

**“EFFICACY OF DIFFERENT DOSES OF PROPOFOL FOR  
TRACHEAL INTUBATION-A RANDOMISED CLINICAL TRIAL”**

**By**

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**Under the guidance of**

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**2017**

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## **LIST OF ABBREVIATIONS USED**

ASA	:	American Society of Anaesthesiologists Classification
IV	:	Intravenous
HR	:	Heart Rate
SBP	:	Systolic Blood Pressure
DBP	:	Diastolic Blood Pressure
MAP	:	Mean Arterial Pressure
PR	:	Pulse Rate
SPO <sub>2</sub>	:	Oxygen Saturation
ECG	:	Electrocardiography
INJ	:	Injection
Bpm	:	beats per minute
mins	:	Minutes
kg	:	Kilogram
µg	:	Microgram
mmHg	:	Millimeters of mercury
BMI	:	Body Mass Index

# ABSTRACT

## **Background and Objectives:**

Endotracheal intubation which is an integral part of General anaesthesia is commonly facilitated by administering muscle relaxants following intravenous induction agent. Keeping the disadvantages of muscle relaxants in mind, intubation without muscle relaxants is an alternative option. Commonly used i.v. induction agent Propofol, because of its unique airway reflex suppression properties, was tried by various authors for endotracheal intubation without the use of muscle relaxants with conflicting conclusions. Opioid supplementation of Propofol apparently improved intubating conditions in some studies.

Hence we undertook this study to evaluate the feasibility / nonfeasibility of endotracheal intubation and safety using prefixed doses of Propofol – 2mg/kg or 4mg/kg bodyweight supplemented with 3µg/kg Fentanyl without the use of muscle relaxants..

## **Methodology:**

Present randomized study was conducted on eighty patients after taking informed written consent, comprising of forty patients each. Patients of either sex were randomly allocated into group P1 and group P2 by computer generated random numbers.

1. Group P1 received 2mg/kg Propofol +3µg/kg Fentanyl.
2. Group P2 received 4mg/kg Propofol+ 3µg/kg Fentanyl.

SPO<sub>2</sub>, HR, BP-SBP, DBP, MAP 1 minute after administration of study drugs were recorded. More than 20 % difference between the Pre induction baseline HR and B.P. readings and the corresponding readings 1 minute after the completion of injection of the study drug but prior to laryngoscopy was considered as effect of the

drug on cardiovascular system. Intubating conditions were assessed - Modified Helbo Hansen Scoring system.

SPO<sub>2</sub>, HR and BP –SBP, DBP, MAP were recorded 1 minute and 3 minutes post intubation. More than 20 % difference between the Pre induction baseline HR and B.P. readings and the corresponding readings 1minute post intubation was considered as pressor response to laryngoscopy and intubation. HR and BP were recorded 3 minutes post intubation to know whether HR and B.P. reached the baseline or not.

### **Results:**

The demographic changes such as Age, Sex, Weight, BMI were comparable in all the groups.

The success rate of endotracheal intubation was 62.5% and 95% in Propofol 2mg/kg + Fentanyl 3µg /kg and Propofol 4mg/kg + Fentanyl 3µg /kg respectively.

The total incidence of hypotension was 40% and 83% in Propofol 2mg/kg + Fentanyl 3 µg /kg and Propofol 4mg/kg + Fentanyl 3µg /kg respectively. The incidence of hypersensitivity was noted only in Propofol 4mg/kg + Fentanyl 3 µg /kg group and was 2.5%.

### **Conclusion:**

We conclude that endotracheal intubation is possible in premedicated adult ASA Grade I patients receiving 3 µg /kg Fentanyl + 2 or 4 mg/kg Propofol for induction without muscle relaxants and the intubating conditions are acceptable. The success of endotracheal intubation , the cardiovascular effects and the side effects are dose related . This technique is an alternative to the use of muscle relaxants on an individualized basis.

We feel that Propofol 4mg/kg + Fentanyl 3µg/kg is the optimal dose required for intubation without the use of muscle relaxants.

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## INTRODUCTION

Tracheal intubation is usually facilitated by using a muscle relaxant to supplement drugs given for the induction of general anaesthesia.

Suxamethonium is the most commonly used muscle relaxant in day to day anaesthetic practice but, it has many potential problems<sup>1</sup> - bradycardia, asystole, increased salivation, increased intraocular and intracranial pressures, hyperkalemia, myalgia<sup>2</sup> and rarely life threatening malignant hyperthermia.

In paediatric anaesthetic practice utmost concern is its potential to cause masseter spasm, unexplained cardiac arrest and death.

Other alternatives like Non-depolarising muscle relaxants are associated with the following disadvantages:

1. Prolonged neuromuscular blockade when compared to Suxamethonium.
2. The inability to reverse the blockade quickly<sup>3</sup> if airway management via mask or tracheal intubation not possible.
3. They are not suitable for surgeries of short duration.

Endotracheal intubation under volatile anaesthetics without the use of muscle relaxants is possible but it has the following disadvantages:

1. Anaesthetic depth required to produce the satisfactory intubating conditions may be difficult to gauge.
2. Premature attempt at intubation can result in life threatening laryngospasm.
3. Time available for intubation is much less when compared to the use of muscle relaxants.

Cardiovascular events-bradycardia, hypotension and myocardial depression can occur



and this may not be acceptable in patients with compromised myocardial reserve and function as in Ischaemic heart disease.

Considering the disadvantages of muscle relaxants and volatile agents in mind there is a need for endotracheal intubation without muscle relaxants.

Propofol is unique in having property to suppress airway reflexes<sup>3</sup> better than any other agent, abducts and immobilizes the vocal cords enabling laryngoscopy.

Keaveny JP and Knell PJ were amongst the first workers to propose the concept of intubation with only Propofol without muscle relaxants. This was the beginning for the thought of elimination of muscle relaxants for intubation.

In some studies, intubating conditions under Propofol without muscle relaxants ranged from impossible / unacceptable to as ideal as produced by Suxamethonium.

Hovorka *et al* in 1991 concluded that Propofol alone without muscle relaxants produced unacceptable intubating conditions and that muscle relaxants need to be used routinely for endotracheal intubation.

Striebel *et al* in 1995 concluded that the intubating conditions produced by Propofol supplemented with Fentanyl but without the use of muscle relaxants produced conditions that were as ideal as that produced by Thiopentone and Suxamethonium.

Fentanyl as a supplement to Propofol for endotracheal intubation has not been extensively studied. Available literature reveals conflicting conclusions regarding feasibility and intubating conditions (not possible / possible but not ideal / possible and ideal as with relaxants<sup>4</sup>) under Propofol without muscle relaxants. No such study had been carried out in our institution so far.

Hence this prospective randomized clinical trial was conducted employing two fixed doses of Propofol 2mg/kg or 4mg/kg supplemented with fixed dose of 3µg/kg Fentanyl (without muscle relaxants) in adult patients with normal airway anatomy for endotracheal intubation. Feasibility, intubating conditions, effect on the haemodynamics and safety were studied & compared.

## **OBJECTIVES OF THE STUDY**

1. Evaluate the intubating conditions and Feasibility / Non feasibility of endotracheal intubation using Propofol (2mg/kg or 4mg/kg) + Fentanyl 3 $\mu$ g/kg without using muscle relaxant.
2. Evaluate the effects of study drug on haemodynamics soon after:
  - a. Induction
  - b. Intubation
3. To find out the optimal dose of study drug based on:
  - a. Success rate of intubation
  - b. Side effects.

## REVIEW OF LITERATURE

1. K. McKeating *et al*<sup>5</sup> in 1988 in a blind randomised prospective study among unpremedicated patients scheduled for elective surgery studied the visualisation of vocal cords by standard laryngoscopy after unsupplemented induction dose of Thiopentone or Propofol without the use of muscle relaxants. Visualisation of vocal cords were more often possible after Propofol than with Thiopentone ( $p < 0.01$ ). The pharyngeal and laryngeal reflexes were depressed more frequently with Propofol. No side effects were noted.
2. J.P. Keaveny and P. J. Knell<sup>6</sup> in 1988 in an open randomised prospective study among 20 unpremedicated ASA I and II adult patients aged 18-65 yrs investigated the ease of tracheal intubation after induction with 2.5mg/kg Propofol without muscle relaxants. Easy laryngoscopy and satisfactory intubation were achieved in 19 patients. No side effects were noted.
3. Kallar S<sup>7</sup> in 1990 evaluated the feasibility of tracheal intubation without muscle relaxant in groups of 3 Patients:

Group	1	-	30 patients received 2.5 mg/kg Propofol,
Group	2	-	30 patients received 4mg/kg Thiopentone,
Group	3	-	30 patients received 2mg /kg Methohexitone.

4 $\mu$ g/kg Fentanyl and 1mg/kg Lidocaine were used as supplements to intravenous induction agents in all the three groups. Tracheal intubation was possible without muscle relaxants in 94%, 34% & 0% of patients in Propofol, Thiopentone and Methohexitone groups respectively.

4. In a prospective randomised blind study Hovorka *et al*<sup>8</sup> in 1991 studied 106 patients giving 1.5mg/kg Lidocaine, 30 µg/kg Alfentanil who were then assigned to receive either 2.5mg/kg Propofol or 4mg/kg Thiopentone for induction. Tracheal intubation was difficult in only 2% of patients in Thiopentone group but 10% of patients in the Propofol group. They concluded that tracheal intubation was more easily accomplished with Thiopentone than with Propofol .
5. In a prospective randomised double blind study L. Saarnivaara and U. M. Kleomala<sup>9</sup> in 1991 evaluated the ease of tracheal intubation in 59 young adults ASA/II, premedicated with 0.1 mg/kg Oxycodone and 0.01mg/kg Atropine i.m. They used Propofol (P) 2-2.5mg/kg preceded by Saline(S) or Alfentanil (A) 20-30 µg/kg for the anaesthetic induction. Intubating conditions were assessed as good, moderate poor and impossible on the basis of jaw relaxation, ease of insertion of tube and coughing reflex on intubation each on a 3 point scale and in impossible cases, Suxamethonium was used.

**TABLE No: 1**  
**INTUBATION SCORING SYSTEM**

CRITERIA	SCORE		
	1	2	3
JAW RELAXATION	COMPLETE	SLIGHT TONE	STIFF
EASE OF TRACHEAL INTUBATION	EASY	SLIGHT DIFFICULTY	IMPOSSIBLE
COUGHING	NONE	SLIGHT	SEVERAL BOUTS

In S+P 2.5 the frequency of good, moderate, poor and impossible intubating conditions were 0,38.8 and 54% respectively and the corresponding figures in A + P 2.5mg/kg was 43%,46.7% and 14 % respectively. Propofol produced pain on injection and a significant decrease in both systolic and diastolic arterial pressures. They concluded that the best method was the combination of Alfentanil 30 µg/kg and Propofol 2.5mg/kg as it caused no pain on injection of Propofol, offers satisfactory intubating conditions in 79% patients and prevented cardiovascular intubation response.

