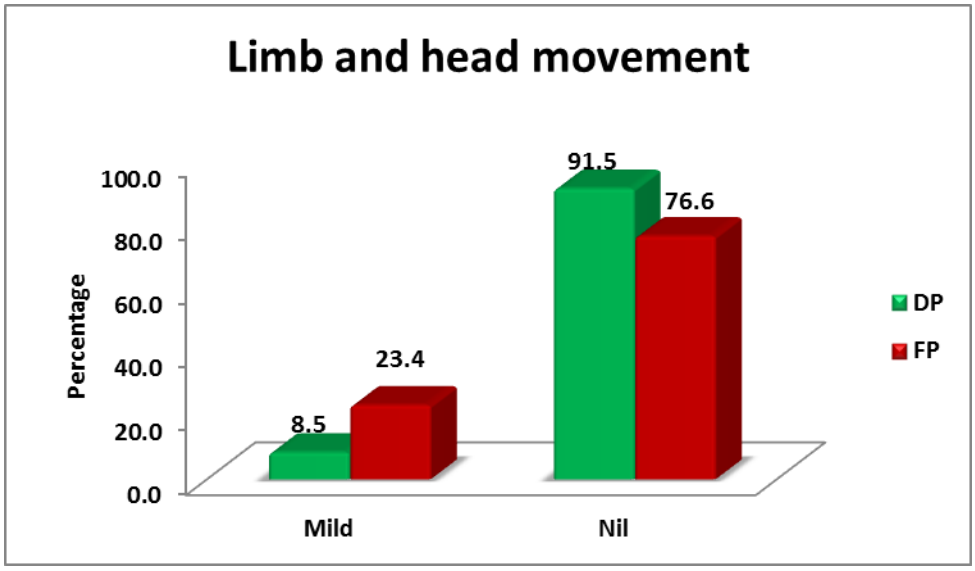


Table 12 and figure 12 shows the comparison of limb and head movement between group D-P and group F-P. Group D-P had 4 patients with limb and head movement while group F-P had 11 such episodes.

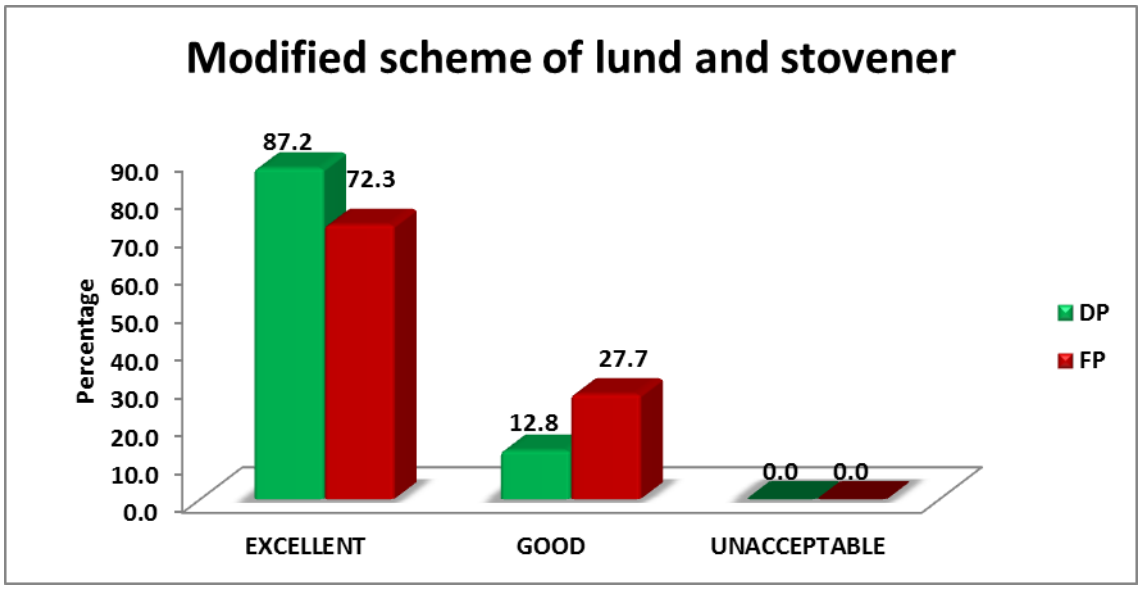
Table 13: Modified scheme of Lund and Stovener

TABLE 13: DISTRIBUTION OF CASES ACCORDING TO MODIFIED SCHEME OF LUND AND STOVENER BETWEEN STUDY GROUPS

Modified scheme of lund and stovener	DP		FP		p value
	N	%	N	%	
EXCELLENT	41	87.2	34	72.3	0.025*
GOOD	6	12.8	13	27.7	
UNACCEPTABLE	0	0.0	0	0.0	
Total	47	100.0	47	100.0	

Note: *means significant at 5% level of significance (p<0.05)

FIGURE 13: DISTRIBUTION OF CASES ACCORDING TO MODIFIED SCHEME OF LUND AND STOVENER BETWEEN STUDY GROUPS



Overall insertion conditions according to modified scheme of Lund and Stovener is depicted in table 13 and figure 13 shows 41 patients out of 47 in group D-P had excellent insertion conditions while 34 patients out of 47 in group F-P had excellent insertion condition.

Table 14: Apnoea > 30 Sec

TABLE 14 : DISTRIBUTION OF CASES ACCORDING TO APNOEA >30 SEC BETWEEN STUDY GROUPS

APNOEA >30 SEC	DP		FP		p value
	N	%	N	%	
No	45	95.7	37	78.7	0.013*
Yes	2	4.3	10	21.3	
Total	47	100.0	47	100.0	

Note: *means significant at 5% level of significance (p<0.05)

FIGURE 14: DISTRIBUTION OF CASES ACCORDING TO APNOEA >30 SEC BETWEEN STUDY GROUPS

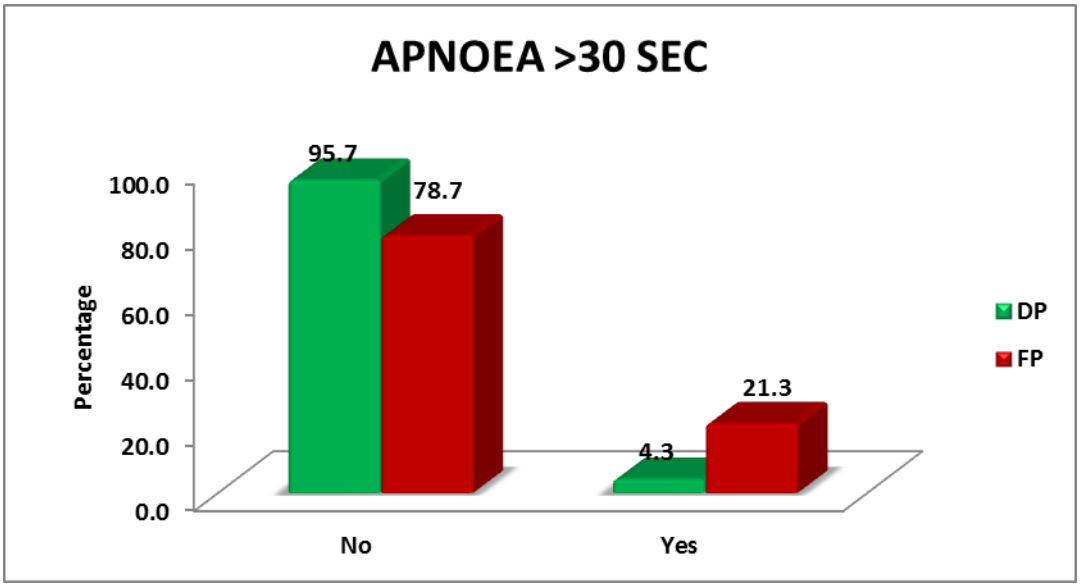


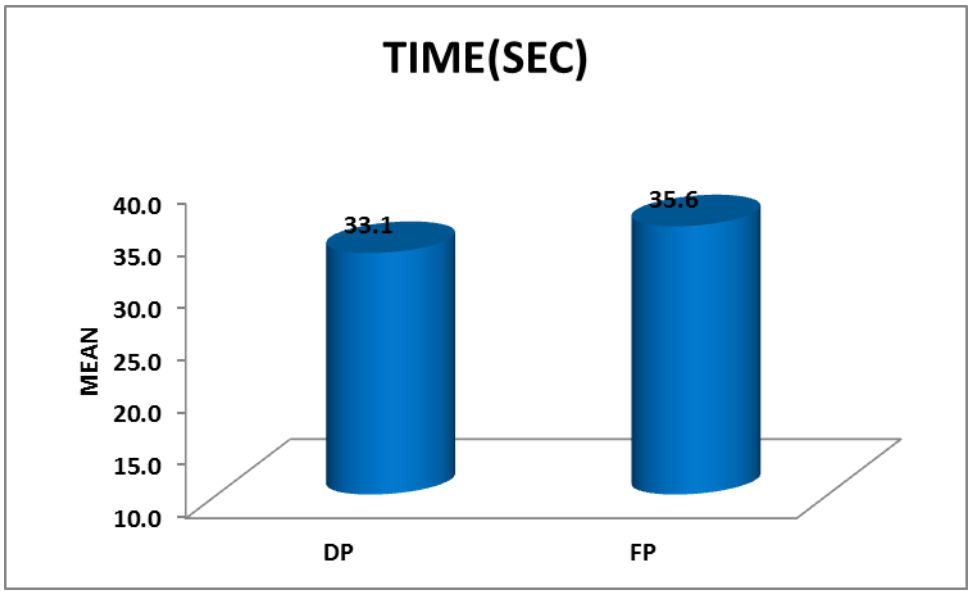
Table 14 and graph 14 shows comparison of apnoea period after induction with Propofol in both groups. Clinically in group F-P 10 patients out of 47 had apnea for > 30 sec. while in group D-P only 2 patients had apnoea more than 30 sec.

Table 15: Time required for PLMA insertion

TABLE 15: COMPARISON OF MEAN PLMA INSERTION TIME BETWEEN STUDY GROUPS

Parameter	DP		FP		p value
	Mean	SD	Mean	SD	
TIME(SEC)	33.1	21.2	35.6	20.9	0.558

FIGURE 15: COMPARISON OF MEAN TIME BETWEEN STUDY GROUPS



Graph 19

Table 15 and figure 15 shows comparison time required for insertion of PLMA between two groups D-P and F-P. Average time required for insertion of PLMA in group D-P is 33.10sec while in group F-P is 35.6sec.