6. Mark S Scheller *et al*<sup>10</sup> in 1992 double blind study to evaluate the intubating conditions after administration of Propofol and Alfentanil in 75 ASA I & II PS patients with Mallampatti class I airway. All patients were premedicated with 1mg Midazolam i.v. before induction of anesthesia. Group 1 (n=15) received d- Tubocurarine 3mg, Thiamylal 4mg/kg and Succinyl Choline 1mg/kg i.v. And group (II - V) patients (n=15each) received Alfentanil 30,40,50 or 60 µg/kg followed by Propofol 2mg/kg i.v. No muscle relaxants were given to patients in II-V groups. 90 seconds after the administration of Propofol/Thiamylal, laryngoscopy was performed and the intubating conditions were assessed using 4 variables: Jaw relaxation, Exposure and Position of vocal cords and Patient movement during attempted intubation of trachea..

**TABLE No: 2**

**INTUBATION SCORING SYSTEM**

SCORE	CRITERIA			
	Jaw mobility	Exposure of vocal cords/arytenoids	Vocal cord position	Patient movement
1	mobile	Completely visible	open	No movement
2	Partly mobile	Partly visible	Mid position	1-2 coughs
3	immobile	Not seen	Closed	Persistent coughing
4	-	-	-	Purposeful movements
If trachea was not intubatable, additional muscle relaxants used ?			YES	NO

Heart rate, Blood pressure were also recorded before and after induction, after tracheal intubation . Suxamethonium 1mg/kg was given to those patients whose trachea could not be intubated after receiving the induction drugs. In patients given Alfentanil 30µg/kg, the incidence of persistent coughing or movement after intubation of trachea was most frequent. All patients receiving Alfentanil had significant decreases in heart rate and arterial blood pressures post induction. Patients receiving Thiamylal and Succinylcholine had significant increases in the heart rate after the induction of anaesthesia.

MAP increased significantly after laryngoscopy and intubation of trachea compared with post induction values in patients receiving Thiamylal and Suxamethonium.

They concluded that in premedicated healthy outpatients with favorable airway anatomy, tracheal intubation may be reliably accomplished with a combination of Propofol 2mg/kg and Alfentanil 40µg/kg. The simultaneous administration of muscle

relaxants may not be necessary to ensure acceptable jaw mobility, mask ventilation, vocal cord exposure and position or patient movement in response to tracheal intubation. They also concluded that in patients who received Alfentanil  $>30\mu\text{g}/\text{kg}$  and Propofol  $2\text{mg}/\text{kg}$  for induction, jaw mobility, exposure and position of the vocal cords during laryngoscopy and patient response to intubation of trachea differs little from that achieved with Thiopental and Succinylcholine.

7. Coghlan SFE *et al*<sup>11</sup> in 1993 in a prospective double blind study investigate the effect of Propofol with Alfentanil for intubation without neuromuscular block in 60 adult patients, aged 16-55yrs, with ASA I and II physical status for elective maxillofacial surgery. They were not premedicated and were randomly assigned to 2 groups of 30 each after giving Glycopyrrolate  $5\mu\text{g}/\text{kg}$  and pre oxygenated for 3 min. Group P received Propofol infusion at a rate of  $2\text{mg}/\text{kg}$  to a total of  $2.5\text{mg}/\text{kg}$  and group A received Alfentanil  $20\mu\text{g}/\text{kg}$  followed by Propofol infusion to a total of  $2.5\text{mg}/\text{kg}$ .

Depth of anaesthesia was assessed 30secs after the completion of infusion by the negative response to verbal stimuli and loss of eyelash reflex.  $20\text{mg}$  bolus dose of Propofol was given if induction was not complete or if moving or coughing occurred during administration, and further doses if necessary. If intubation was unsuccessful after 2 attempts, Suxamethonium  $1\text{mg}/\text{kg}$  was given.

Quality of intubation was assessed with criteria mainly jaw relaxation on a point scale and position with movement of the cords on a point scale



**TABLE No:3**  
**INTUBATION SCORING SYSTEM**

SCORE	CRITERIA	
	JAW RELAXATION	POSITION AND MOVEMENT OF VOCAL CORDS
1	Complete relaxation with easy laryngoscopy	Abducted and no movement on intubation
2	Partial relaxation, laryngoscopy possible	Abducted cords but movement during intubation
3	Laryngoscopy not possible	Vocal cords moving/adducted, Intubation possible
4	-	Intubation not possible

Intubation was successful in 73% patients in group P and 83% in group A.

In group P there were significant increases in the MAP and HR after intubation whereas a small increase in MAP and no change in HR was noted in group A. They concluded that

- a) tracheal intubation was readily achieved with a combination of Propofol and Alfentanil without the use of neuromuscular blockers.
  - b) Tracheal intubation conditions were significantly better when Propofol was augmented with Alfentanil 20µg/kg - Jaw relaxation was improved, Vocal cord movements were reduced and the cords were abducted
  - c) Coughing and Pressor response to intubation were attenuated.
8. M.P. Steyn *et al*<sup>12</sup> in 1994 studied 80 children aged 2-14 years undergoing adenotonsillectomy in a double blind design. Tracheal intubation was facilitated with either Suxamethonium 1.5mg/kg or Alfentanil 5µg/kg was compared after the induction of anesthesia with Propofol 3-4 mg/kg. The quality of tracheal intubation was

graded according to the Jaw relaxation, ease of laryngoscopy, position of vocal cords, coughing, and patient movement of limbs.

Helbo-Hansen, Raulo, Trap-Anderson scoring for intubating conditions consisted of three criteria-Laryngoscopy, Movement of vocal cords and Coughing response. M P Steyn modified the above scoring system by including two additional criteria- Jaw relaxation and Limb movements. Intubating condition scoring was done as per the scoring system given vide infra :

**TABLE No: 4**

**M P Steyn Modification of Helbo- Hansen intubating scoring system:**

CRITERIA	SCORE			
	1	2	3	4
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal Cords	Open	Moving	Closing	Closed
Coughing	None	Slight	Moderate	Severe
Jaw relaxation	Complete	Slight	Stiff	Rigid
Limb movement	None	Slight	Moderate	Severe

Acceptable intubating conditions = 5 to 10 (each individual criteria was 2 or less). Unacceptable intubating conditions if total score is greater than 10 (each score greater than 2 ) There were no significant differences in the assessment of intubating conditions and few patients coughed and limb movements were less common. They concluded that intubation without neuromuscular blockade using Propofol-Alfentanil is feasible and safe in majority of children. Adjusting the dose of Alfentanil or Lidocaine improves the intubating conditions while minimizing coughing and limb movements. Alfentanil attenuated the pressor responses to tracheal intubation.

9. P.Mc Conaghy and H. E. Bunting<sup>13</sup> in 1994 assessed tracheal intubating conditions in 60 ASA I and II unpremedicated children aged 3-12 years after induction of anesthesia with Alfentanil 5,10 or 15µg/kg(each n=20) given over 10 seconds followed by titrated induction dose of Propofol (2.8 to 3.4mg/kg) 30 seconds later without using any muscle relaxants. Laryngoscopy and intubation were attempted 60 seconds after induction of anaesthesia. Intubating conditions were scored based on the Helbo-Hansen scoring system

**TABLE No: 5**

**HELBO HANSEN SCORING SYSTEM:**

CRITERIA	SCORE			
	1	2	3	4
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	Slight	Moderate	Severe

Overall conditions for intubation was excellent if total score was 6 or less.

Intubation was unsuccessful if

- 1) Laryngoscopy was not possible
- 2) Vocal cords were closed

In those patients in whom intubation was impossible, anaesthesia was deepened either with Halothane or Propofol and intubation attempted. Suxamethonium was used if second intubation attempt failed. The number of patients in whom each component of the assessment was satisfactory, increased with the dose of Alfentanil. Successful intubation was noted in 70%, 95% and 95% patients after Alfentanil 5, 10, 15µg/kg respectively and conditions were considered to be excellent in 20%,70% and 80% patients respectively.

Side effects of Propofol induction included pain on injection, excitatory movements and bradycardia. They concluded that adequate conditions of Laryngoscopy and intubation were produced in children after induction of anaesthesia with Propofol (2.8 to 3.4 mg/kg) and Alfentanil ( 5 to 15µg/kg) and no additional benefits were noted by increasing the dose of Alfentanil to 15 µg/kg.

10. James B Stevens and La Dona Wheatley<sup>14</sup> in 1998 in a double blind randomized study evaluated 80 ASA 1 and II patients aged 18-55 years who were premedicated with i.v midazolam 0.03mg/kg 5 minutes before the induction of anaesthesia. All patients were randomly assigned to receive Remifentanil 1, 2, 3, 4 µg/kg (groups 1 to 4, n=20 ). 60 seconds later, patients were induced with 2mg/kg Propofol. 90 seconds after the Propofol administration, Laryngoscopy and intubation were attempted. Intubating conditions were assessed - Ease of mask ventilation, Jaw relaxation, Vocal cord position, patient response to intubation and slow inflation of tube cuff.

**TABLE No: 6****INTUBATION SCORING SYSTEM**

Overall score	Criteria
Excellent	Easy mask ventilation, mobile jaw, Open vocal cords, No cough or patient movement to Intubation
Good	Easy mask ventilation, mobile jaw, open vocal cords ,one to two bouts of cough in response to intubation
Poor	Difficult/impossible mask ventilation, Immobile jaw, Closed vocal cords, Persistent coughing and patient movement to laryngoscopy

Those patients who could not be intubated in the first attempt were given Suxamethonium 1mg/kg iv to facilitate endotracheal intubation. They concluded that the administration of 2mg/kg Propofol in combination with Remifentanil 3-4 $\mu$ g/kg reliably allows tracheal intubation and rapid return of spontaneous ventilation in most healthy premedicated patients with favorable airway anatomy. Clinically acceptable intubating conditions (i.e. jaw relaxed, vocal cords open, and fewer than two coughs in response to intubation) were observed in 35%, 75% ,95% and100% of patients in group 1-1V. Clinically acceptable intubating conditions were significantly less likely to occur ( $p<0.05$ )in group 1 compared with all the other groups. Excellent intubating conditions were observed in 30%, 50%, 80% and 80% of patients in group I to IV. They suggested that this technique maybe appropriate for tracheal intubation in outpatients when neuromuscular blockade is undesirable or not required for planned surgical procedure.MAP values were significantly decreased ( $p<0.05$ ), HR decreased significantly ( $p<0.05$ ) in all the 4 study groups..

Remifentanyl can result in severe bradycardia muscle rigidity, apnoea and increased incidence of post operative nausea and vomiting.

11. S Grant *et al*<sup>15</sup> in 1998 carried out a prospective randomized double blind study to assess intubating conditions in 60 ASA I and II adult patients undergoing elective inpatient surgery. All patients were premedicated with Temazepam 20-30/kg and Rantac 150mg. Patients were allocated randomly (using a computer program) to one of the 3 study groups:

Group I 2mg/kg Propofol+ 0.5µg/kg Remifentanyl

Group II 2mg/kg Propofol + 1µg/kg Remifentanyl

Group III 2 mg/kg Propofol + 2µg/kg Remifentanyl

Anaesthesia induced with 2mg/kg Propofol after the administration of 0.5,1 or 2µg/kg remifentanyl. Laryngoscopy was attempted 90 seconds after Propofol was administered.

Tracheal intubation was graded according to Jaw relaxation, Exposure of vocal cords, Position of vocal cords, Coughing, Patient limb movement

**TABLE No: 7**

**MP Steyn modification of Helbo Hansen Ravlo Scoring <sup>30</sup>**

CRITERIA	SCORE			
	1	2	3	4
Jaw relaxation	Complete	Slight tone	Stiff	Rigid
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	Sight	Moderate	Severe
Limb movements	None	Slight	Moderate	Severe

Intubating conditions were graded as

- Acceptable when each parameter score was 2 or less OR TOTAL SCORE was 5-10
- Unacceptable- each parameter score was 3 or more OR TOTAL SCORE was 15-20.

Overall intubating conditions were acceptable in 20%, 50% and 80% patients in Group I, II and III respectively. The decrease in MAP and HR observed were both statistically insignificant. It was concluded that the intubating conditions were best after induction with Propofol 2mg/kg and Remifentanyl 2µg/kg.

They saw the potential for this technique in

- Out patient ENT and Gynaecological surgery
- Cases in which intubation is required but neuromuscular block is not required to facilitate surgical access
- Cases where neuromuscular blocking agents are contraindicated (eg: myopathies)
- Cases wherein Suxamethonium is contraindicated (Hyperkalemia, Burns, penetrating eye injury)

12. R. Alexander *et al*<sup>16</sup> in 1999 in a randomized double blind design studied the ease of tracheal intubation among 60 ASA I and II patients undergoing elective surgical procedures. Patients were premedicated with Midazolam 0.03mg/kg i.v 10 minutes before the induction of anaesthesia. The patients were randomly allocated to one of the three groups using a computer generated table:-Group R3 received Remifentanil 3µg/kg, Group R4 received 4µg/kg and Group R5 received Remifentanil 5µg/kg.

After 3 minutes of preoxygenation, anaesthesia was induced with Propofol 2mg/kg at an infusion rate of 40mg every 10 seconds followed immediately by Remifentanil 3,4 or 5µg/kg as rapid bolus over 10 seconds. Laryngoscopy was performed 60 seconds after the drug was given. Relaxed jaw, Open vocal cords, coughing and patient movement were the criteria used to assess the ease of intubation.

**TABLE No: 8**

**INTUBATION SCORING SYSTEM**

GRADE	CRITERIA
Excellent	Relaxed jaw, Open vocal cords, no coughing or no limb movement during or after intubation, No rigidity
Good	Relaxed jaw, Fully or half open vocal cords Coughing < or slight limb movement during or after intubation, No rigidity.
Poor	Resistance to jaw opening ,Closed vocal cords, Sustained coughing or purposeful movements to intubation ,Rigidity present



MAP, HR, SPO<sub>2</sub> were measured before induction, before intubation and 1 minute after intubation for 5 minutes. Good to excellent intubating conditions were observed in 12 patients in Group R3 compared with the 19 patients each in groups R4 and R5 (p= 0.004) Sustained gross airway reaction in 6 patients (n=20) in group R3 indicated inadequate depth of anaesthesia for intubation.

Significant reductions in MAP and HR were observed in each group. There was however no difference in mean MAP and HR between the three groups at all time points. More patients in Group R5 (30%) required use of vasopressors for hypotension than in the other two groups (10% and 25% respectively)

They concluded that the combination of 2mg/kg Propofol with 4-5µg/kg Remifentanyl provided reliable conditions for intubation.

13. Harald Andel *et al*<sup>17</sup> in 2000 in a randomized double blind design studied the Propofol dose required for conventional tracheal intubation /Fibreoptic intubation in 32 adult patients aged 17-72 under going maxillofacial surgery. ECG, MAP, ETCO<sub>2</sub> and baseline vitals were recorded. Respiration was monitored continuously via impedance measurement along with ECG. Patients were randomly allocated to the conventional or the fibreoptic intubation group (n=16). Anaesthesia was then induced slow i.v administration of 3µg/kg Fentanyl and the respiratory rate was recorded. If there was no significant change of less than 10 breaths per minute then additional 1.5µg/kg was given. Propofol was then titrated iv until loss of verbal response.

Endotracheal tube was placed nasally in the pharynx and the vocal cords visualized using a fibrescope inserted via the tube. In the conventional group, the larynx was visualized with a Miller laryngoscope blade. After the visualization of the vocal cords

Propofol was given titrated to allow relaxation of the vocal cords in both the groups. The amount of Propofol given, degree of jaw relaxation (complete, moderate, none) at the time of intubation, patient coughing (vigorous, slight, none) were recorded. Vitals were recorded post induction as well as post intubation. Haemodynamics remained stable in all patients.

They concluded that in all patients the trachea could be intubated without the use of muscle relaxants. The amount of Propofol required in the conventional direct laryngoscopy group were significantly ( $p < 0.0001$ ) more (1.95-7.07mg/kg) than in the fiberoptic group (0.72-2.8mg/kg).

14. De Fatima de Assuncao *et al*<sup>18</sup> in 2001 in a randomized blind study evaluated the intubating conditions and cardiovascular responses in 60 ASA I and II children. 0.1mg/kg Midazolam was given as premedication. The children were randomly allocated to receive different doses of Propofol (G1 2.5mg/kg, G2 3mg/kg & G3 3.5mg/kg) preceded by 3µg/kg Fentanyl. No neuromuscular blockers were administered. The intubating conditions were assessed using a four point scoring system based on the degree of difficulty of laryngoscopy, position of vocal cords and the intensity of coughing.

Tracheal intubating conditions were adequate in 20% of patients in G1, 75% in G2, and in 80% in G3 ( $p < 0.05$  for G1 v/s G2). They concluded that 3mg/kg Propofol preceded by 3µg/kg Fentanyl was adequate for induction of anaesthesia in children and provided adequate trachea intubating conditions without significant haemodynamic changes.

15. Dr Uma Srivastava *et al*<sup>19</sup> in 2001 in a randomized blind study compared tracheal intubation and haemodynamic response after induction of anaesthesia Propofol supplemented with Fentanyl with the standard technique of using Thiopentone followed by Succinylcholine in 70 unpremedicated children aged 3-12 years of ASA grade I and II. Patients were randomly allocated to two groups Group F Propofol supplemented with Fentanyl or Group S Thiopentone followed by Succinylcholine . 0.01mg/kg Atropine was injected prior to induction.

In Group F 1µg/kg Fentanyl was given i.v followed 60 seconds later by Propofol Lignocaine 0.2mg/kg was added to Propofol to abolish pain on injection. Titrated i.v induction with Propofol over 10 seconds was performed with loss of verbal response or tolerance of face mask as the end point. Laryngoscopy and intubation were attempted 60 seconds after the induction of anaesthesia using Macintosh laryngoscope blade of appropriate size and latex tracheal tube of appropriate diameter. Additional bolus of 1mg/kg Propofol was given if laryngoscopy was not possible due to muscle spasm, coughing or excessive movement. In those patients where intubation was not possible after two attempts were given 1mg/kg Suxamethonium and intubation completed. In the control group S, anaesthesia was induced by Thiopentone 3-5mg/kg followed by Suxamethonium 1mg/kg and endotracheal intubation was performed 60 seconds later. The intubating conditions were assessed using a 4 point scoring system :

**TABLE No: 9****INTUBATION SCORING SYSTEM**

	SCORE			
	1	2	3	4
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	Sight	Moderate	Severe
Limb movement	None	Slight	Moderate	Vigorous

Overall intubating conditions were labeled acceptable if total score was 4 to 8 (individual scores were 2 or less). Pulse rate, systolic arterial pressure and SPO<sub>2</sub> were recorded at one minute interval from the time of iv. cannulation till one minute after intubation. Tracheal intubation was successful in 78% patients receiving Propofol and Fentanyl and in 100% patients receiving Thiopentone and Suxamethonium. The overall assessment of intubating conditions was acceptable (score of 2 or less in all categories) in 27 of 40 (67.5%) children given Fentanyl and Propofol. Nine patients required Suxamethonium for intubation in Propofol group with failure rate of 22%. Significantly more patients coughed ( $p < 0.05$ ) and had limb movement ( $p < 0.01$ ) after intubation in Propofol Group.

Thiopentone- Suxamethonium group patients showed a significant increase in pulse rate and blood pressure (both  $p < 0.01$ ) after intubation. The cardiovascular pressor response was attenuated in Propofol-Fentanyl group but not in Thiopentone-Suxamethonium group. They concluded that Propofol and Fentanyl in combination suppress haemodynamic response but intubating conditions are not ideal as seen after Thiopentone and Suxamethonium in children.

16. Tsuda A *et al*<sup>20</sup> in 2001 in a randomized blind study evaluated the airway and intubating conditions without muscle relaxants in 55 adult patients posted for elective surgery. Patients were randomly allocated to receive different doses of Fentanyl (G1 0µg/kg, G2 2µg/kg, G3 3µg/kg, G4 4µg/kg) followed by 2mg/kg Propofol and 2mg/kg Lidocaine topical. Laryngoscopy and tracheal intubation was attempted. Visualisation of vocal cords was possible in 60 % patients who receive 2mg/kg Propofol and 4µg/kg Fentanyl. They concluded that tracheal intubation without muscle relaxants produced unacceptable conditions and this cannot be recommended.
17. J.M. Blair *et al*<sup>21</sup> in 2004 did a prospective randomized blind trial to evaluate the intubating conditions and haemodynamic responses in 112 unpremedicated children of ASA I and II aged 3-12 years posted for elective otorhinolaryngological surgery. Children were randomly allocated to four groups. G 1 received Propofol 3mg/kg and Atropine 10 µg/kg +1 µg/kg Remifentanyl (n= 28), G 2 Propofol 3mg/kg and Atropine 10 µg/kg +2 µg/kg Remifentanyl (n =26), G 3 Propofol 3mg/kg and Atropine 10 µg/kg +3µg/kg Remifentanyl (n = 27), G 4 Propofol 3mg/kg and Atropine 10 µg/kg + 0.2mg/kg Mivacurium (n =28). After Remifentanyl, 3mg/kg Propofol and Atropine 10µg/kg was given over 5 seconds. 60 seconds after the propofol administration, laryngoscopy and endotracheal intubation was attempted. Intubating conditions were graded with Modified Helbo Hansen's scoring system *vide infra*.

**TABLE No: 10****MP Steyn modification of Helbo Hansen Ravlo Scoring<sup>30</sup>**

CRITERIA	SCORE			
	1	2	3	4
Jaw relaxation	Complete	Slight tone	Stiff	Rigid
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	Sight	Moderate	Severe
Limb movements	None	Slight	Moderate	Severe

Intubating conditions were unacceptable if any variable score was > 2. Single attempt intubation within 60 seconds was deemed successful. Heart rate increased significantly after induction and after intubation in G 1group without the relaxant Mivacurium ( $p < 0.05$ ) and the mean systolic blood pressure decreased significantly from the baseline value in G1( $p < 0.05$ ), G2 ( $p < 0.001$ ) and G3 ( $p < 0.001$ ) whereas there was no significant change in the relaxant group ( $p > 0.05$ ). The mean systolic blood pressure did not increase significantly in G2 and G 3 groups ( $p > 0.05$ ) while it increased significantly in G1 ( $p < 0.01$ ) and in the relaxant group ( $p < 0.001$ ). Acceptable tracheal intubation was observed in 50%, 69 %, 82 % and 100% children respectively. They concluded that Propofol 3mg/kg + 10 $\mu$ g/kg Atropine + 2-3 $\mu$ g/kg Remifentanil given over 30 - 60 seconds is optimal and safe dose for tracheal intubation considering the intubating conditions, haemodynamic stability and the rapid return of ventilation post induction. Remifentanil 3 $\mu$ g/kg + Propofol 3mg/kg + 10 $\mu$ g/kg Atropine provides similar intubating conditions to 0.2mg/kg mivacurium and provides significantly better intubating conditions than 1 $\mu$ g/kg Remifentanil.