Table 16: Heart rate (beat per minute)

TABLE: CHANGE IN MEAN HR ACCORDING TO TIME BETWEEN STUDY GROUPS

HR	DP		FP		p value
	Mean	SD	Mean	SD	
BASELINE WITH PREMEDICATION	91.3	12.4	91.1	9.5	0.941
BEFORE INDUCTION	93.5	12.4	94.8	9.3	0.575
AFTER INDUCTION	97.8	17.4	99.1	10.1	0.665
AFTER LMA INSERTION	99.7	14.9	104.5	10.5	0.076
1MIN AFTER INSERTION	94.4	13.5	97.6	8.4	0.172
3 MIN AFTER INSERTION	88.7	12.7	90.6	7.4	0.384
5MIN AFTER INSERTION	87.2	13.7	86.4	7.6	0.732
10 MIN AFTER INSERTION	85.2	14.0	86.0	5.9	0.702
15 MIN AFTER INSERTION	83.9	11.9	84.0	6.1	0.965
20 MIN AFTER INSERTION	82.4	11.6	81.5	5.6	0.650

FIGURE16: CHANGE IN MEAN HR ACCORDING TO TIME BETWEEN STUDY GROUPS

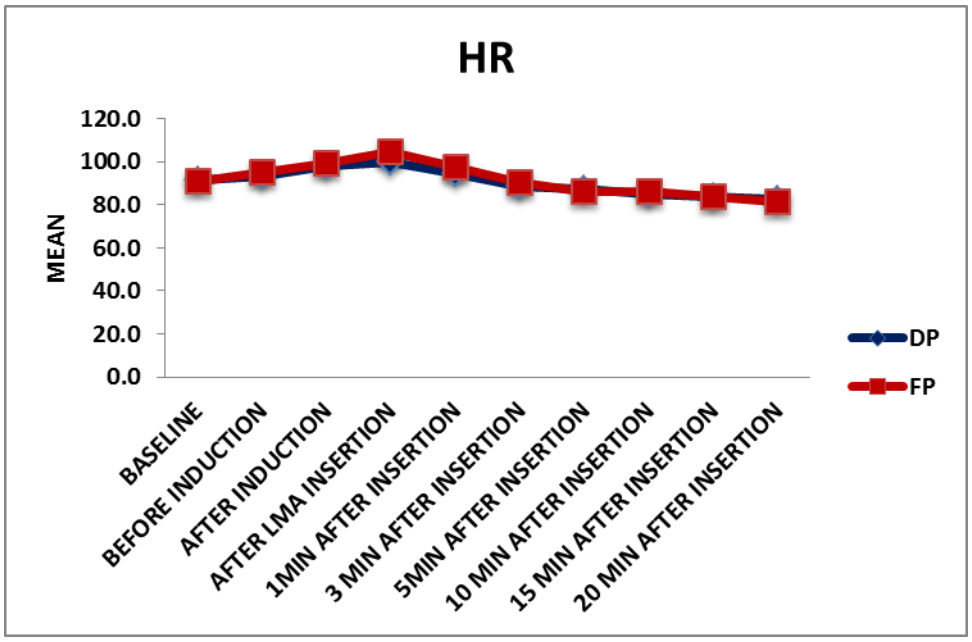


Table 16 and figure 16 shows comparison of mean heart rate between group D-P and group F-P. Though group F-P shows rise in heart rate at the time of insertion of PLMA, the values are statistically comparable in both the groups.

Table 17: Systolic blood pressure (mmHg)

TABLE 17: CHANGE IN MEAN SBP ACCORDING TO TIME BETWEEN STUDY GROUPS

SBP	DP		FP		p value
	Mean	SD	Mean	SD	
BASELINE WITH PREMEDICATION	117.7	15.1	116.0	10.7	0.519
BEFORE INDUCTION	117.1	13.8	116.5	9.9	0.817
AFTER INDUCTION	108.7	11.0	112.5	10.9	0.097
AFTER LMA INSERTION	110.9	11.5	117.7	10.8	0.004*
1MIN AFTER INSERTION	108.3	11.1	114.7	10.2	0.005*
3 MIN AFTER INSERTION	107.1	9.1	109.7	8.3	0.159
5MIN AFTER INSERTION	105.6	8.3	108.9	8.5	0.059
10 MIN AFTER INSERTION	105.4	7.6	107.9	7.8	0.126
15 MIN AFTER INSERTION	108.2	7.2	109.9	6.7	0.227
20 MIN AFTER INSERTION	107.4	6.8	109.3	7.1	0.195

Note: *means significant at 5% level of significance ($p<0.05$)

FIGURE 17: CHANGE IN MEAN SBP ACCORDING TO TIME BETWEEN STUDY GROUPS

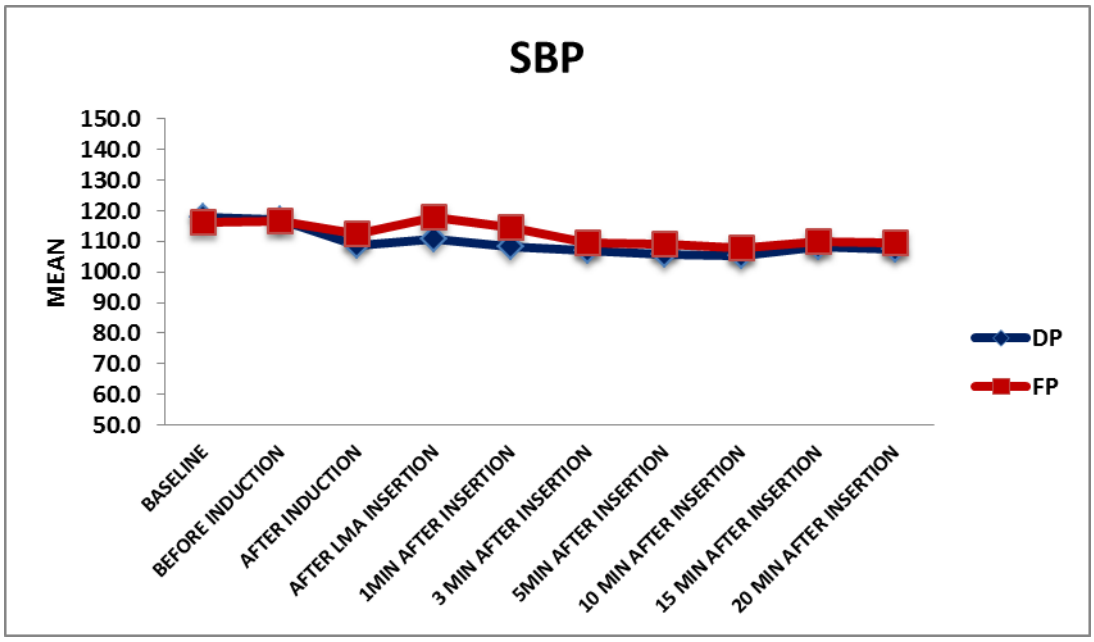


Table 17 and figure 17 shows comparison of systolic blood pressure between two groups. Mean systolic blood pressure after PLMA insertion in group D-P is 110.9 and group F-P is 117.7, which is calculated by unpaired T test with p value 0.024 and this is statistically significant. Thus mean systolic blood pressure is significantly higher in group F-P. Similarly mean systolic blood pressure 1 minute after PLMA insertion in group D-P is 108.3 and in group F-P is 114.7, which is higher in group F-P.

Table 18: Diastolic blood pressure (mmHg)

TABLE 18: CHANGE IN MEAN DBP ACCORDING TO TIME BETWEEN STUDY GROUPS

DBP	DP		FP		p value
	Mean	SD	Mean	SD	
BASELINE WITH PREMEDICATION	77.1	11.0	75.7	10.2	0.512
BEFORE INDUCTION	76.3	11.3	76.9	10.6	0.778
AFTER INDUCTION	72.4	10.0	76.0	10.9	0.095
AFTER LMA INSERTION	75.8	11.0	77.9	10.2	0.344
1MIN AFTER INSERTION	74.0	10.9	76.8	8.8	0.180
3 MIN AFTER INSERTION	73.4	8.9	76.3	8.5	0.109
5MIN AFTER INSERTION	72.1	8.0	74.9	8.0	0.098
10 MIN AFTER INSERTION	71.4	8.0	73.7	7.8	0.163
15 MIN AFTER INSERTION	71.6	7.7	73.7	6.8	0.161
20 MIN AFTER INSERTION	71.0	7.8	73.0	6.0	0.166

FIGURE18: CHANGE IN MEAN DBP ACCORDING TO TIME BETWEEN STUDY GROUPS

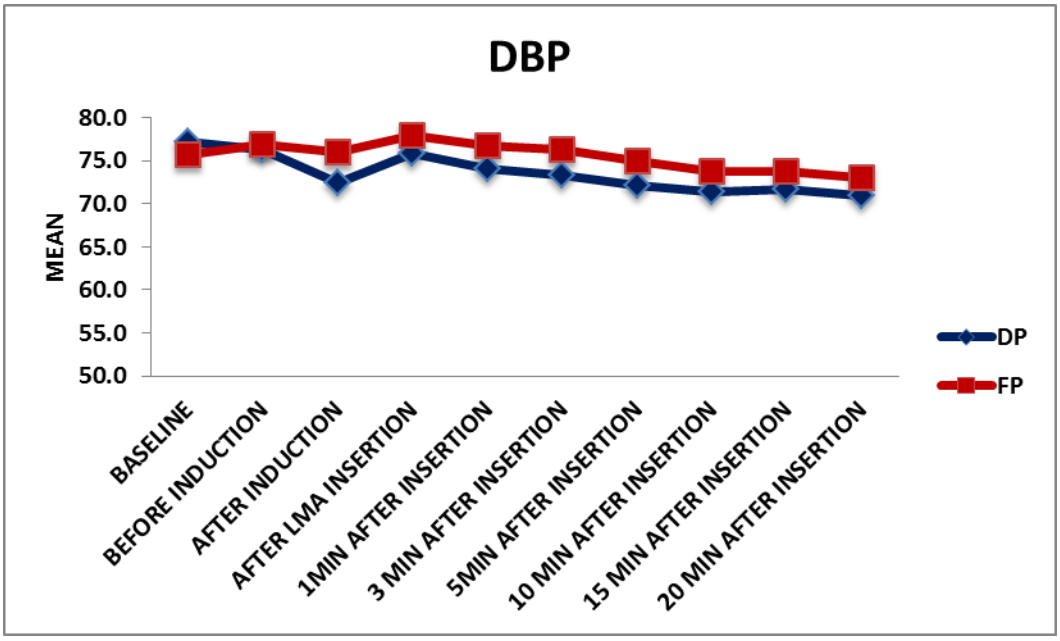


Table 18 and figure 18 shows comparison of mean diastolic blood pressure between groups D-P and group F-P. All the mean values calculated and compared statistically and found to be statistically not significant and mean diastolic blood pressure In both groups is comparable.

Table 19:SPO2 %

TABLE19: COMPARISON OF MEAN SPO2% BETWEEN STUDY GROUPS

	DP		FP		p value
	Mean	SD	Mean	SD	
SPO2%	98.9	0.6	98.8	0.7	0.430

FIGURE: COMPARISON OF MEAN SPO2% BETWEEN STUDY GROUPS

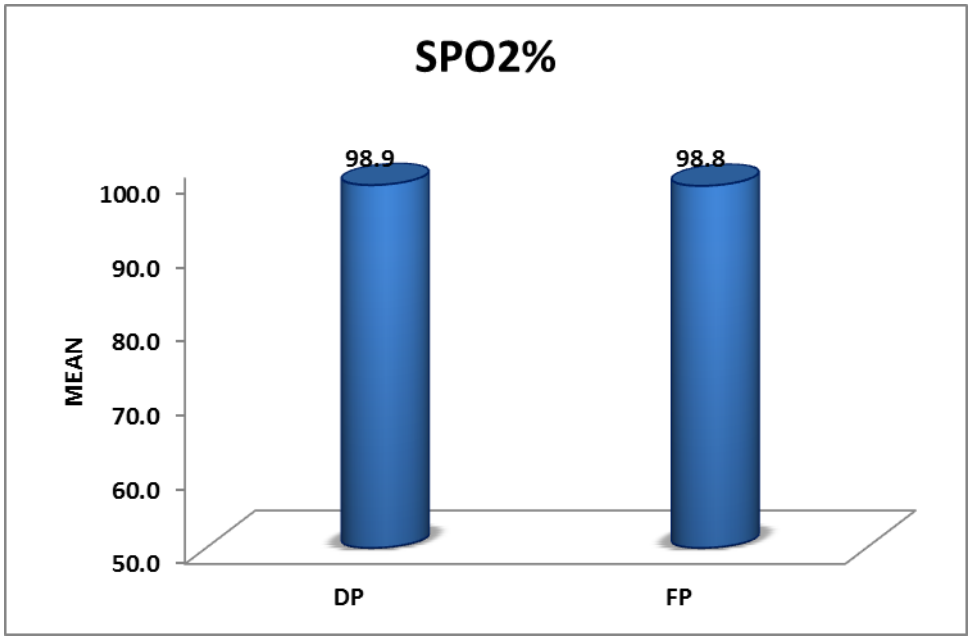


Table 19 and figure 19 compares the oxygen saturation between two groups D-P and F-P.

DISCUSSION

Using general anaesthesia for surgical procedure mandates the procurement of airway . Conventionally the endotracheal tube is used to serve this purpose and endotracheal intubation is considered as gold standard for this. Endotracheal intubation has its own set of complications, such as use of laryngoscope, has added risk of injury to oral structures, vocal cord injury and associated haemodynamic changes. Laryngoscopy and intubation stimulates neural pathway in pharynx by direct laryngoscopy leading to hypertension and tachycardia. This response is hazardous in patients with compromised cardiovascular system especially if this response is left unchecked [35]. To minimize these complications new set of device used, as supraglottic airway devices like classic LMA, intubating LMA, supreme LMA, etc. A relatively newer device, the PLMA, Pro-seal laryngeal mask airway designed. It is an improved version of the Classic LMA and offers some added safety features over the Classic LMA such as providing a better glottic seal at low mucosal pressures, better for positive pressure ventilation with twice the seal pressure than classic LMA and facilities insertion of drain tube to vent out air and regurgitated material from the stomach [23].

It is considered better over tracheal intubation with respect to ease of insertion and haemodynamic responses; it has specific considerations like adequate depth of anaesthesia, mouth opening, Mallampatti grade of patients, jaw relaxation. Induction of general anaesthesia and insertion of PLMA are associated with changes in the cardiovascular parameters due to both the effects of anaesthetic agent administered and adrenergic state of the patients.

Different induction agents like Thiopentone, Propofol, Etomidate and Sevoflurane were tried for smooth and safe insertion of LMA as inhalational and intravenous induction agents [95, 96, 97]. Since time required for LMA insertion is longer with inhalational agents, intra-venous anaesthetics are preferred. In a study conducted by **Mrunalini Parasa** [40] to compare Propofol and Thiopentone sodium for LMA insertion, they found Inj. Propofol to be a better induction agent than Thiopentone with respect to average induction and apnoea time, proportion of jaw relaxation, number of attempts for LMA insertion, limb head movement, coughing, gagging and laryngospasm than Thiopentone.

Propofol has been preferred the most, because of its potential suppressor effects on upper airway reflexes. **Sudeep Krishnappa** [30] assessed loss of motor response to jaw thrust as the clinical indicator of insertion of LMA and found 2.55 mg/kg of Propofol to be coinciding with clinical indicator.

Similarly obtundation of airway reflexes is essential for PLMA insertion and requires sufficient depth of anaesthesia for jaw muscles relaxation and for the device to be tolerated within the hypo-pharynx without undue coughing, gagging, and patient movement. It has been found that Propofol when used alone without premedication, it provides conditions for PLMA insertion far from satisfactory and can cause cardio respiratory depression [39]. Hence in order to avoid use of inadvertent high dose of Propofol for PLMA insertion, various co-induction agents such as Midazolam, Ketamine, low dose Succinylcholine and opioids[13, 71, 37] have been tried to achieve the optimal insertion conditions with minimum hemodynamic response. Although Ketamine as an adjuvant to Propofol may provide good conditions for LMA insertion, it produces sympathetic stimulation leading to increase in myocardial contractility and vascular

resistance, which in turn leads to increased arterial pressure and heart rate. Previous studies [71] have demonstrated marked synergism between Midazolam and Alfentanyl with Propofol on hypnotic and anaesthetic endpoints. Addition of Midazolam was found to significantly reduce the Propofol requirements and provide better jaw relaxation without significant hemodynamic changes.

The hemodynamic response to PLMA insertion expected to manifest in form of rise in HR and BP, that can be attenuated by using adjuvants such as Fentanyl and recently introduced Dexmedetomidine. **C.M. Wong et al** [69] tried different doses of Fentanyl (placebo, 0.5 mcg/kg, 1 mcg/kg, 1.5 mcg/kg and 2.0 mcg/kg) to find out optimal insertion conditions for cLMA with fixed dose Propofol 2.5 mg/kg. They found that Fentanyl in a dose of 0.5 mcg/kg was associated with optimal insertion condition in 50% of patients and 65 % with a standard dose of 1 mcg/kg. In a study conducted by **Akanksha Dutt et al** [31]**,** they assessed two different doses of Fentanyl 1 mcg/kg and 2 mcg/kg. The patients who received Fentanyl 1 mcg/kg remained more haemodynamically stable compared to those receiving Fentanyl 2 mcg/kg. While overall insertion conditions, time required for insertion, number of attempts for insertion and incidence of sore throat were comparable in both the groups. Inj. Fentanyl 2 mcg/kg though caused statistically significant decrease in blood pressure it did not require any intervention, it may be deleterious in patients with poor hemodynamic profiles (e.g., ASA III and IV, patients with history of ischemic heart disease, patients with valvular heart disease/using beta blockers), where a tight control of blood pressures and heart rates would be required, the same fall in pressures could become clinically significant. In such cases Fentanyl 1 mcg/kg would be a better option, as it would provide optimum LMA insertion conditions

along with a more stable hemodynamic profile. **Goyagi et al** [24] have also shown the effect of Fentanyl on Propofol requirement for cLMA insertion, where Fentanyl 2 mcg/kg reduced the Propofol requirement by 60%, but at the expense of prolonged respiratory depression.

Dexmedetomidine is being considered for attenuation of cardiovascular responses, specific and selective α-2 adrenoceptor agonist. Dexmedetomidine has anaesthetic and analgesic effects in addition to its sedative effects appearing at 0.5 - 2 mcg/kg dose intervals. When Dexmedetomidine is used perioperatively , the doses of Propofol for induction and maintenance were significantly reduced [72]. Dexmedetomidine was also shown to diminish airway and circulatory responses during intubation and extubation [16]. **Volkan Hanci et al** [70] in 2010 studied these two drugs Dexmedetomidine and Fentanyl as an adjuvant to Inj. Propofol for intubation. They found that intubation conditions and haemodynamic responses were significantly better with Dexmedetomidine over Fentanyl. Similarly **F Uzumcugil** [15] 2008 have tried these two drugs Dexmedetomidine and Fentanyl to assess insertion condition of LMA and found both are comparable without clinically significant effect on respiratory function at 1 mcg/kg dose given 30 sec before Propofol induction.

Though dexmeditomedine is known to cause hypertension initially after the administration, it was not that significant as the drug administered was over 10min through a syringe pump.

As per study done by **ASB Tan et al** [44] they used Propofol 2.5 mg/kg with Fentanyl to assess LMA insertion condition and found that optimal dose for Fentanyl is 1

mcg/kg, here we are also using the same dose of Fentanyl. Dose of Dexmedetomidine was based on a study conducted by **Sowmya Jayaram et al** [39] for assessing Dexmedetomidine against Fentanyl for LMA insertion. Similarly **Suparto et al** [16] studied Dexmedetomidine and Fentanyl in a dose of 1 mcg/kg each for attenuating haemodynamic responses during laryngoscopy followed by tracheal intubation.

As Propofol does not have any analgesic property, opioids are added which reduces the effective concentration ($EC_{50\ LMA}$) for PLMA insertion of Propofol for various noxious stimuli with minimal respiratory depression. In this study, Dexmedetomidine in D-P group and Fentanyl in the F-P group at the rate of 1mcg/kg/10mins was administered. Premedication was given to the patients in both the groups with minimum dose of 0.02 mg/kg of Midazolam [74] to produce anxiolysis. This sequence of the drug dosing and timings were adjusted to attain the peak onsets at a similar range of time for the insertion of the PLMA.

Based on these studies we have used the same dose of Propofol (2.5 mg/kg) and Dexmedetomidine or Fentanyl (1 mcg/kg) to assess the insertion conditions of PLMA. Many studies have been conducted to assess insertion conditions for cLMA; very few studies have tried PLMA to assess insertion conditions, which is a newer airway device. The cLMA is not a very popular device for positive pressure ventilation, it involves risk of gastric distension, aspiration of gastric contents and inadequate ventilation. PLMA is superior to the Classic LMA for providing positive pressure ventilation and, at a given intra-cuff pressure, provides twice the seal pressure of the cLMA [2]. We are using PLMA in our study to maintain airway in short surgical procedures done under general anaesthesia. Earlier very few studies have done with Dexmedetomidine-Propofol for

assessing LMA insertion conditions; there is limited literature on PLMA, also in our study we did it on wide range of short surgical procedures that may require different levels of analgesia and different duration of anaesthesia so only insertion conditions and insertion haemodynamics were studied.

With reference to demographic data as age, sex, weight and ASA physical status and MPC, the patients selected in our study were statistically comparable in two groups, group D-P and group F-P.

In this trial, the study drug was given by blinded investigator by an infusion pump, either Dexmedetomidine or Fentanyl 1 mcg/kg over 10 min, before giving induction dose Propofol. Propofol was given gradually till central fixation of eyeball up to a maximum dose of up to 2.5 mg/kg. Dose of Inj. Propofol required to achieve the endpoint was recorded. We required mean induction dose of Inj. Propofol in D-P group 94.88 mg and for group F-P 110.7, which is significantly higher in group F-P statistically. Thus we found that dose of Propofol required for PLMA insertion in group F-P is significantly higher than group D-P. This maximum induction dose of 2.5mg/kg of Propofol for PLMA insertion was decided on the basis of previous studies that found this dose to be optimum for jaw relaxation [15, 30, 11]. Reduction in the requirement of induction dose of Propofol below the maximum predecided dose of 2.5mg/kg following both Fentanyl and Dexmedetomidine was noted.