18. Gupta A *et al*<sup>22</sup> in 2006 conducted a prospective randomized double blind study in 60 ASA I and II children aged between 3- 10 years undergoing elective surgery to determine the optimal dose of Propofol preceded with Fentanyl or endotracheal intubation and its effectiveness to blunt the haemodynamic pressor response following laryngoscopy. Patients were randomly allocated to three groups of 20 each. G I received 2.5mg/kg Propofol, G II 3mg/kg Propofol, and G III 3.5mg/kg Propofol. All patients received a fixed dose of 3µg/kg Fentanyl preceding the dose of Propofol. The tracheal intubation was assessed on a 4 point scale as per the scoring system based on Modified Helbo Hansen scoring system *vide infra*.

**TABLE No:11**  
**MP Steyn modification of Helbo Hansen Ravlo Scoring<sup>30</sup>**

CRITERIA	SCORE			
	1	2	3	4
Jaw relaxation	Complete	Slight tone	Stiff	Rigid
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	Sight	Moderate	Severe
Limb movements	None	Slight	Moderate	Severe

Acceptable intubating conditions were observed in 20%, 80% and 90% patients in GI, GII and GIII respectively. Pressor response was noted to be effectively blunted in G II and G III while there was a 17% increase in heart rate in G I. A fall of 16% in MAP and a fall in heart rate of 11% was seen in G III.

They concluded that 3mg/kg Propofol + 3µg/kg Fentanil is the optimal dose for endotracheal intubation providing acceptable intubating conditions in 80% patients and it

also effectively blunted the pressor response without any significant cardiovascular depression.

19. J.M. Morgan *et al*<sup>23</sup> in 2007 conducted a prospective randomized double blind trial in 60 ASA I and II unpremedicated children aged 2- 16 years who presented for elective surgery to evaluate the intubating conditions, haemodynamic response and the duration of apnea following 4mg/kg Propofol combined with either 1.25 µg /kg Remifentanil ( Group R, n = 30) or 1mg/kg Suxamethonium ( Group S, n = 30).Tracheal intubating conditions were assessed based on a scoring system developed by Viby – Mogenson and colleagues *vide infra* :

**TABLE No: 12**  
**INTUBATION CONDITION SCORE**

CRITERIA	SCORE		
	1	2	3
Jaw relaxation	Relaxed	Increased tone	Rigid
Laryngoscopy	Easy	Difficult	Impossible
Vocal cords	Open	Moving	Closed
Coughing	None	Sight	Severe
Limb movements	None	Slight	Severe

Overall intubating conditions were recorded as excellent if all the variables scored 1, good if any scored 2 and poor if there were any score of 3. Successful intubation was observed in single attempt in 93 % patients of Group Remifentanil while 100 % could be intubated in Group Suxamethonium. Overall intubating conditions were excellent in 67% in remifentanil group and 87% in Suxamethonium group ( $p < 0.05$ ).



## Post intubation

- 1) Heart rate increased significantly in Group S unlike in Group R ( $p < 0.001$ )
- 2) Fall in mean systolic and diastolic pressures in Remifentanil group was significantly higher than in Suxamethonium group ( $p < 0.01$ ).

They concluded that Suxamethonium provided better intubating conditions and shorter apnoea. Intubation without muscle relaxant cannot be recommended in children with difficult airway or in an emergency scenario or as an alternative in rapid sequence intubation.

20. Mir Mohammed Taghi Mortazavi *et al*<sup>24</sup> in 2010 performed a prospective double blind trial in 60 ASA I and II unpremedicated children aged between 3- 12 years to evaluate the intubating conditions without neuromuscular blockade . Patients were randomly allocated to 4 groups (n =15) G I ,G II and G III received 3mg/kg Propofol preceded by 1 $\mu$ g/kg ,2 $\mu$ g/kg and 3  $\mu$ g/kg Remifentanil respectively, G IV 0.5mg/kg Atracurium + 3mg/kg Propofol. Remifentanil was injected over 30 seconds and 3mg/kg Propofol was given as rapid i.v. bolus over 10 seconds. 60 seconds after the administration of Propofol, laryngoscopy and endotracheal intubation was attempted and the intubating conditions were assessed based on the Helbo Hansen's scoring system vide infra :

## HELBO HANSEN SCORING SYSTEM:<sup>31</sup>

TABLE No: 13

CRITERIA	SCORE			
	1	2	3	4
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	Slight	Moderate	Severe

Score of 1 or 2 from each variable in the scoring system is considered as acceptable while a score of 3 or 4 for each variable was non acceptable intubating conditions. In non acceptable conditions, intubation was carried out after further injection of the study drugs .Intubation time of less than 30 seconds was considered acceptable.

Where intubation had failed, in study groups I ,II and III (where relaxant was not used) authors used additional bolus administration of Propofol and Remifentaniol to facilitate intubation

They concluded from this study that 3µg/kg Remifentaniol + 3mg/kg Propofol without neuromuscular blockade provided satisfactory intubating conditions in children.

21. Shaikh SI and Bellagali VP<sup>25</sup> in 2010 in an prospective randomized study in 80 ASA I and II children aged 4- 12 years who presented for elective surgical procedures (n= 40) evaluated the intubating condition haemodynamic responses in children after induction of anaesthesia with Inj. Fentanyl 4 µg/kg + Inj. Propofol 3 mg/kg(Group F) or Inj. Propofol 3 mg/kg + Inj. Suxamethonium 1 mg/kg (GroupS). All the patients were pre-medicated with Inj. Midazolam 0.05 mg/kg and Atropine 0.01 mg/kg I.V., 10 minutes prior to induction. Group F (study group)- Inj. Fentanyl 4µg/kg was given I.V. over 30 seconds. Five minutes later, the children received

Propofol 3mg/kg over a period of 30 seconds (Lignocaine 0.2 mg/kg was added to Propofol solution to abolish pain on injection). Laryngoscopy and intubation were attempted 60 seconds after induction of anaesthesia in both the groups. Additional bolus of 1 mg/kg of Propofol was given if laryngoscopy was not possible due to muscle spasm, coughing or excessive movements. In those patients where intubation was impossible after two attempts due to any cause, Suxamethonium 1 mg/kg was injected and intubation completed.

In Group S (control group), anaesthesia was induced by Inj. Propofol 3 mg/kg followed by Inj. Suxamethonium 1 mg/kg; endotracheal intubation was performed 60 seconds later. The quality of intubation was graded the scoring system devised by Helbo-Hansen Raulo and Trap-Anderson.

**TABLE No: 14**

CRITERIA	SCORE			
	1	2	3	4
Jaw relaxation	Complete	Slight tone	Stiff	Rigid
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	Sight	Moderate	Severe

Excellent intubating conditions (intubation score 3-4) were achieved in 14 (35%) out of 40 patients in group F and 36 (90%) out of 40 patients in group S which was not statistically significant. Good intubating conditions (intubation score 5-8) were achieved in 24 (60%) patients in group F and 4 (10%) patients in group (not statistically significant). They concluded that in pre-medicated healthy children, tracheal intubation may be accomplished using a combination of Fentanyl (4 µg/kg) and Propofol (3 mg/kg).

22. Dr.Mangesh S Gore and Dr.Kalpana D Harnagale<sup>26</sup> in 2011 evaluated the tracheal intubating conditions with different doses of propofol without neuromuscular blockade in 90 ASA I and II adult patients aged between 20 - 65 years who presented for elective surgical procedures. All patients were premedicated with Inj. Glycopyrrolate 0.005mg/kg, Inj Midazolam 0.02mg/kg , 2µg/kg Fentanyl and randomly allocated to 3 groups

5 minutes after the injection of Fentanyl, Propofol (2mg/kg, 2.5mg/kg or 3mg/kg) was given over 10 seconds followed by Inj. Lignocaine 1.5 mg/kg i.v. bolus. 90 seconds after the administration of Propofol, laryngoscopy and intubation was attempted with 8.5mm Cuffed endotracheal tube and 7.5mm Cuffed endotracheal tube for males and females respectively. Intubating condition was assessed as follows :

**TABLE No: 15**  
**INTUBATION SCORING SYSTEM**

CRITERIA	SCORE			
	1	2	3	4
Laryngoscopy	Fully relaxed	Mild resistance	Tight but open	Impossible
Vocal cords	Widely Open	Mid position	Moving but open	Closed
Coughing	None	Diaphragmatic movements	Slight	Severe

Excellent = score 3 , Good = score 4 – 6 , Inadequate = score > 7

First attempt endotracheal intubation without the use of muscle relaxants was possible in 66.7 % , 96.7% and 100% patients in the 3 groups respectively.

During laryngoscopy and intubation there was a significant increase of heart rate in all the three groups but were comparable amongst each other. In Group I there was a significant rise in MAP (p <0.05) overshooting the baseline during intubation and 5

minutes post intubation. In Group II and III, there was a rise in MAP but remained well below the baseline values.

They concluded that 3mg/kg Propofol + 2µg/kg Fentanyl + 1.5mg/kg Lignocaine provided ideal intubating conditions without muscle relaxants and also effectively attenuated the pressor response to laryngoscopy.

23. Motlb E A E and Deeb A <sup>27</sup> in 2011 conducted a prospective double blind randomized study in 100 ASA I and II parturients scheduled for elective cesarean delivery to evaluate the intubation conditions for cesarean section with Fentanyl without muscle relaxant administration to obtain clinically acceptable intubation conditions and cardiovascular responses. Patients were randomly allocated to receive both Fentanyl 2 µg/kg and Propofol 2 mg/kg in group F, Propofol 2 mg/kg and Succinylcholine 1 mg/kg in group S. In group F Fentanyl 2 µg/kg was given, and then Propofol 2 mg/kg was injected over 30 s. Once the parturient became unconscious, ventilation was maintained via a face mask. Ninety seconds after completion of drug administration, laryngoscopy and intubation was attempted using a Macintosh 3 laryngoscope blade and a 7.0 mm endo-tracheal tube.

The quality of intubation was graded by anesthesiologist blinded to induction agents using the following scoring system:

(a) excellent defined by flaccid relaxation of jaw muscles, mouth open widely, good cord visualization, well separated, abducted cord, and no bucking at intubation;

(b) satisfactory defined by mouth easily opened, well relaxed jaw muscles, good cord visualization, slight cord movement when touched but abducted, and no bucking on intubation;

(c) fair defined by conditions less favorable, jaw muscles not well relaxed, cord visualization fair but allowing intubation, and bucking on intubation;

(d) unsatisfactory defined by resistance to mouth opening, poor relaxation of jaw muscles, poor cord visualization or none, cord abducted if viewed, superior pharyngeal constrictor muscle activity and intubation cannot be done or marked bucking and body movement on intubation

Patients who could not be intubated on the first attempt in group F were given Succinylcholine 1 mg/kg, and intubation was completed.