Incremental dose of 0.5mg/kg of Propofol was repeated after each unsuccessful attempt at PLMA insertion. The number of attempts required for PLMA insertion after unsuccessful first time insertion, in this study in group D-P 6 patients required second

attempt while in group F-P 10 patients required second attempt. These findings are in line with study by **Surabhi Lande et al** [17] on insertion of LMA they had 1 patient in group D-P and 5 patients in group F-P who required second attempt for insertion of LMA. Though this is clinically significant, statistical significance is not there. For each second attempt tried an incremental dose of Propofol 0.5 mg/kg was given and patient is allowed to ventilate for 1 minute. Thus this additional dose of Propofol summed and the total dose is calculated, which in group D-P found to be 98.7 mg and in group F-P it was 115.7 mg. This total dose required in group F-P is significantly higher than group D-P. This may either be due to the more number of second attempt required in group F-P or higher induction dose required in group F-P.

Insertion conditions were assessed only after the first attempt of PLMA insertion by the Young's criteria, Limb and head movements, coughing and gagging, laryngospasm and lacrimation. These overall conditions were summed up by modified scheme of Lund and Stovener. These parameters were based on study conducted by **Asha Gupta** [29] and colleagues. In this study 41 patients of F-P group and 34 patients in D-P group had absolutely relaxed jaw.

The overall insertion conditions were excellent by modified scheme of Lund and Stovener[93] in which 41/47 patients from D-P group and 34/47 patients from F-P group had excellent insertion conditions.

Apnoea >30 sec is known to occur after Inj. Fentanyl followed by Propofol induction. In this study 10/47 patients in F-P group and 2/47 patients in D-P group had

apnoea. Similarly **Sowmya Jayaram et al**[39] also found higher incidence of apnoea in F-P group, 22/30 (73.33%) than in group D-P, 12/30 (40%) patients.

In this study the average time required for PLMA insertion for group D-P is 33.1sec while for group F-P is 35.5sec. group F-P required more time compared to group D-P, still the data is statistically not significant.

Bimla Sharma et al [23] showed that the PLMA is a safe airway device in patients undergoing laparoscopic surgery as judged by stable haemodynamics, good oxygenation and adequate ventilation. **Suparto et al** [16] compared Dexmedetomidine and Fentanyl for attenuating sympathetic responses to laryngoscopy and intubation and they found that decrease in heart rate in Dexmedetomidine group is significantly lower than in Fentanyl group (p 0.000). Here in this study baseline heart rate was nearly similar in both groups initially. Heart rate in group D-P and group F-P was gradually decreased after induction but there was transient rise in heart rate at the time of insertion of PLMA then till the time we recorded the values it was less than baseline heart rate. The rise in heart rate is higher in group F-P than in group D-P, and this finding is similar to study conducted by **Surabhi Lande et al** [17].

Systolic blood pressure found to rise in group F-P at the time of insertion of PLMA and 1 min after insertion of PLMA and this difference found to be statistically significant with p value < 0.05. After 1 min of PLMA insertion systolic blood pressure found to be in decreasing trend in both groups though the mean SBP in group F-P was higher than group D-P. These findings are resembling with study conducted by **Surabhi Lande et al** [17].

Diastolic blood pressure in our study had decreasing trend after induction of patient in both groups. Mean DBP in group F-P was higher in group D-P till the end of study though this difference is not statistically significant. There was a rise in diastolic blood pressure after insertion of PLMA in both groups which was falling after 1 min of insertion till the end of study.

Regarding adverse events 4 patients in group F-P had evidence of blood stains around the cuff that was seen after removal of PLMA following the surgical procedure, probably from the oropharyngeal mucosa. There was no evidence of gastric regurgitation in both groups. No trauma to lips, tongue and teeth was found.

It can be said that when PLMA is being used for short surgical procedures, Propofol is a preferred induction agent. The dose of Propofol when used alone is neither satisfactory for smooth insertion of PLMA nor from haemodynamic point of view. Thus the Dexmedetomidine , used in a dose of 1 mcg/kg gives better insertion conditions and haemodynamic stability compared to Fentanyl used in a dose of 1 mcg/kg.

SUMMARY AND CONCLUSION

Using general anaesthesia for surgical procedure, requires the airway to be secured for maintaining the patency of airway and ventilation of the patient for the period of apnoea. Conventionally endotracheal intubation is considered for the same. Over a period of time newer devices have been developed for securing airway, of which supraglottic airway is a major achievement. Newly developed supraglottic airway PLMA, now increasingly used with added advantages for better glottic seal and provision of drain tube insertion.

In a prospective, randomized, comparative, open study 94 ASA class I and II patients undergoing short surgical procedures were allotted in 2 different groups. One receiving Dexmedetomidine (group D-P) and the other receiving Fentanyl (F-P). Study drug was given at a dose of 1 mcg/kg over 10 minutes by an infusion pump . After standard premedication, all the patients were induced with Inj. Propofol up to a dose of 2.5 mg/kg fixed in protocol, till the end point of centralization of pupils was achieved. PLMA was introduced with the help of introducer technique described. Every unsuccessful attempt was topped up with Propofol 0.5 mg/kg, followed by successive attempt. Total of three such attempts were tried and even after that if successful insertion was not achieved, then the case was withdrawn from the study. In this study the induction dose required for successful insertion of PLMA in first attempt in group D-P was and in group F-P it was 94.8mg and in group F-P it was 110.7mg , this higher dose of Propofol required in group F-P is statistically significant. The total dose of Propofol required after considering the successive attempts following unsuccessful first attempt was also significantly higher in group D-P than in group F-P. Insertion conditions of PLMA were

assessed with adequate jaw relaxation, limb and head movements, coughing and gagging, lacrimation and laryngospasm. Overall insertion conditions were assessed by modified scheme of Lund and Stovener on a scale of excellent, moderate, poor and unacceptable. Haemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure and were recorded for the baseline value and then at interval of before induction, after induction, at the time of insertion, 1 min after induction and then at 3 min, 5 min, 10 min, 15 min and 20 min interval. Arterial oxygen saturation was observed throughout the procedure.

To start with the study both the groups, group D-P and group F-P were comparable in demographic and baseline haemodynamic parameters. The insertion conditions assessed were comparable on the basis of findings of Jaw relaxation, coughing and gagging, limb and head movements, laryngospasm and lacrimation, though the coughing and limb movements observed more in group F-P. Jaw relaxation was comparable in both the groups statistically. More number of patients in group F-P had apnoea > 30 sec than in group D-P. We also observed that more number of patients in group F-P required second attempt of PLMA insertion than group D-P. Considering haemodynamic parameters, the heart rate was comparable at baseline, which was comparable till 20 min after PLMA insertion. Though the trend was decreasing in both study groups, mean heart rate was lower in group D-P. Systolic blood pressure was comparable in both groups till the time of induction. SBP after PLMA insertion and 1 min after PLMA insertion was raised in group F-P and this rise is statistically significant.

Arterial oxygen saturation was maintained around 98% in both groups and no episode of desaturation was observed throughout procedure. At the end of procedure 4

patients in group F-P we observed the cuff was blood stained in group F-P, this may be due to interindividual variation between investigators introducing PLMA. There was no evidence of trauma to lip, tongue and teeth; also there was no evidence of gastric contents regurgitation seen on the cuff of PLMA.

From this study we came to conclusion that though the insertion conditions were comparable statistically with the use of either Dexmedetomidine or Fentanyl as an adjuvant with Inj. Propofol (up to 2.5mg/kg) for the use of PLMA in short surgical procedures, Dexmedetomidine (1 mcg/kg) can be used with more favorable overall insertion conditions and less chances of coughing and movements; also lower incidence of apnoea than Fentanyl (1mcg/kg). Use of Dexmedetomidine also reduces the requirement of induction and incremental doses of Inj. Propofol. Attenuation of haemodynamic responses is also better with use of Dexmedetomidine as an adjuvant , compared to use of Fentanyl as an adjuvant. Thus Dexmedetomidine has better potential as a co -induction agent used with Propofol for insertion of PLMA in short surgical procedures in given doses with improved overall insertion conditions and better haemodynamic profile than Fentanyl.

The study results could have been better if the more number of patients were involved in the study or the end point for induction using Propofol was considered as adequate jaw relaxation.

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ANNEXURES

ETHICAL CERTIFICATE

B.L.D.E.UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR – 586103
INSTITUTIONAL ETHICAL COMMITTEE

No/58/2015
20/11/15

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 17/11/2015 *at* 03 pm *scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has accorded Ethical Clearance.*

Title A prospective randomised comparative study of efficacy & saftey of combination of inj. Dexmedetomidine inj-propofol & inj-Fentanyl-inj-propofol for the insertion conditions of proseal LMA"

Name of P.G. Student : Dr Prashanth Vadiger.
Dept of Anaesthesiology

Name of Guide/Co-investigator : Dr. Vidya patil
professor of Anaesthesiology

DR.TEJASWINI VALLABHA
CHAIRMAN
CHAIRMAN
Institutional Ethical Committee
BLDEU's Shri B.M. Patil
Medical Collego,BIJAPUR-586103.

Following documents were placed before E.C. for Scrutinization
1)Copy of Synopsis/Research Project
2)Copy of informed consent form.
3)Any other relevant documents.

PROFORMA

A PROSPECTIVE RANDOMISED COMPARATIVE STUDY OF EFFICACY AND SAFETY OF COMBINATION OF INJ.DEXMEDETOMIDINE–PROPOFOL AND INJ.FENTANYL-PROPOFOL FOR THE INSERTION CONDITIONS OF PROSEAL LARYNGEAL MASK AIRWAY

Serial no: - Group D [Dexmedetomidine + Propofol group] [ ]

Group F [Fentanyl + Propofol group] [ ]

Name:

Age /sex: Weight: kg. Date:

I.P.D no: ward: unit: D.O.A:

Diagnosis:

Proposed procedure:

Mouth opening: MPC class:

ECG: (FOR INDIVIDUALS>40 YRS):

ASA class: I / II / III / IV / V

Premedication:

Inj. Glycopyrrolate 0.004 mg/kg IV. [ ]

Study drug: Dose:

Inj. Midazolam 0.02 mg / kg IV. [ ]

Induction:

Inj. Propofol _____mg/kg

Maintenance:

Intraoperative monitoring:-

Parameters for insertion condition:-

1) Ease of insertion: jaw relaxation according to **Young's criteria**-

Grade I [ ]

Grade II [ ]

Grade III [ ]

Young's criteria-

Absolutely relaxed muscle tone- Grade I

Moderately relaxed muscle tone- Grade II

Poorly relaxed muscle tone- Grade III

2) Coughing gagging

Grade I (nil) [ ]

Grade II (mild) [ ]

Grade III (sever) [ ]

3) Laryngospasm

Grade I (nil) [ ]

Grade II (mild) [ ]

Grade III (sever) [ ]

4) Limb and head movements -

Grade I (nil) [ ]

Grade II (mild) [ ]

Grade III (sever) [ ]

5) Lacrimation

Yes [ ]

No [ ]

6) Overall insertion condition by **modified scheme of Lund and Stovener**-

Excellent [ ]

Good [ ]

Poor [ ]

Unacceptable [ ]

Modified scheme of Lund and Stovener, As-

1.Excellent: No gagging or coughing, no patient movement or laryngospasm

2.Good: mild to moderate gagging, coughing, or patient movement with no laryngospasm

3. Poor: moderate to severe gagging, coughing, or patient movement with no laryngospasm

4. Unacceptable: sever gagging, coughing, or patient movement or laryngospasm

7) Presence of apnoea >30 sec.