Measurements of heart rate, mean arterial pressure and arterial O<sub>2</sub> saturation were noted at different time intervals (pre-induction, post-induction, post-intubation at 0, 1, 3 and 5 min).

Acceptable intubating conditions (excellent and satisfactory) were observed in 45 patients in group F (90%) and in 48 patients in group S (94%) (not statistically significant). Unacceptable intubating conditions (fair and unsatisfactory) were observed in 5 patients of group F (10%) and 2 patients in group S (4%); which was not statistically significant. They concluded that in healthy pre-medicated women with favorable airway anatomy who are scheduled for cesarean section can be reliably intubated 90 s after co-administration of Fentanyl 2 µg/kg and Propofol 2 mg/kg with satisfactory fetal outcome.

24. Srivastava M *et al*<sup>28</sup> in 2014 conducted prospective randomized 100 ASA Grade I & II patients, undergoing surgeries under general anaesthesia were randomly allocated into two Groups to receive - Midazolam (0.04 mg/kg), Lignocaine (1.5 mg/kg), Propofol (2 mg/kg) and study drug Fentanyl 2 mcg/kg or 3 mcg/kg

During and within 1 min of laryngoscopy and intubation, the intubating anesthesiologist assessed each patient for five variables using MARK S. SCHELLER scoring criteria for various airway conditions Table No.16.

Criteria	Score
Jaw relaxation	
Jaw freely mobile & relaxed	1
Jaw partially mobile	2
Jaw Immobile	3
Mask Ventilation	
Mask ventilation easy	1
Mask ventilation difficult	2
Mask ventilation impossible	3
Exposure of Vocal cords	
Vocal cords and arytenoids completely visible	1
Vocal cords and arytenoids partly visible	2
Vocal cords and arytenoids not visible	3
Position of Vocal cords	
Vocal cords open	1
Vocal cords mid position	2
Vocal cords closed	3
Cough/Movements after intubation	
No movements	1
One or two coughs	2
Persistent coughing	3
Purposeful movements	4
Tracheal intubation with out additional drugs given	
Yes	1
No	2

In case where intubation was not possible, Succinylcholine 2mg/kg was given to facilitate laryngoscopy and intubation.

Once the patient was intubated, vital signs like pulse rate, BP were recorded at 1, 2, 5, 10, 15 and 30 minutes and side effects were noted.

They concluded that Fentanyl 3mcg/kg with Propofol, Midazolam and Lignocaine provides better intubating conditions and effective in blunting hemodynamic responses to intubation when compared to Fentanyl 2mcg/kg. Fentanyl 3mcg/kg with Propofol, Midazolam and Lignocaine

25. Naziri S *et al*<sup>29</sup> in 2015 conducted a prospective randomized study in 60 ASA I and II children aged 3- 12 years ( n= 30) who presented for elective surgical procedures . All the children were premedicated with 0.05 mg/kg Midazolam and 1.5 mg/kg Lidocaine 5 min before the induction of anesthesia. They were allocated randomly to receive with Propofol 3mg /kg, Supplemented with 2 µg/kg Remifentanyl (Group R) or with 1.5mg/kg Suxamethonium (Group S) Tracheal intubation was attempted 90 s after the administration of propofol. The quality of intubation was assessed by using Copenhagen score based on jaw relaxation, ease of laryngoscopy, position of vocal cord, coughing and limb movement. Heart rate and blood pressure were recorded before and after induction, and 1, 3, 5 min after intubation.



**TABLE No: 17****INTUBATION CONDITION SCORE**

CRITERIA	SCORE		
	1	2	3
Jaw relaxation	Relaxed	Increased tone	Rigid
Laryngoscopy	Easy	Difficult	Impossible
Vocal cords	Open	Moving	Closed
Coughing	None	Sight	Severe
Limb movements	None	Slight	Severe

There was no significant difference in intubating condition between the two groups ( $P = 0.11$ ). Intubation condition was excellent in 26 of 30 (86.7%) patients in the group R compared with 30 (100%) patients in the group S..

Tracheal intubation was made in both groups at the first attempt without any intervention. The intubating conditions were excellent in 86.7% in group R as compared to 100% of the patients in group S. However, not considering the reaction to endotracheal intubation, the quality of intubation in group R was 100% and it was great. Jaw was relaxed, and laryngoscopy was done easily in all of the patients in group R and vocal cord was open during laryngoscopy. Only 4 patients had coughing and mild limb movement after intubation.

There were significant difference in systolic blood pressure and heart rate over time between two groups ( $P = 0.03$ ,  $P = 0.02$ , respectively) . In group R, values of heart rate and systolic blood pressure showed a significant decrease after administration of induction drugs compared to baseline values ( $P = 0.012$ ,  $P = 0.000$ , respectively). They

concluded that in premedicated children, propofol-remifentanyl combination adequate conditions for tracheal intubation that is comparable with succinylcholine.

## **MATERIAL AND METHODS**

After the approval by the institutional ethical committee, consenting adult in-patients of Shri B.M.Patil Medical College Hospital requiring general anaesthesia via endotracheal tube for elective surgical procedures entered this PROSPECTIVE RANDOMISED CLINICAL TRIAL

***STUDY PERIOD:*** DEC 2014 TO JUNE 2016

### **INCLUSION CRITERIA:**

- Adult ASA Grade 1 patients of either sex.
- Age group 21-40 yrs.
- BMI 18.5-24.9
- Modified Mallampati Class I airway anatomy.
- Elective surgical procedure under general anaesthesia.

### **EXCLUSION CRITERIA:**

1. Anticipated difficult intubation<sup>32</sup>.
2. Upper airway pathology<sup>17</sup>.
3. Heart Diseases<sup>33</sup>.
4. Pregnancy.
5. Obesity.
6. Emergency surgeries.

During preanaesthetic evaluation, history of any significant medical illness (Endocrine / Metabolic derangement, Hypertension, Valvular cardiac lesions, Bronchial asthma) or drug hypersensitivity if any was elicited. Weight, pulse rate and blood pressure were recorded during the general examination of the patients.

**Airway assessment:**

Mouth opening, temporomandibular joint movement, Mallampati<sup>35</sup> view of upper airway, submandibular space and cervical spine movement was assessed

Patients were asked to sit with head in neutral position, the mouth wide open and tongue protruding to its maximum and the airway assessed at eyelevel Patients with

- a) one finger insinuation at the temporomandibular joint
- b) more than 2 finger breadths (>4cms) of mouth opening (inter- incisor distance)
- c) more than 3 finger breadths of thyromental distance (>6cms ) - submandibular space
- d) Mallampati class I view –visualization possible of the soft palate, entire uvula, anterior and the posterior tonsillar pillars.
- e) Normal neck movements – Flexion, Extension and side to side movements were included in our study.

Patients fulfilling above criteria were included in our study.

In addition to the airway assessment, respiratory system and cardiovascular system were assessed.

Following investigations were done before taking any patient for surgery :

1. Complete blood count.
2. Urine – sugar, albumin and microscopy.
3. Random blood sugar, Serum creatinine, Blood urea.

4. Electro-cardio-gram (if necessary).
5. Tests to detect infection with Human Immunodeficiency Virus and Hepatitis B Virus

Only ASA Grade I patients with normal airway anatomy were taken into our study. Patients likely to be included in the study were kept fasting over night .Patients were given 0.1mg/kg Tab Diazepam per oral HS and 2 hours preoperatively on the morning of surgery.

A written informed consent was taken.

#### **RANDOMISATION :**

Patients of either sex were randomly allocated into group P1 and group P2 by computer generated random numbers.

1. Group P1 received 2mg/kg Propofol +3µg/kg Fentanyl.
2. Group P2 received 4mg/kg Propofol+ 3µg/kg Fentanyl.

#### **DESIGN OF THE STUDY:**

IV line was secured using 18G canula and all patients were preloaded with 10ml/kg body weight crystalloid over 15 min.

ECG, NIBP, SPO<sub>2</sub> were monitored. Baseline Heart rate, SPO<sub>2</sub> and Blood Pressure (Systolic, Diastolic, MAP) were recorded.

The study drugs were injected into the forearm vein in the following sequence- contents of the 5 ml syringe –Fentanyl 3 µg/kg over 15 seconds and after 1 minute, administration of the contents of the 50 ml syringe containing Xylocard 0.2 mg/kg and Propofol 2 or 4 mg/kg over 30 seconds.

SPO<sub>2</sub>, HR, BP-SBP, DBP, MAP 1 minute after administration of study drugs were recorded.

Difference between the Pre induction baseline HR and B.P. readings and the corresponding readings 1 minute after the completion of injection of the study drugs but prior to laryngoscopy and intubation was taken as the effect of drugs on the cardiovascular system.

1minute after the administration of the study drugs, direct laryngoscopy was performed using appropriate Mcintosh curved blade and the intubating conditions were assessed as per the MODIFIED HELBO- HANSEN'S SCORING SYSTEM<sup>24,34</sup>

**TABLE No:18**  
**MODIFIED HELBO-HANSEN'S SCORING SYSTEM OF INTUBATING**  
**CONDITIONS :**

Variable	1	2	3	4
Jaw relaxation	Complete	Slight tone	Stiff	Rigid
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	1-2 bouts	3-4 bouts	>4bouts, persistent
Limb movements	None	Slight	Moderate	Severe

**We have considered:**

- a) Unacceptable intubating conditions - Total score of 8 or more
- b) Acceptable intubating conditions - Total score of 7 or less
- c) Successful intubation - Total score of 7 or less coupled with first attempt endotracheal intubation with appropriate sized cuffed endotracheal tubes .
- d) Failure- Inability to intubate in the first attempt was considered as failure. In these cases Suxamethonium was used before second attempt at endotracheal intubation.

More than 20 % difference between the Pre induction baseline HR and BP readings and the corresponding readings 1 minute after the completion of injection of the study drug but prior to laryngoscopy was considered as effect of the drug on cardiovascular system.

SPO<sub>2</sub>, HR and BP –SBP, DBP, MAP were recorded 1 minute and 3 minutes post intubation. More than 20 % difference between the Pre induction baseline HR and BP readings and the corresponding readings 1 minute post intubation was considered as pressor response to laryngoscopy and intubation. HR and BP were recorded 3 minutes post intubation to know whether HR and BP reached the baseline or not.

Any side effects of the study drugs used like:

- 1. Pain on injection
- 2. Myoclonus
- 3. Apnoea
- 4. Hypersensitivity
- 5. Cardio-Vascular Events like
  - a) Bradycardia-Heart rate less than 60 bpm
  - b) Hypotension B.P- fall > 20 % from baseline was noted

B.P fall 30 % was treated with volume infusion and vasopressor  
- Inj. Mephentermine, in incremental doses titrated to patient response.

After recording the vitals and assessing the intubating conditions, anaesthesia was maintained with 34% Oxygen + 66% Nitrous oxide + Inhalational agent + Non-depolarizing muscle relaxants with intermittent positive pressure ventilation using Bain's circuit. At the end of the surgical procedure, patients were reversed with Neostigmine 0.05mg/kg and Atropine 0.02 mg/kg.



## STATISTICAL METHODS

- All characteristics were summarized descriptively.
- For continuous variables, the summary statistics of N, mean, standard deviation (SD) were used.
- For categorical data, the number and percentage were used in the data summaries. Chi-square ( $\chi^2$ )/Fisher exact test was employed to determine the significance of differences between groups for categorical data.
- The difference of the means of analysis variables was tested with the unpaired t-test. If the p-value was  $< 0.05$ , then the results will be considered to be significant.
- Data were analyzed using SPSS software v.23.0.

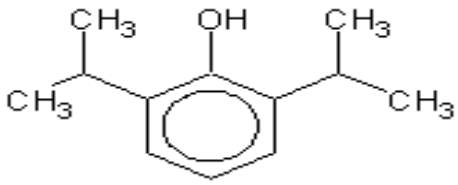
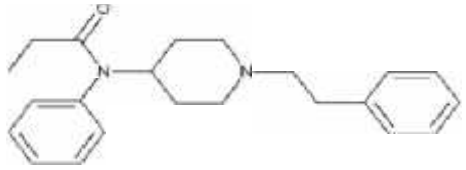
**TABLE No: 19**

**HISTORICAL REVIEW OF USE OF PROPOFOL**

AUTHOR AND YEAR	STUDY
1977- Kay and Rolley <sup>32</sup>	Ist clinical trial with ICI 35868(PROPOFOL) as i.v. anaesthetic agent
1980 Rogers KM et al <sup>33</sup>	I V induction agent Propofol
1980 Rutter D V et al <sup>34</sup>	I V induction agent Propofol
1990 Kallar S <sup>7</sup>	Tried tracheal intubation with Propofol without muscle relaxant.

**TABLE NO. 20**

**COMPARATIVE PHARMACOLOGY OF PROPOFOL AND FENTANYL<sup>36</sup>**

STRUCTURAL FORMULAE:	
<b>PROPOFOL</b> 	<b>FENTANYL</b> 

	PROPOFOL	FENTANYL
APPEARANCE	Milky white emulsion	Clear solution
STABILITY:	Stable at room temperature	Stable at room temperature
<b>PHYSICOCHEMICAL PROPERTIES:<sup>36</sup></b>		

PHARMACOKINETICS: <sup>36</sup>		
	PROPOFOL	FENTANYL
pH	6.8-7	4-7.5
Pka	11	8.4
Protein binding (%)	98%	84%
Volume of distribution(l/kg)	2- 10	3 - 5
Clearance rate(ml/min/kg)	20 - 30	10-20
Elimination t 1 / 2 /(hrs)	4 - 23	3 - 5

**TABLE NO.20** <sup>36,40,41</sup>

	PROPOFOL	FENTANYL
HEART RATE	or	
MEAN ARTERIAL PRESSURE		No effect or
CARDIAC OUTPUT		No effect
SYSTEMIC VASCULAR RESISTANCE		No effect
dP/Dt (Contractility)	( Negative inotropic effect)	No effect
Venodilatation		No effect or
Pressor response to intubation		

**Heart rate:**

Propofol does not alter the sinoatrial or the atrioventricular nodal function in normal patients or even in those with Wolff Parkinson White syndrome. Heart rate often remains unchanged despite the decreases in systolic blood pressure. Profound bradycardia may occur and it is treated with agonists like Isoproterenol.

**Blood pressure:**

Inhibition of sympathetic vasoconstrictor nerve activity and negative inotropic effect of Propofol contributes to the decrease in blood pressure.

Blood pressure effects are exaggerated in hypovolemic, elderly and the patients with compromised LV function due to coronary artery disease. Adequate hydration before rapid intravenous administration of Propofol is therefore recommended.

**PHARMACODYNAMICS:**<sup>36,39</sup>

**TABLE No: 20**

**RESPIRATORY SYSTEM:**

	PROPOFOL	FENTANYL
Airway reflexes: Supraglottic	making insertion of and infraglottic airways easier.	No data regarding instrumentation.
Mechanics:  Respiratory rate:  Tidal volume :  Minute ventilation :  Apnoea :	     23 – 35% patients	     Normal /   Yes
Bronchial tone :	Mild bronchodilatation	No effect
Ventilatory response to hypoxia and hypercarbia:		

**INSTRUMENTATION:**

Propofol depresses the pharyngeal reflexes and the laryngeal tone making the insertion of supraglottic airways (nasopharyngeal/oropharyngeal/laryngeal mask) easier.

Dose dependent depression of ventilation with apnoea produced by Propofol may also facilitate endotracheal intubation.

Subsequent studies by various authors opined that insertion of endotracheal tube insertion was possible without the use of muscle relaxants after induction with Propofol alone. The intubating conditions therein was acceptable but not as ideal as with relaxants.

**TABLE No: 21 A**  
**CENTRAL NERVOUS SYSTEM:<sup>36</sup>**

	PROPOFOL	FENTANYL
Cerebral Blood Flow :		or
Cerebral Perfusion Pressure:		No effect
Cerebral Metabolic Requirement of :		
Intracranial pressure :		or
Intraocular pressure :		No effect
EEG effect :	initial increase in $\alpha$ and then shift to $\delta$ and $\theta$ frequency. Maybe used to treat seizures but can also stimulate seizures.	Depression progressing to high voltage waves with ceiling effect.

**TABLE No: 21 B**

**Plasma concentrations – effects relationships of Propofol :<sup>37</sup>**

1.6µg/ml plasma concentration	Concentration beyond which awakening is lost
2.2µg/ml plasma concentration	Concentration beyond which orientation is lost
2.2 to 3.3µg /ml plasma concentration	Cp 50 preventing response to verbal response
16µg /ml plasma concentration	Cp 50 preventing response to surgical stimulus

**MATERNAL AND FETAL EFFECTS:<sup>36</sup>**

DRUG	UTERINE BLOOD FLOW	ABILITY TO CROSS PLACENTA	UTERINE TONE	FETAL EFFECTS
PROPOFOL	No change	Yes	No effect reported	No effect at lower doses.
FENTANYL	No change	Yes	No effect	Respiratory depression

**TABLE No: 22****METABOLISM:<sup>36,38</sup>**

DRUG	HEPATIC	CYT-P 450	PULMONARY	RENAL	ELIMINATION
PROPOFOL	Conjugation producing water soluble sulfates and glucuronides	Ring hydroxylation to produce 4-OH Propofol	30% of the total metabolism producing , - diisopropyl-, - quinol.	<0.3% excreted unchanged in urine	kidneys
FENTANYL	N-dealkylation and hydroxylation producing Norfentanyl, Hydroxypropionyl Norfentanyl			<10% excreted unchanged in urine	kidneys



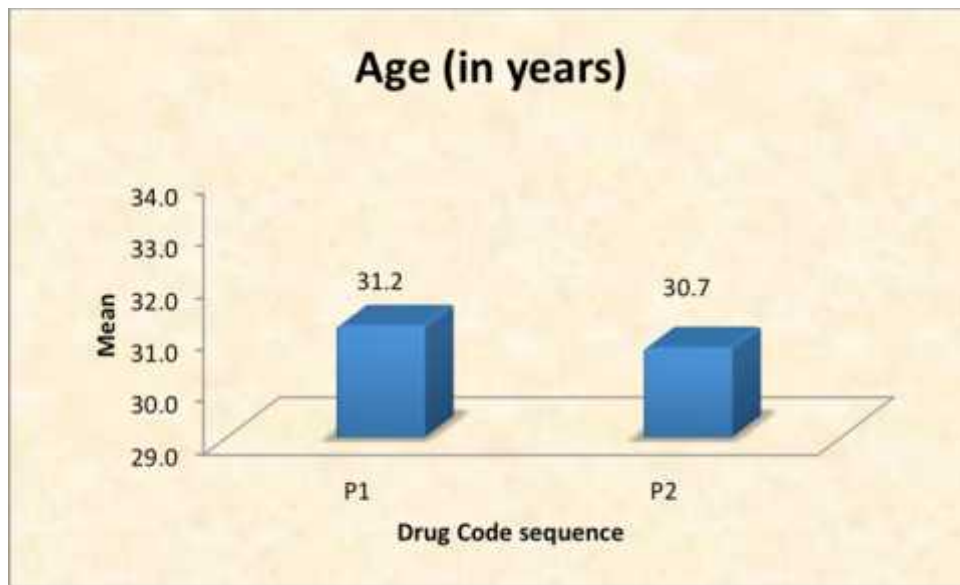
## OBSERVATIONS

**Table 23: Mean distribution of Age and weight of cases between study groups**

Parameters	P1		P2		p value
	Mean	SD	Mean	SD	
Age (in years)	31.2	5.9	30.7	5.6	0.741
Wt. (in Kg)	53.1	7.1	53.4	5.4	0.832

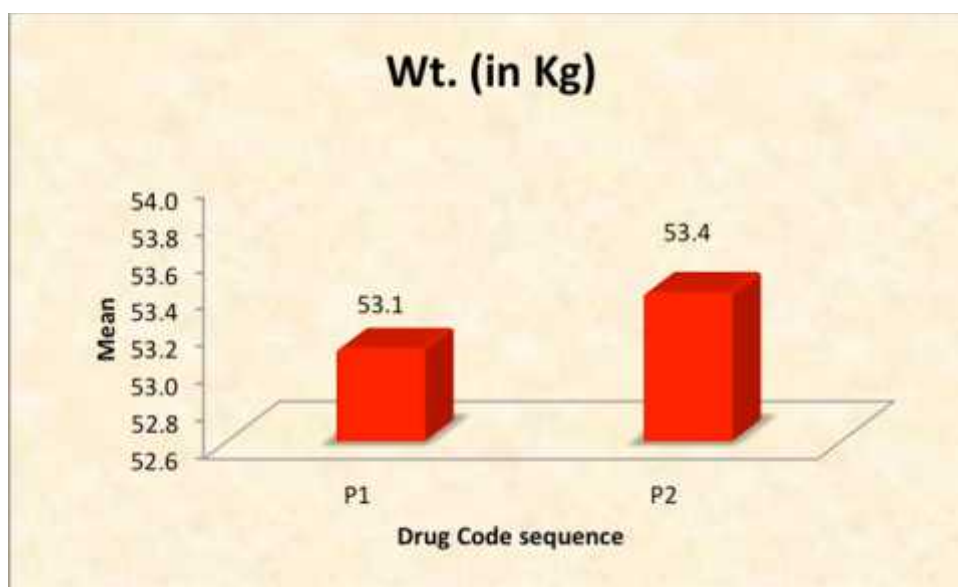
(Group P1 : Propofol 2mg/kg + Fentanyl 3 $\mu$ g/kg, Group P2 : Propofol 4mg/kg + Fentanyl 3 $\mu$ g/kg)

**Figure 1 : Mean distribution of Age of cases between study groups**



Group P1 : Propofol 2mg/kg + Fentanyl 3 $\mu$ g/kg, and Group P2 : Propofol 4mg/kg + Fentanyl 3 $\mu$ g/kg are comparable with respect to age in years(p=0.741).