Yes [ ]

No [ ]

8) Time required for insertion of Proseal LMA: _____ Minutes.

9) No. of attempts required for insertion of Proseal LMA: 1 / 2 / 3

Haemodynamic parameters:-

Event	HR/ min	SBP	DBP	MBP	SPO2	ECG	RR/ min
Basal reading							
Before induction							
After induction							
After LMA insertion							
1 min after insertion							
3min after insertion							
5 min after insertion							
10 min after insertion							
15 min after insertion							
20 min after insertion							

Adverse effects assessed:

1) Evidence of trauma to –

   Lip [ ]

   Tongue [ ]

   Teeth [ ]

2) Evidence of regurgitation –

   Yes [ ]

   No [ ]

PATIENT INFORMATION SHEET

A PROSPECTIVE RANDOMISED COMPARATIVE STUDY OF EFFICACY AND SAFETY OF COMBINATION OF INJ.DEXMEDETOMIDINE–PROPOFOL AND INJ.FENTANYL-PROPOFOL FOR THE INSERTION CONDITIONS OF PROSEAL LARYNGEAL MASK AIRWAY

Proseal LMA is a device that has been used for general anaesthesia in various surgical procedures to maintain patency of airway. A medicine named Fentanyl can be used as drug for easier and safer insertion of Proseal LMA. It can also be carried out using same dose of a newer drug named Dexmedetomidine. As compared to Fentanyl, no extra harmful effects are seen with it. You are invited to participate in the study that compares these two drugs.

You will not be advised any extra tests or extra stay in operation theater for participating in the study. Surgeries have been performed safely using both the drugs. You will not be given any compensation for participating in the study. Your participation is voluntary and refusal to participate would not affect your treatment. You have a right to withdraw at any point of time without giving any reason. Your reports will be kept confidential.

CONSENT FORM

A PROSPECTIVE RANDOMISED COMPARATIVE STUDY OF EFFICACY AND SAFETY OF COMBINATION OF INJ.DEXMEDETOMIDINE–PROPOFOL AND INJ.FENTANYL-PROPOFOL FOR THE INSERTION CONDITIONS OF PROSEAL LARYNGEAL MASK AIRWAY

I have been explained about this study in the language which I understand. I have been told that my participation in above study is voluntary and I am aware that I can opt out of the study at any time without giving any reason to do so. I am also hereby informed that my refusal to participate in the above study will not affect my treatment by any means.

I agree to participate in the study and cooperate fully and agree to follow the doctor's instructions and recommendation about my case and treatment to the best of my ability.

Doctor's signature	**Witness's signature**	**patient's signature**
Name	**Name**	**Name**
Date	**Date**	**Date**