**Figure 2: Mean distribution of weight of cases between study groups**



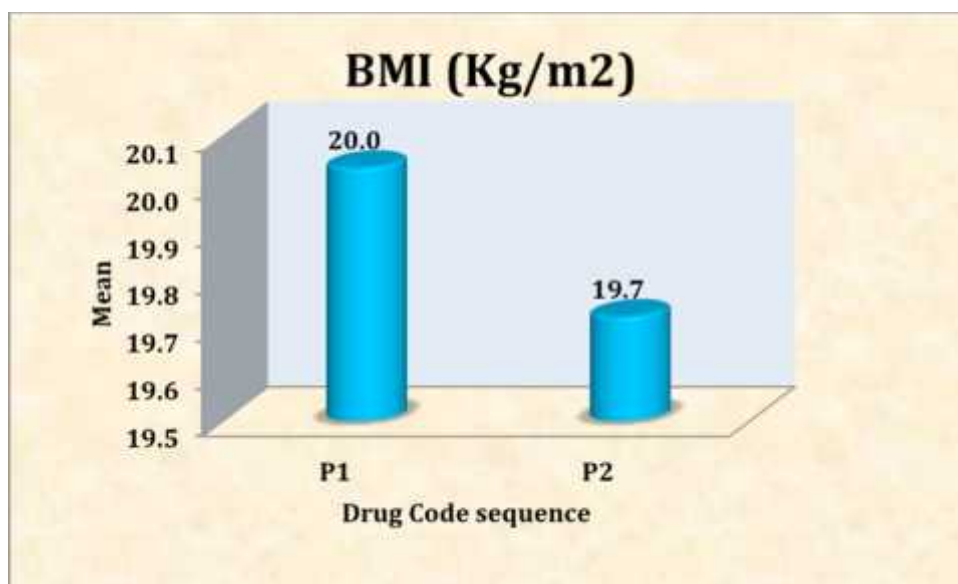
Group P1 : Propofol 2mg/kg + Fentanyl 3 $\mu$ g/kg, and Group P2 : Propofol 4mg/kg + Fentanyl 3 $\mu$ g/kg are comparable with respect to weight in kgs(p=0.832)

**Table 24: Mean distribution of BMI between study Groups**

BMI (Kg/m <sup>2</sup> )	P1		P2		p value
	Mean	SD	Mean	SD	
	20.0	1.3	19.7	1.0	0.242

(Group P1 : Propofol 2mg/kg + Fentanyl 3µg/kg, Group P2 : Propofol 4mg/kg + Fentanyl 3µg/kg)

**Figure 3: Mean distribution of BMI between study groupS**



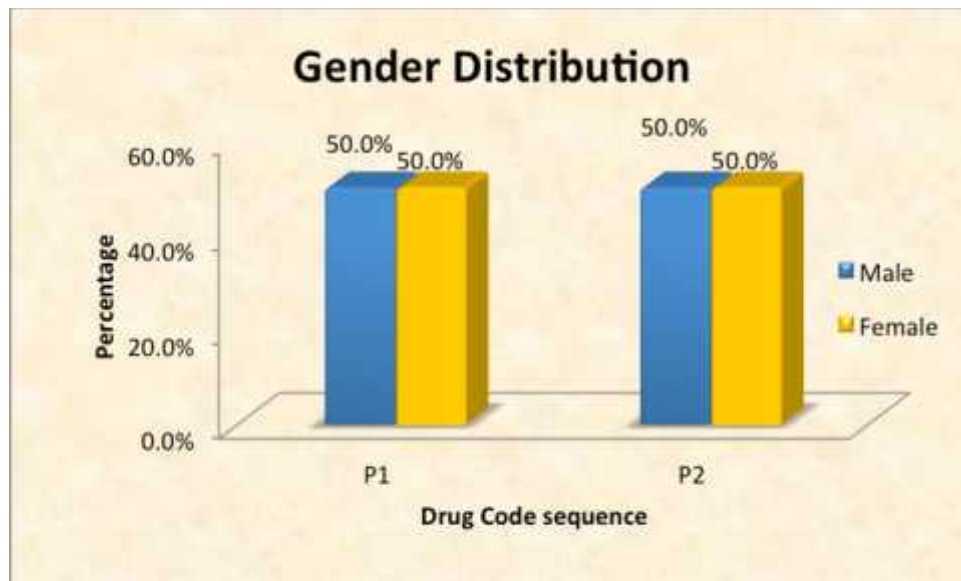
Group P1 : Propofol 2mg/kg + Fentanyl 3µg/kg, and Group P2 : Propofol 4mg/kg + Fentanyl 3µg/kg are comparable with respect to BMI (ht/m<sup>2</sup>) (p=0.242)

**Table 25: Distribution of cases between study groups according to Gender**

Gender	P1		P2		Total	
	N	%	N	%	N	%
Male	20	50.0%	20	50.0%	40	50.0%
Female	20	50.0%	20	50.0%	40	50.0%
Total	40	100.0%	40	100.0%	80	100.0%

(Group P1 : Propofol 2mg/kg + Fentanyl 3 $\mu$ g/kg, Group P2 : Propofol 4mg/kg + Fentanyl 3 $\mu$ g/kg)

**Figure 4: Distribution of cases between study groups according to Gender**

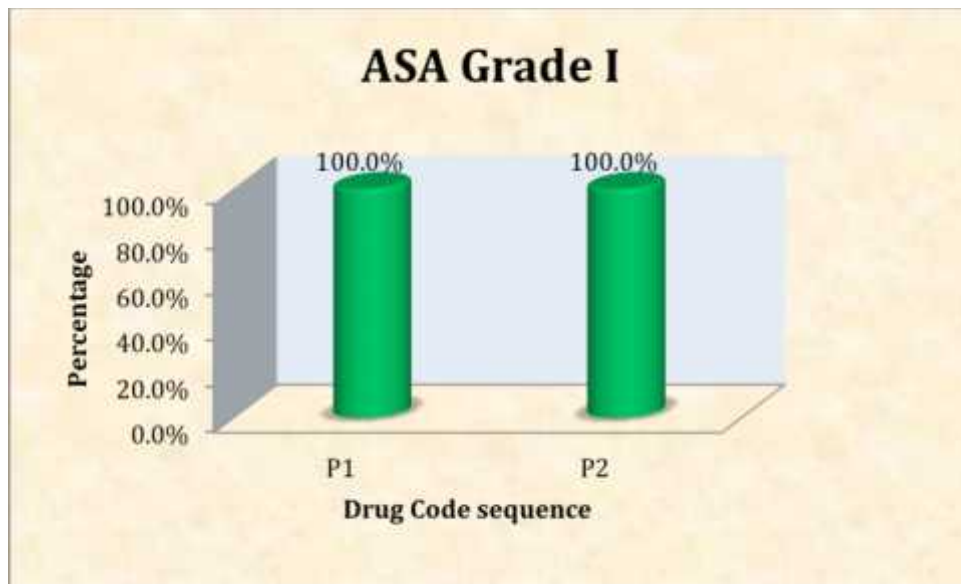


Sex distribution, male:female 50% : 50 % in both the groups.

**Table 26: Distribution of cases between study groups according to ASA Grading**

ASA Grade	P1		P2		Total	
	N	%	N	%	N	%
Grade I	40	100.0%	40	100.0%	80	100.0%
Total	40	100.0%	40	100.0%	80	100.0%

**Figure 5: Distribution of cases between study groups according to ASA Grading**



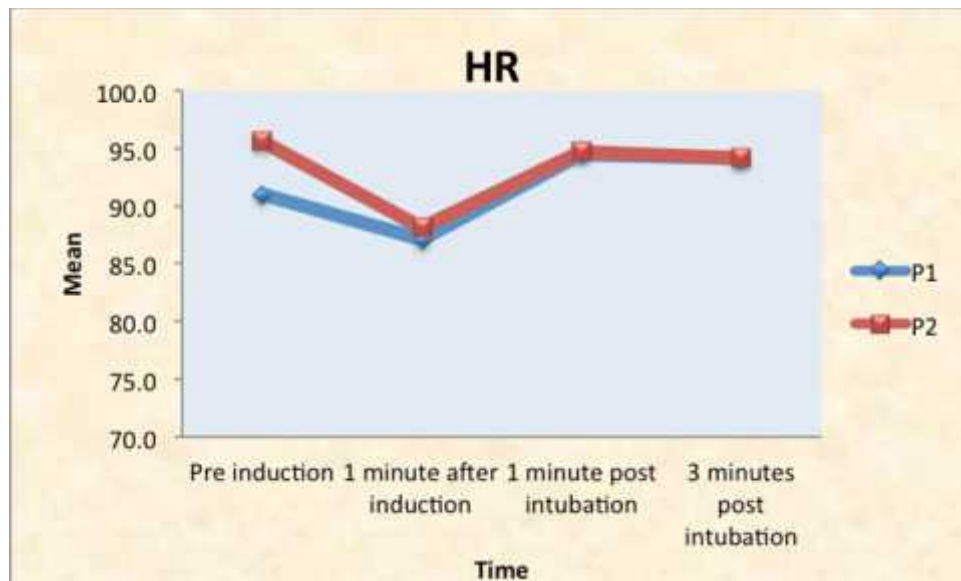
All the 80 patients belonged to ASA Grade I.

**Table 27: Comparison of Mean HR of cases between study groups according to different time point**

HR	P1		P2		p value
	Mean	SD	Mean	SD	
<b>Pre induction</b>	91.0	16.8	95.7	16.6	0.21
<b>1 minute after induction</b>	87.0	12.6	88.1	10.9	0.676
<b>1 minute post intubation</b>	94.5	16.5	94.7	13.2	0.947
<b>3 minutes post intubation</b>	94.1	17.5	94.2	14.2	0.972

(Group P1 : Propofol 2mg/kg + Fentanyl 3 $\mu$ g/kg, Group P2 : Propofol 4mg/kg + Fentanyl 3 $\mu$ g/kg)

**Figure 6: Variation of Mean HR of cases between study groups according to different time point**



Preinduction heart rates in Group P1 ( $91 \pm 16.8$ ) and Group P2 ( $95.7 \pm 16.6$  bpm) are comparable ( $p = 0.21$ ).

### **1 minute after Induction :**

After the injection of the study drugs, there was a reduction in the heart rate in both the study groups with respect to preinduction values. 1 minute after induction heart rate were Group P1 ( $87 \pm 12.6$ ) and Group P2 ( $88.1 \pm 10.9$ ). There was no statistically significant difference between the post induction heart rates of the study groups. ( $p = 0.676$ ).

### **One minute post intubation:**

After the post induction decrease, the heart rates gradually increased in both the groups. In Group P1 ( $94.5 \pm 16.5$ ) the heart rates (bpm) reached preinduction values and overshoot the preinduction values by 2-3 beats. But in Group P2 ( $95 \pm 14$ ), the heart rate (bpm) remained below the baseline preinduction values. At one minute post intubation, the heart rates in both the groups were comparable with no statistically significant difference. ( $p = 0.947$ ).