KEY TO MASTER CHART

1. Jaw relaxation according to **Young's criteria**-

    Absolutely relaxed muscle tone-1

    Moderately relaxed muscle tone-2

    Poorly relaxed muscle tone-3

2. Overall insertion conditions by **Modified scheme of Lund and Stovener**, as-

    1. Excellent: No gagging or coughing, no patient movement or laryngospasm.

    2. Good: mild to moderate gagging, coughing, or patient movement with no laryngospasm

    3. Poor: moderate to severe gagging, coughing, or patient movement with no laryngospasm

    4. Unacceptable: severe gagging, coughing, or patient movement or laryngospasm.

MASTER CHART

MASTER CHART FOR DEXMEDETOMEDINE-PROPOFOL

SR NO	AGE(YR)	SEX(M/F)	ASA	WEIGHT	MPC	DOSE	INDUCTION DOSE OF PROPOFOL	PARAMETERS OF INSERTION						APNOEA >30 SEC	TIME(SEC)	ATTEMPTS	DOSE OF PROPOFOL		HEART RATE (beats per minute)									SYSTOLIC BLOOD PRESSURE (mmHg)									DIASTOLIC BLOOD PRESSURE (mmHg)									MEAN BLOOD PRESSURE (mmHg)									SPO_2	ECG	RR	ADVERSE EVENTS	
	years	male (M) / female (F)		kilogram (kg)		mg/kg	mg	young"s criteria(grade 1/2/3)	coughing, gagging (nil/ mild / sever)	laryngospasm (nil / mild / sever)	limb and head movement (nil / mild /sever)	lacrimation (yes / no)	modified scheme of lund and stovener	YES(Y) / NO (N)			increments (mg)	total (mg)	BASELINE	BEFORE INDUCTION	AFTER INDUCTION	AFTER LMA INSERTION	1MIN AFTER INSERTION	3 MIN AFTER INSERTION	5MIN AFTER INSERTION	10 MIN AFTER INSERTION	15 MIN AFTER INSERTION	20 MIN AFTER INSERTION	BASELINE	BEFORE INDUCTION	AFTER INDUCTION	AFTER LMA INSERTION	1MIN AFTER INSERTION	3 MIN AFTER INSERTION	5 MIN AFTER INSERTION	10 MIN AFTER INSERTION	15 MIN AFTER INSERTION	20 MIN AFTER INSERTION	BASELINE	BEFORE INDUCTION	AFTER INDUCTION	AFTER LMA INSERTION	1 MIN AFTER INSERTION	3MIN AFTER INSERTION	5 MIN AFTER INSERTION	10 MIN AFTER INSERTION	15 MIN AFTER INSERTION	20 MIN AFTER INSERTION	BASELINE	BEFORE INDUCTION	AFTER INDUCTION	AFTER LMA INSERTION	1MIN AFTER LMA INSERTION	3 MIN AFTER INSERTION	5 MIN AFTER INSERTION	10 MIN AFTER INSERTION	15 MIN AFTER INSERTION	20 MIN AFTER INSERTION	%		PER MINUTE	TRAUMA YES (Y) /NO (N)	REGURGITATION YES (Y) / NO(N)
1	30	M	I	58	I	1.5	87	I	N	N	N	N	EXCELLENT	N	15	1	0	87	118	114	120	114	106	100	98	98	96	92	130	114	90	96	94	98	96	100	104	100	80	60	60	64	58	60	62	64	66	64	96.67	78.00	70.00	74.67	70.00	72.67	73.33	76.00	78.67	76.00	99	WNL	24	N	N
2	24	F	I	45	I	1.2	54	I	N	N	N	N	EXCELLENT	N	10	1	0	54	80	88	90	86	82	80	84	78	76	80	104	106	98	108	110	104	100	102	104	104	60	68	60	64	66	68	64	66	66	64	74.67	80.67	72.67	78.67	80.67	80.00	76.00	78.00	78.67	77.33	99	WNL	16	N	N
3	28	M	I	62	I	2	124	I	N	N	M	N	GOOD	N	60	2	20	144	98	96	100	102	100	96	96	92	90	90	118	124	106	104	110	108	112	106	108	104	72	76	66	68	68	72	72	66	60	58	87.33	92.00	79.33	80.00	82.00	84.00	85.33	79.33	76.00	73.33	98	WNL	14	N	N
4	24	F	I	48	I	1.2	58	I	N	N	N	N	EXCELLENT	N	15	1	0	58	98	94	82	92	88	82	81	76	72	72	102	105	94	106	102	104	92	96	100	102	58	62	65	76	60	62	60	64	60	62	72.67	76.33	74.67	86.00	74.00	76.00	70.67	74.67	73.33	75.33	99	WNL	18	N	N
5	25	M	II	62	I	1.3	80	I	N	N	N	N	EXCELLENT	N	18	1	0	80	102	96	104	102	100	100	96	94	94	92	100	100	104	110	102	96	98	92	96	98	64	66	62	70	66	68	66	58	60	62	76.00	77.33	76.00	83.33	78.00	77.33	76.67	69.33	72.00	74.00	99	WNL	16	N	N
6	45	M	I	60	II	1.5	90	II	N	N	N	N	EXCELLENT	N	75	1	0	90	92	90	98	106	104	100	98	96	98	94	108	110	100	98	102	100	108	106	110	104	68	70	62	60	64	66	72	72	72	68	81.33	83.33	74.67	72.67	76.67	77.33	84.00	83.33	84.67	80.00	99	WNL	14	N	N
7	43	F	I	60	II	1.6	96	I	N	N	N	N	EXCELLENT	N	30	1	0	96	86	80	72	76	74	76	74	72	68	66	118	120	130	128	130	116	118	114	118	114	88	84	84	86	78	80	84	80	72	70	98.00	96.00	99.33	100.00	95.33	92.00	95.33	91.33	87.33	84.67	100	WNL	16	N	N
8	53	F	I	50	I	1.4	70	I	N	N	N	N	EXCELLENT	N	20	1	0	70	114	84	82	80	80	78	76	70	68	66	154	132	114	120	116	108	106	112	114	116	94	84	72	88	80	82	80	84	82	84	114.00	100.00	86.00	98.67	92.00	90.67	88.67	93.33	92.67	94.67	99	WNL	18	N	N
9	20	F	I	45	I	1.2	52	I	N	N	N	N	EXCELLENT	N	15	1	0	52	110	120	134	126	128	124	126	122	115	110	134	153	132	138	136	126	118	116	118	120	98	112	100	102	100	96	84	82	78	80	82.00	125.67	110.67	114.00	112.00	106.00	95.33	93.33	91.33	93.33	98	WNL	14	N	N
10	19	F	I	48	I	1.3	58	I	N	N	N	N	EXCELLENT	N	12	1	0	58	78	80	92	100	104	100	100	98	86	82	100	118	114	116	108	104	106	102	106	112	68	76	74	86	80	82	84	80	84	86	78.67	90.00	87.33	96.00	89.33	89.33	91.33	87.33	91.33	94.67	99	WNL	14	N	N
11	20	M	I	70	I	1.8	136	I	N	N	N	N	EXCELLENT	N	40	1	0	136	64	70	72	76	80	72	76	78	76	72	140	128	118	114	108	106	100	110	114	112	90	76	74	74	72	74	68	70	70	70	106.67	93.00	88.67	87.33	84.00	84.67	78.67	83.33	84.67	84.00	99	WNL	14	N	N
12	24	F	I	50	I	1.5	68	I	N	N	N	N	EXCELLENT	N	18	1	0	68	72	74	70	70	68	64	66	60	58	60	136	130	112	108	104	100	98	94	110	114	94	84	76	68	70	72	66	62	64	70	108.00	99.33	88.00	81.33	81.33	81.33	76.67	72.67	79.33	84.67	98	WNL	14	N	N
13	20	F	I	52	II	1.5	78	I	N	N	N	Y	EXCELLENT	N	30	1	0	78	87	94	84	80	74	70	68	60	72	70	108	116	118	110	106	106	104	100	104	104	78	78	76	74	72	74	72	68	70	68	88.00	90.67	90.00	86.00	83.33	84.67	82.67	78.67	81.33	80.00	98	WNL	14	N	N
14	26	F	II	50	II	1.4	70	I	N	N	N	N	EXCELLENT	N	12	1	0	70	68	66	56	80	76	68	58	56	62	58	136	127	114	124	122	106	112	120	126	122	86	76	61	101	98	72	74	84	86	82	102.67	93.00	78.67	108.67	106.00	83.33	86.67	96.00	99.33	95.33	99	WNL	16	N	N
15	42	F	II	62	II	2	124	II	N	M	N	N	GOOD	Y	70	2	50	174	90	86	88	86	84	88	94	96	82	80	114	96	116	114	108	100	98	98	100	102	74	62	76	80	78	72	68	68	70	72	87.33	73.33	89.33	91.33	88.00	81.33	78.00	78.00	80.00	82.00	99	WNL	18	N	N
16	18	M	I	64	I	1.6	102	I	N	N	N	N	EXCELLENT	N	25	1	0	102	94	100	104	100	94	90	92	86	84	88	100	110	98	118	110	110	104	116	114	114	58	64	56	68	64	64	60	70	70	68	72.00	79.33	70.00	84.67	79.33	79.33	74.67	85.33	84.67	83.33	99	WNL	14	N	N
17	26	F	I	52	I	1.4	72.8	I	N	N	N	N	EXCELLENT	N	15	1	0	72.8	96	98	108	106	100	90	86	86	84	80	102	102	102	100	98	98	100	96	98	96	60	62	64	60	58	60	62	58	60	60	74.00	75.33	76.67	73.33	71.33	72.67	74.67	70.67	72.67	72.00	98	WNL	16	N	N
18	32	F	I	46	I	1.2	55	I	N	N	N	N	EXCELLENT	N	15	1	0	55	94	100	110	116	108	94	98	94	90	94	94	90	92	88	88	94	92	96	98	98	62	60	66	60	60	58	58	56	58	56	72.67	70.00	74.67	69.33	69.33	70.00	69.33	69.33	71.33	70.00	100	WNL	14	N	N
19	28	F	I	58	I	1.8	105	I	N	N	N	N	EXCELLENT	N	35	1	0	105	86	94	104	108	98	88	82	80	82	82	112	114	102	110	104	106	102	104	106	104	76	80	70	74	74	72	70	70	72	68	88.00	91.33	80.67	86.00	84.00	83.33	80.67	81.33	83.33	80.00	98	WNL	14	N	N
20	36	M	II	72	II	1.8	134	II	N	N	N	N	EXCELLENT	N	40	1	0	134	92	100	112	110	102	92	90	88	88	84	120	124	110	108	106	110	108	102	108	104	76	84	78	74	72	68	70	68	72	70	90.67	97.33	88.67	85.33	83.33	82.00	82.67	79.33	84.00	81.33	99	WNL	16	N	N
21	42	M	I	70	I	1.8	126	I	N	N	N	N	EXCELLENT	N	50	1	0	126	78	84	100	98	90	84	84	86	86	82	128	122	114	120	116	122	120	114	116	116	86	82	82	86	86	84	82	82	84	84	100.00	95.33	92.67	97.33	96.00	96.67	94.67	92.67	94.67	94.67	99	WNL	14	N	N
22	44	M	I	72	II	2.1	150	II	N	N	N	N	EXCELLENT	N	80	2	20	170	100	104	114	116	106	96	92	88	86	86	142	136	122	126	122	130	122	114	110	108	88	84	78	76	84	82	82	80	76	76	106.00	101.33	92.67	92.67	96.67	98.00	95.33	91.33	87.33	86.67	99	WNL	14	N	N
23	36	F	II	66	II	2	132	I	N	N	N	N	EXCELLENT	N	60	1	0	132	94	96	106	100	92	82	80	80	84	82	132	128	110	106	106	112	108	108	106	110	84	80	80	78	78	80	78	74	74	76	100.00	96.00	90.00	87.33	87.33	90.67	88.00	85.33	84.67	87.33	99	WNL	16	N	N
24	24	F	I	60	I	1.4	84	I	N	N	N	N	EXCELLENT	N	20	1	0	84	90	94	102	98	90	86	82	80	80	76	104	102	96	96	94	98	96	98	100	102	74	76	72	72	68	72	70	70	70	72	84.00	84.67	80.00	80.00	76.67	80.67	78.67	79.33	80.00	82.00	100	WNL	14	N	N
25	30	M	I	70	I	1.2	84	I	N	N	N	N	EXCELLENT	N	15	1	0	84	84	90	94	96	88	82	78	78	74	76	114	118	104	110	106	104	106	102	104	106	78	80	68	72	70	72	74	72	74	76	90.00	92.67	80.00	84.67	82.00	82.67	84.67	82.00	84.00	86.00	99	WNL	14	N	N
26	28	F	II	64	I	1.5	96	II	N	N	M	N	GOOD	N	25	1	0	96	98	104	110	118	102	92	88	90	92	88	108	112	100	98	96	100	102	104	106	104	72	80	76	76	74	76	76	78	76	78	84.00	90.67	84.00	83.33	81.33	84.00	84.67	85.33	87.33	85.33	99	WNL	18	N	N
27	32	M	I	68	II	1.7	115	I	N	N	N	N	EXCELLENT	N	30	1	0	115	96	106	108	112	104	98	94	94	94	90	124	120	114	120	120	118	118	114	116	114	84	82	82	86	86	88	86	82	84	82	97.33	94.67	92.67	97.33	97.33	98.00	96.67	92.67	94.67	92.67	99	WNL	14	N	N
28	35	M	I	58	I	1.5	87	I	N	N	N	N	EXCELLENT	N	20	1	0	87	92	100	104	116	108	100	98	96	92	94	100	104	102	102	100	100	96	98	102	102	78	80	80	84	82	84	80	80	80	78	85.33	88.00	87.33	90.00	88.00	89.33	85.33	86.00	87.33	86.00	99	WNL	16	N	N
29	27	M	I	61	I	1.5	90	I	N	N	N	N	EXCELLENT	N	25	1	0	90	88	94	98	104	94	88	82	84	80	80	118	114	108	110	108	116	112	108	110	112	78	76	70	68	70	72	68	66	68	70	91.33	88.67	82.67	82.00	82.67	86.67	82.67	80.00	82.00	84.00	100	WNL	14	N	N
30	25	F	I	52	I	1.3	68	I	N	N	N	N	EXCELLENT	N	15	1	0	68	80	90	92	98	84	82	76	78	76	78	120	126	114	116	110	110	110	108	112	110	86	88	86	82	84	82	82	80	82	80	97.33	100.67	95.33	93.33	92.67	91.33	91.33	89.33	92.00	90.00	99	WNL	14	N	N
31	28	F	II	64	I	1.5	96	II	N	N	M	N	GOOD	N	25	1	0	96	98	104	110	118	102	92	88	90	92	88	108	112	100	98	96	100	102	104	106	104	72	80	76	76	74	76	76	78	76	78	84.00	90.67	84.00	83.33	81.33	84.00	84.67	85.33	87.33	85.33	99	WNL	18	N	N
32	36	F	II	66	II	2	132	I	N	N	N	N	EXCELLENT	N	60	1	0	132	94	96	106	100	92	82	80	80	84	82	132	128	110	106	106	112	108	108	106	110	84	80	80	78	78	80	78	74	74	76	100.00	96.00	90.00	87.33	87.33	90.67	88.00	85.33	84.67	87.33	99	WNL	16	N	N
33	36	M	II	72	II	1.8	134	II	N	N	N	N	EXCELLENT	N	40	1	0	134	92	100	112	110	102	92	90	88	88	84	120	124	110	108	106	110	108	102	108	104	76	84	78	74	72	68	70	68	72	70	90.67	97.33	88.67	85.33	83.33	82.00	82.67	79.33	84.00	81.33	99	WNL	16	N	N
34	32	F	I	46	I	1.2	55	I	N	N	N	N	EXCELLENT	N	15	1	0	55	94	100	110	116	108	94	98	94	90	94	94	90	92	88	88	94	92	96	98	98	62	60	66	60	60	58	58	56	58	56	72.67	70.00	74.67	69.33	69.33	70.00	69.33	69.33	71.33	70.00	100	WNL	14	N	N
35	18	M	I	64	I	1.6	102	I	N	N	N	N	EXCELLENT	N	25	1	0	102	94	100	104	100	94	90	92	86	84	88	100	110	98	118	110	110	104	116	114	114	58	64	56	68	64	64	60	70	70	68	72.00	79.33	70.00	84.67	79.33	79.33	74.67	85.33	84.67	83.33	99	WNL	14	N	N
36	20	F	I	52	II	1.5	78	I	N	N	N	Y	EXCELLENT	N	30	1	0	78	87	94	84	80	74	70	68	60	72	70	108	116	118	110	106	106	104	100	104	104	78	78	76	74	72	74	72	68	70	68	88.00	90.67	90.00	86.00	83.33	84.67	82.67	78.67	81.33	80.00	98	WNL	14	N	N
37	20	M	I	70	I	1.8	136	I	N	N	N	N	EXCELLENT	N	40	1	0	136	64	70	72	76	80	72	76	78	76	72	140	128	118	114	108	106	100	110	114	112	90	76	74	74	72	74	68	70	70	70	106.67	93.00	88.67	87.33	84.00	84.67	78.67	83.33	84.67	84.00	99	WNL	14	N	N
38	42	F	II	62	II	2	124	II	N	M	N	N	GOOD	Y	70	2	50	174	90	86	88	86	84	88	94	96	82	80	114	96	116	114	108	100	98	98	100	102	74	62	76	80	78	72	68	68	70	72	87.33	73.33	89.33	91.33	88.00	81.33	78.00	78.00	80.00	82.00	99	WNL	18	N	N
39	20	F	I	45	I	1.2	52	I	N	N	N	N	EXCELLENT	N	15	1	0	52	110	120	134	126	128	124	126	122	115	110	134	153	132	138	136	126	118	116	118	120	98	112	100	102	100	96	84	82	78	80	82.00	125.67	110.67	114.00	112.00	106.00	95.33	93.33	91.33	93.33	98	WNL	14	N	N
40	43	F	I	60	II	1.6	96	I	N	N	N	N	EXCELLENT	N	30	1	0	96	86	80	72	76	74	76	74	72	68	66	118	120	130	128	130	116	118	114	118	114	88	84	84	86	78	80	84	80	72	70	98.00	96.00	99.33	100.00	95.33	92.00	95.33	91.33	87.33	84.67	100	WNL	16	N	N
41	25	M	II	62	I	1.3	80	I	N	N	N	N	EXCELLENT	N	18	1	0	80	102	96	104	102	100	100	96	94	94	92	100	100	104	110	102	96	98	92	96	98	64	66	62	70	66	68	66	58	60	62	76.00	77.33	76.00	83.33	78.00	77.33	76.67	69.33	72.00	74.00	99	WNL	16	N	N
42	45	M	I	60	II	1.5	90	II	N	N	N	N	EXCELLENT	N	75	1	0	90	92	90	98	106	104	100	98	96	98	94	108	110	100	98	102	100	108	106	110	104	68	70	62	60	64	66	72	72	72	68	81.33	83.33	74.67	72.67	76.67	77.33	84.00	83.33	84.67	80.00	99	WNL	14	N	N
43	44	M	I	72	II	2.1	150	II	N	N	N	N	EXCELLENT	N	80	2	20	170	100	104	114	116	106	96	92	88	86	86	142	136	122	126	122	130	122	114	110	108	88	84	78	76	84	82	82	80	76	76	106.00	101.33	92.67	92.67	96.67	98.00	95.33	91.33	87.33	86.67	99	WNL	14	N	N
44	26	F	II	50	II	1.4	70	I	N	N	N	N	EXCELLENT	N	12	1	0	70	68	66	56	80	76	68	58	56	62	58	136	127	114	124	122	106	112	120	126	122	86	76	61	101	98	72	74	84	86	82	102.67	93.00	78.67	108.67	106.00	83.33	86.67	96.00	99.33	95.33	99	WNL	16	N	N
45	30	M	I	58	I	1.5	87	I	N	N	N	N	EXCELLENT	N	15	1	0	87	118	114	120	114	106	100	98	98	96	92	130	114	90	96	94	98	96	100	104	100	80	60	60	64	58	60	62	64	66	64	96.67	78.00	70.00	74.67	70.00	72.67	73.33	76.00	78.67	76.00	99	WNL	24	N	N
46	28	M	I	62	I	2	124	I	N	N	M	N	GOOD	N	60	2	20	144	98	96	100	102	100	96	96	92	90	90	118	124	106	104	110	108	112	106	108	104	72	76	66	68	68	72	72	66	60	58	87.33	92.00	79.33	80.00	82.00	84.00	85.33	79.33	76.00	73.33	98	WNL	14	N	N
47	28	F	I	58	I	1.8	105	I	N	N	N	N	EXCELLENT	N	35	1	0	105	86	94	104	108	98	88	82	80	82	82	112	114	102	110	104	106	102	104	106	104	76	80	70	74	74	72	70	70	72	68	88.00	91.33	80.67	86.00	84.00	83.33	80.67	81.33	83.33	80.00	98	WNL	14	N	N

MASTER CHART

MASTER CHART FOR FENTANYL-PROPOFOL

SR NO	AGE(YR)	SEX(M/F)	ASA	WEIGHT	MPC	DOSE	INDUCTION DOSE OF PROPOFOL	PARAMETERS OF INSERTION						APNOEA > 30 SEC	TIME(SEC)	ATTEMPTS	DOSE OF PROPOFOL		HEART RATE (beats per minute)									SYSTOLIC BLOOD PRESSURE (mmHg)									DIASTOLIC BLOOD PRESSURE (mmHg)									MEAN BLOOD PRESSURE (mmHg)									SPO_2	ECG	RR	ADVERSE EVENTS	
	years	male (M) / female (F)		kilogram (kg)		mg/kg	mg	young's criteria(grade 1/2/3)	coughing, gagging (nil/ mild / sever)	laryngospasm (nil / mild / sever)	limb and head movement (nil / mild /sever	lacrimation (yes / no)	modified scheme of lund and stovener	YES(Y) / NO (N)	increments (mg)	total (mg)		BEFORE INDUCTION	AFTER LMA INSERTION	1MIN AFTER INSERTION	3 MIN AFTER INSERTION	5MIN AFTER INSERTION	10 MIN AFTER INSERTION	15 MIN AFTER INSERTION	20 MIN AFTER INSERTION	BASELINE	BEFORE INDUCTION	AFTER INDUCTION	AFTER LMA INSERTION	1MIN AFTER INSERTION	3 MIN AFTER INSERTION	5 MIN AFTER INSERTION	10 MIN AFTER INSERTION	15 MIN AFTER INSERTION	20 MIN AFTER INSERTION	BASELINE	BEFORE INDUCTION	AFTER INDUCTION	AFTER LMA INSERTION	1 MIN AFTER INSERTION	3MIN AFTER INSERTION	5 MIN AFTER INSERTION	10 MIN AFTER INSERTION	15 MIN AFTER INSERTION	20 MIN AFTER INSERTION	BASELINE	BEFORE INDUCTION	AFTER INDUCTION	AFTER LMA INSERTION	1MIN AFTER LMA INSERTION	3 MIN AFTER INSERTION	5 MIN AFTER INSERTION	10 MIN AFTER INSERTION	15 MIN AFTER INSERTION	20 MIN AFTER INSERTION	%		per minute	TRAUMA YES (Y) /NO (N)	REGURGITATION YES (Y) / NO(N)
1	30	F	I	52	I	1.6	84	I	N	N	N	N	EXCELLENT	N	25	2	20	104	94	100	104	106	102	100	102	90	88	84	118	112	114	124	122	114	108	112	106	104	64	68	66	76	70	66	64	62	60	62	82.00	82.67	82.00	92.00	87.33	82.00	78.67	78.67	75.33	76.00	99	WNL	20	N	N
2	31	F	I	56	II	2.5	140	I	M	N	M	N	GOOD	Y	20	1	0	140	80	82	76	74	71	76	82	82	80	78	98	100	140	146	144	136	138	134	128	130	70	72	100	102	90	84	84	82	80	76	79.33	81.33	113.33	116.67	108.00	101.33	102.00	99.33	96.00	94.00	98	WNL	16	Y	N
3	28	M	I	63	I	1.8	113.4	I	N	N	N	N	EXCELLENT	N	20	1	0	113.4	98	102	106	110	100	96	96	92	90	86	118	124	106	114	112	108	112	106	110	108	72	76	66	70	68	70	68	62	68	66	87.33	92.00	79.33	84.67	82.67	82.67	82.67	76.67	82.00	80.00	98	WNL	14	N	N
4	32	M	I	68	I	2	136	I	N	N	M	N	GOOD	N	35	1	0	136	96	94	82	92	88	82	80	76	72	72	102	105	94	106	106	104	92	96	98	102	68	62	65	76	60	60	56	58	60	62	79.33	76.33	74.67	86.00	75.33	74.67	68.00	70.67	72.67	75.33	99	WNL	18	N	N
5	33	F	II	60	II	2.2	132	II	N	N	M	N	GOOD	Y	90	2	30	162	100	106	110	118	110	106	100	96	94	90	122	124	120	128	126	120	110	112	114	112	76	84	84	88	86	86	82	82	80	80	91.33	97.33	96.00	101.33	99.33	97.33	91.33	92.00	91.33	90.67	99	WNL	20	N	N
6	26	F	I	50	I	1.5	75	I	N	N	N	N	EXCELLENT	N	20	1	0	75	88	92	100	108	100	96	90	88	90	86	118	120	116	122	120	114	116	112	118	110	78	86	88	86	84	84	80	78	78	76	91.33	97.33	97.33	98.00	96.00	94.00	92.00	89.33	91.33	87.33	99	WNL	16	N	N
7	32	F	II	48	I	1.8	86	I	N	N	N	N	EXCELLENT	N	35	1	0	86	114	116	120	124	112	106	102	98	94	92	130	126	124	130	128	118	112	110	112	110	90	94	88	90	84	86	82	80	80	78	103.33	104.67	100.00	103.33	98.67	96.67	92.00	90.00	90.67	88.67	100	WNL	14	N	N
8	30	M	I	59	II	1.8	122	I	N	N	N	N	EXCELLENT	Y	30	1	0	122	76	78	88	98	94	88	74	76	74	72	132	130	122	126	122	114	108	112	116	120	88	88	84	82	80	82	76	76	78	76	102.67	102.00	96.67	96.67	94.00	92.67	86.67	88.00	90.67	90.67	99	WNL	16	N	N
9	28	M	I	63	I	1.9	130	I	N	N	N	M	GOOD	N	70	2	20	150	84	88	96	104	100	92	84	86	86	82	112	110	114	118	116	110	116	108	108	114	74	76	76	74	78	76	78	74	72	72	86.67	87.33	88.67	88.67	90.67	87.33	90.67	85.33	84.00	86.00	98	WNL	14	N	N
10	26	F	I	58	I	1.6	90	I	N	N	N	N	EXCELLENT	N	20	1	0	90	90	96	98	106	98	90	80	84	82	78	106	110	106	110	108	108	110	106	108	104	68	66	68	72	74	72	74	70	72	70	80.67	80.67	80.67	84.67	85.33	84.00	86.00	82.00	84.00	81.33	99	WNL	14	N	N
11	26	M	I	66	I	1.8	135	I	N	N	N	N	EXCELLENT	N	25	1	0	135	84	86	92	100	96	88	82	80	78	76	114	118	114	118	116	112	110	102	104	100	66	70	68	70	74	74	76	72	68	68	82.00	86.00	83.33	86.00	88.00	86.67	87.33	82.00	80.00	78.67	99	WNL	16	N	N
12	35	F	I	64	I	2	128	I	N	N	N	N	EXCELLENT	N	30	1	0	128	92	94	98	104	102	92	88	88	86	84	124	122	120	124	122	116	120	118	116	114	86	86	86	88	90	86	86	84	82	84	98.67	98.00	97.33	100.00	100.67	96.00	97.33	95.33	93.33	94.00	98	WNL	16	N	N
13	28	F	I	50	I	1.6	80	I	N	N	N	N	EXCELLENT	N	20	1	0	80	80	84	92	98	92	86	80	84	82	80	126	120	112	118	114	106	108	106	112	116	88	76	72	74	78	80	76	76	78	74	100.67	90.67	85.33	88.67	90.00	88.67	86.67	86.00	89.33	88.00	98	WNL	18	N	N
14	32	F	I	55	II	2.5	137	II	M	N	M	N	GOOD	Y	65	2	25	162	94	96	100	110	104	94	90	92	88	88	138	136	132	136	126	118	110	112	108	108	92	94	90	92	88	88	84	84	86	84	107.33	108.00	104.00	106.67	100.67	98.00	92.67	93.33	93.33	92.00	97	WNL	20	Y	N
15	38	M	II	65	I	2	130	I	N	N	N	N	EXCELLENT	Y	30	1	0	130	76	82	90	98	96	88	78	80	76	74	106	104	100	104	104	100	104	102	106	102	66	62	58	60	64	64	66	64	66	66	79.33	76.00	72.00	74.67	77.33	76.00	78.67	76.67	80.67	78.00	99	WNL	16	N	N
16	26	F	I	50	I	1.5	75	I	N	N	N	N	EXCELLENT	N	20	1	0	75	82	86	92	96	92	86	80	82	84	82	124	126	118	122	118	108	110	114	110	108	68	70	72	70	74	72	72	74	76	74	86.67	88.67	87.33	87.33	88.67	84.00	84.67	87.33	87.33	85.33	99	WNL	16	N	N
17	30	M	I	65	I	1.8	118	I	N	N	N	N	EXCELLENT	N	25	1	0	118	102	108	112	116	108	100	92	90	88	86	114	110	104	108	106	102	106	110	106	106	70	70	66	68	68	68	66	64	66	64	84.67	83.33	78.67	81.33	80.67	79.33	79.33	79.33	79.33	78.00	98	WNL	14	N	N
18	32	M	II	64	I	2.2	145	I	N	N	M	N	GOOD	Y	30	1	0	145	82	86	94	100	94	88	82	84	84	80	130	124	114	116	112	104	110	106	104	102	88	76	76	80	78	78	74	72	74	70	102.00	92.00	88.67	92.00	89.33	86.67	86.00	83.33	84.00	80.67	100	WNL	16	N	N
19	34	F	I	58	I	1.8	105	I	N	N	N	N	EXCELLENT	N	30	1	0	105	80	88	94	98	94	84	78	80	76	72	110	108	100	104	102	102	104	102	100	100	84	82	78	76	76	78	74	72	68	70	92.67	90.67	85.33	85.33	84.67	86.00	84.00	82.00	78.67	80.00	98	WNL	14	N	N
20	30	F	I	45	I	1.5	68	I	N	N	N	N	EXCELLENT	N	25	1	0	68	84	92	96	102	96	86	80	82	80	78	116	118	110	114	112	104	100	98	100	98	78	84	84	82	80	80	74	72	68	70	90.67	95.33	92.67	92.67	90.67	88.00	82.67	80.67	78.67	79.33	99	WNL	16	N	N
21	32	M	I	64	I	2	128	I	N	N	N	N	EXCELLENT	N	40	1	0	128	78	84	90	94	90	82	78	80	78	78	110	108	102	108	106	102	100	98	104	106	66	68	64	68	70	72	68	70	70	68	80.67	81.33	76.67	81.33	82.00	82.00	78.67	79.33	81.33	80.67	99	WNL	16	N	N
22	27	F	I	50	I	1.8	90	I	N	N	N	N	EXCELLENT	N	30	1	0	90	86	92	98	104	94	88	84	84	82	80	108	112	108	112	108	104	108	102	106	102	58	60	62	66	68	68	70	70	68	66	74.67	77.33	77.33	81.33	81.33	80.00	82.67	80.67	80.67	78.00	99	WNL	14	N	N
23	30	M	I	59	I	1.7	110	I	N	N	N	N	EXCELLENT	N	25	1	0	110	94	98	102	110	100	92	92	90	88	84	114	120	108	114	106	108	112	114	116	112	86	90	82	84	86	82	82	84	80	80	95.33	100.00	90.67	94.00	92.67	90.67	92.00	94.00	92.00	90.67	99	WNL	14	N	N
24	34	F	II	62	II	2	125	I	M	N	M	N	GOOD	N	80	2	15	140	100	104	110	116	104	92	88	90	86	84	126	126	116	120	116	110	106	110	118	114	90	90	84	84	82	84	82	80	78	78	102.00	102.00	94.67	96.00	93.33	92.67	90.00	90.00	91.33	90.00	100	WNL	16	N	N
25	31	F	I	50	I	1.8	90	I	N	N	N	N	EXCELLENT	N	30	1	0	90	94	98	104	106	98	90	86	84	80	78	106	104	100	104	102	100	102	100	106	108	72	70	66	68	70	70	72	68	70	72	83.33	81.33	77.33	80.00	80.67	80.00	82.00	78.67	82.00	84.00	99	WNL	16	N	N
26	27	M	I	55	I	1.6	105	I	N	N	N	N	EXCELLENT	N	25	1	0	105	108	112	116	120	108	100	98	94	92	90	122	120	114	118	114	110	110	112	118	120	74	76	78	76	78	76	80	80	78	74	90.00	90.67	90.00	90.00	90.00	87.33	90.00	90.67	91.33	89.33	99	WNL	18	N	N
27	32	F	I	50	I	1.5	75	I	N	N	N	N	EXCELLENT	N	30	1	0	75	96	100	104	108	100	92	88	90	88	84	104	106	102	106	102	100	100	104	110	116	64	66	62	64	66	68	68	70	68	72	77.33	79.33	75.33	78.00	78.00	78.67	78.67	81.33	82.00	86.67	99	WNL	14	N	N
28	25	M	I	64	I	2	145	I	N	N	N	N	EXCELLENT	N	25	1	0	145	98	98	104	104	96	84	80	82	80	78	98	100	96	100	100	98	102	100	106	112	56	60	60	62	60	58	58	62	66	68	70.00	73.33	72.00	74.67	73.33	71.33	72.67	74.67	79.33	82.67	99	WNL	14	N	N
29	38	F	I	58	I	1.8	105	I	N	N	N	N	EXCELLENT	N	25	1	0	105	88	86	94	92	86	78	80	78	74	74	110	114	110	114	108	104	100	106	110	108	76	78	76	76	78	80	80	78	82	80	87.33	90.00	87.33	88.67	88.00	88.00	86.67	87.33	91.33	89.33	100	WNL	14	N	N
30	31	F	I	60	I	2.2	132	I	N	N	N	N	EXCELLENT	Y	75	2	35	167	106	110	116	118	104	94	96	94	94	90	128	132	126	130	122	118	110	108	112	106	90	94	90	92	92	86	88	88	84	82	102.67	106.67	102.00	104.67	102.00	96.67	95.33	94.67	93.33	90.00	99	WNL	16	N	N
31	31	F	I	50	I	1.8	90	I	N	N	N	N	EXCELLENT	N	30	1	0	90	94	98	104	106	98	90	86	84	80	78	106	104	100	104	102	100	102	100	106	108	72	70	66	68	70	70	72	68	70	72	83.33	81.33	77.33	80.00	80.67	80.00	82.00	78.67	82.00	84.00	99	WNL	16	N	N
32	25	M	I	64	I	2	145	I	N	N	N	N	EXCELLENT	N	25	1	0	145	98	98	104	104	96	84	80	82	80	78	98	100	96	100	100	98	102	100	106	112	56	60	60	62	60	58	58	62	66	68	70.00	73.33	72.00	74.67	73.33	71.33	72.67	74.67	79.33	82.67	99	WNL	14	N	N
33	30	M	I	59	I	1.7	110	I	N	N	N	N	EXCELLENT	N	25	1	0	110	94	98	102	110	100	92	92	90	88	84	114	120	108	114	106	108	112	114	116	112	86	90	82	84	86	82	82	84	80	80	95.33	100.00	90.67	94.00	92.67	90.67	92.00	94.00	92.00	90.67	99	WNL	14	N	N
34	33	F	II	60	II	2.2	132	II	N	N	M	N	GOOD	Y	90	2	30	162	100	106	110	118	110	106	100	96	94	90	122	124	120	128	126	120	110	112	114	112	76	84	84	88	86	86	82	82	80	80	91.33	97.33	96.00	101.33	99.33	97.33	91.33	92.00	91.33	90.67	99	WNL	20	N	N
35	30	F	I	45	I	1.5	68	I	N	N	N	N	EXCELLENT	N	25	1	0	68	84	92	96	102	96	86	80	82	80	78	116	118	110	114	112	104	100	98	100	98	78	84	84	82	80	80	74	72	68	70	90.67	95.33	92.67	92.67	90.67	88.00	82.67	80.67	78.67	79.33	99	WNL	16	N	N
36	34	F	II	62	II	2	125	I	M	N	M	N	GOOD	N	80	2	15	140	100	104	110	116	104	92	88	90	86	84	126	126	116	120	116	110	106	110	118	114	90	90	84	84	82	84	82	80	78	78	102.00	102.00	94.67	96.00	93.33	92.67	90.00	90.00	91.33	90.00	100	WNL	16	N	N
37	31	F	I	56	II	2.5	140	I	M	N	M	N	GOOD	Y	20	1	0	140	80	82	76	74	71	76	82	82	80	78	98	100	140	146	144	136	138	134	128	130	70	72	100	102	90	84	84	82	80	76	79.33	81.33	113.33	116.67	108.00	101.33	102.00	99.33	96.00	94.00	98	WNL	16	Y	N
38	36	F	I	50	I	1.5	75	I	N	N	N	N	EXCELLENT	N	20	1	0	75	82	86	92	96	92	86	80	82	84	82	124	126	118	122	118	108	110	114	110	108	68	70	72	70	74	72	72	74	76	74	86.67	88.67	87.33	87.33	88.67	84.00	84.67	87.33	87.33	85.33	99	WNL	16	N	N
39	28	F	I	50	I	1.6	80	I	N	N	N	N	EXCELLENT	N	20	1	0	80	80	84	92	98	92	86	80	84	82	80	126	120	112	118	114	106	108	106	112	116	88	76	72	74	78	80	76	76	78	74	100.67	90.67	85.33	88.67	90.00	88.67	86.67	86.00	89.33	88.00	98	WNL	18	N	N
40	23	M	I	66	I	1.8	135	I	N	N	N	N	EXCELLENT	N	25	1	0	135	84	86	92	100	96	88	82	80	78	76	114	118	114	118	116	112	110	102	104	100	66	70	68	70	74	74	76	72	68	68	82.00	86.00	83.33	86.00	88.00	86.67	87.33	82.00	80.00	78.67	99	WNL	16	N	N
41	32	F	I	55	II	2.5	137	II	M	N	M	N	GOOD	Y	65	2	25	162	94	96	100	110	104	94	90	92	88	88	138	136	132	136	126	118	110	112	108	108	92	94	90	92	88	88	84	84	86	84	107.33	108.00	104.00	106.67	100.67	98.00	92.67	93.33	93.33	92.00	97	WNL	20	Y	N
42	26	F	I	58	I	1.6	90	I	N	N	N	N	EXCELLENT	N	20	1	0	90	90	96	98	106	98	90	80	84	82	78	106	110	106	110	108	108	110	106	108	104	68	66	68	72	74	72	74	70	72	70	80.67	80.67	80.67	84.67	85.33	84.00	86.00	82.00	84.00	81.33	99	WNL	14	N	N
43	32	F	II	48	I	1.8	86	I	N	N	N	N	EXCELLENT	N	35	1	0	86	114	116	120	124	112	106	102	98	94	92	130	126	124	130	128	118	112	110	112	110	90	94	88	90	84	86	82	80	80	78	103.33	104.67	100.00	103.33	98.67	96.67	92.00	90.00	90.67	88.67	100	WNL	14	N	N
44	28	M	I	63	I	1.9	130	I	N	N	N	M	GOOD	N	70	2	20	150	84	88	96	104	100	92	84	86	86	82	112	110	114	118	116	110	116	108	108	114	74	76	76	74	78	76	78	74	72	72	86.67	87.33	88.67	88.67	90.67	87.33	90.67	85.33	84.00	86.00	98	WNL	14	N	N
45	26	F	I	50	I	1.5	75	I	N	N	N	M	EXCELLENT	N	20	1	0	75	88	92	100	108	100	96	90	88	90	86	118	120	116	122	120	114	116	112	118	110	78	86	88	86	84	84	80	78	78	76	91.33	97.33	97.33	98.00	96.00	94.00	92.00	89.33	91.33	87.33	99	WNL	16	N	N
46	32	M	I	68	I	2	136	I	N	N	M	N	GOOD	N	35	1	0	136	96	94	82	92	88	82	80	76	72	72	102	105	94	106	106	104	92	96	98	102	68	62	65	76	60	60	56	58	60	62	79.33	76.33	74.67	86.00	75.33	74.67	68.00	70.67	72.67	75.33	99	WNL	18	N	N
47	28		I	63	I	1.8	113.4	I	N	N	N	N	EXCELLENT	N	20	1	0	113.4	98	102	106	110	100	96	96	92	90	86	118	124	106	114	112	108	112	106	110	108	72	76	66	70	68	70	68	62	68	66	87.33	92.00	79.33	84.67	82.67	82.67	82.67	76.67	82.00	80.00	98	WNL	14	N	N