### **3 minutes post intubation:**

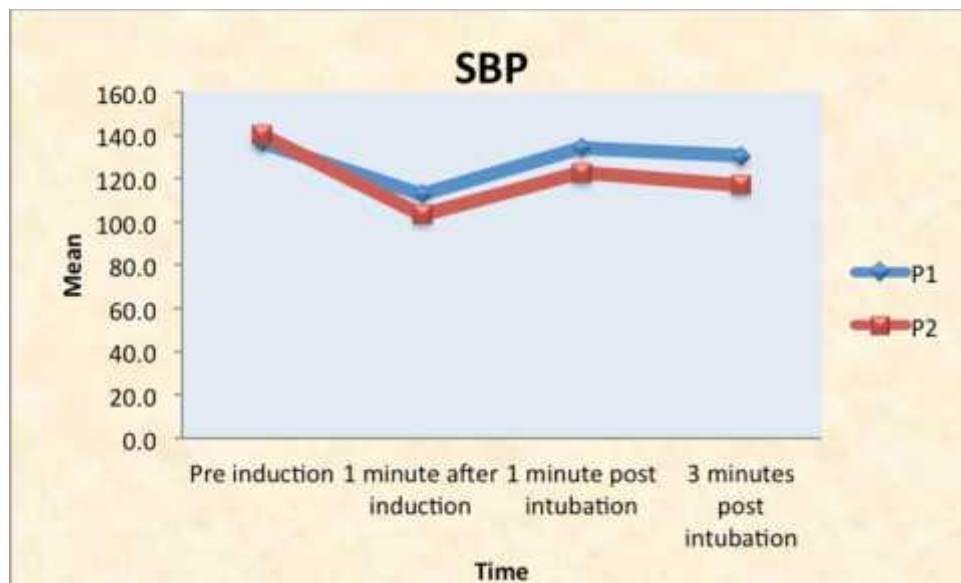
There is no statistically significant difference between the heart rates in both groups. ( $p = 0.972$ ). The heart rates (bpm) in Group P1 ( $94.1 \pm 17.5$ ) overshoot the preinduction values unlike in Group P2 ( $94.2 \pm 14.2$ ) which was still below the preinduction value.

**Table 28: Comparison of Mean SBP of cases between study groups according to different time point**

SBP	P1		P2		p value
	Mean	SD	Mean	SD	
<b>Pre induction</b>	137.0	20.9	140.2	17.1	0.459
<b>1 minute after induction</b>	112.8	19.9	103.2	15.0	0.018 (sig)
<b>1 minute post intubation</b>	134.3	28.5	122.8	21.7	0.045(sig)
<b>3 minutes post intubation</b>	130.5	31.3	116.9	19.7	0.023(sig)

Group P1 : Propofol 2mg/kg + Fentanyl 3µg/kg, Group P2 : Propofol 4mg/kg + Fentanyl 3µg/kg)

**Figure 7: Variation of Mean SBP of cases between study groups according to different time point**



**Preinduction:**

The systolic blood pressures (mmHg) in Group P1( $137 \pm 20.9$ ) and Group P2 ( $140.2 \pm 17.1$ ) are comparable with no significant statistical difference (p = 0.459).



**1 minute after induction:**

Post injection of the study drugs, there was a reduction in the systolic blood pressures in both the groups. Post induction systolic blood pressures (mmHg) were - Group P1 ( $112.8 \pm 19.9$ ) > Group P2 ( $103.2 \pm 15$ ).

There was significant statistical difference between the post induction systolic blood pressure values of both the groups ( $p = 0.018$ ).

**1 minute post intubation:**

After the initial reduction post induction, the systolic blood pressure values (mmHg) gradually increased in both the groups. In Group P1 ( $134.3 \pm 28.5$ ), and Group P2 ( $121 \pm 20$ ), the systolic blood pressure values still remained below the preinduction values. Systolic blood pressures in Group P2 was significantly lower ( $p = 0.045$ ) than that of Group P1.

**3 minute post intubation:**

Increase in systolic blood pressures 3 minute post intubation was observed. But systolic blood pressure values (mmHg) were below the preinduction values in both the groups. Group P1 ( $130.5 \pm 31.3$ ) > Group P2 ( $116.9 \pm 19.7$ ).

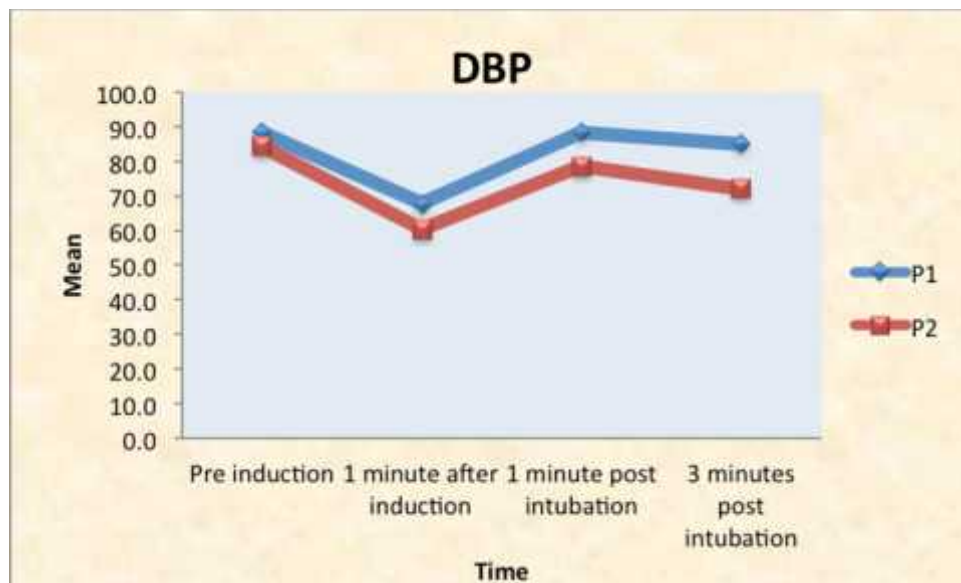
There was statistically significant difference between the systolic blood pressures of both the groups ( $p = 0.018$ )

**Table 29: Comparison of Mean DBP of cases between study groups according to different time point**

DBP	P1		P2		p value
	Mean	SD	Mean	SD	
<b>Pre induction</b>	88.5	20.0	84.2	18.3	0.316
<b>1 minute after induction</b>	67.8	12.9	60.3	13.5	0.013(sig)
<b>1 minute post intubation</b>	88.3	20.2	78.6	14.5	0.015(sig)
<b>3 minutes post intubation</b>	85.0	25.4	71.9	17.1	0.009(sig)

Group P1 : Propofol 2mg/kg + Fentanyl 3µg/kg, Group P2 : Propofol 4mg/kg + Fentanyl 3µg/kg)

**Figure 8: Variation of Mean DBP of cases between study groups according to different time point**



The preinduction diastolic blood pressures(mmHg) of Group P1 ( $88.5 \pm 20$ ) and Group P2 ( $84.2 \pm 18.3$ ) are comparable with no significant statistical difference ( p = 0.316)

### **1 minute after induction:**

The diastolic blood pressures (mmHg) are -

Group P1 ( $67.8 \pm 12.9$ ) > Group P2 ( $60.3 \pm 13.5$ ).

Statistically significant difference was observed in the post induction diastolic blood pressures both the groups ( $p = 0.013$  sig)

1 minute post intubation: After the post induction diastolic blood pressures gradually increased in both groups.

1 minute post intubation, the diastolic blood pressures Group P2 ( $78.6 \pm 14.5$ ) still remained below the baseline while the diastolic blood pressures of Group P1 ( $88.3 \pm 20.2$ ) almost reached the preinduction values.

The diastolic blood pressure values in Group P2 were significantly lower than Group P1 ( $p = 0.015$ ).

### **3 minute post intubation:**

The diastolic blood pressures (mmHg) 3 minute post intubation in Group P1 ( $85 \pm 25.4$ ) and Group P2 ( $71.9 \pm 17.1$ ) group remained below the preinduction value.

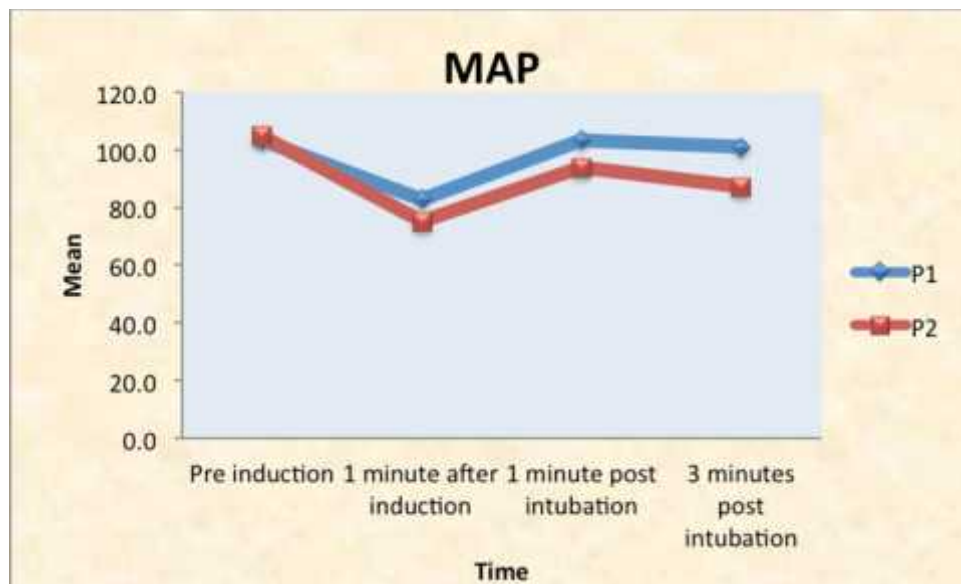
Diastolic blood pressures in Group P2 were significantly lower than the diastolic blood pressure observed Group P1 ( $p = 0.009$ )

**Table 30: Comparison of Mean MAP of cases between study groups according to different time point**

MAP	P1		P2		p value
	Mean	SD	Mean	SD	
<b>Pre induction</b>	103.3	14.3	104.6	13.5	0.671
<b>1 minute after induction</b>	82.8	14.6	74.8	13.2	0.012(sig)
<b>1 minute post intubation</b>	103.4	21.9	93.8	15.9	0.028(sig)
<b>3 minutes post intubation</b>	100.9	25.9	87.2	16.8	0.006(sig)

Group P1 : Propofol 2mg/kg + Fentanyl 3µg/kg, Group P2 : Propofol 4mg/kg + Fentanyl 3µg/kg)

**Figure 9: Variation of Mean MAP of cases between study groups according to different time point**



**Pre induction:**

The MAP (mmHg) of Group P1 (103.3±14.3) and Group P2 (104.6±13.5) are comparable with no statistically significant difference (  $p = 0.671$  ).

**1 minute after induction:**

There is a reduction in the MAP values calculated post injection of the study drugs.

MAP (mmHg) observed were -

Group P1 (82.8±14.6) > Group P2 (74.8±13.2).

The reduction in MAP is seen to be directly proportional to the dose of Propofol. Group P2 having the maximum reduction compared to Group P1. The mean arterial pressure values in Group P2 were significantly lower than Group P1 ( $p=0.012$ ).

**1 minute post intubation:**

Following an initial reduction post induction, MAP gradually increased in both the groups with Group P1(103.4±21.9) MAP reaching the preinduction value while in Group P2(93.8±15.9) study group MAP values remaining below the preinduction values.

1 minute post intubation, MAP in Group P2 was almost significantly lower than Group P1. (  $p = 0.028$  ).

**3 minutes post intubation:**

Group P1 (100.9±25.9) > Group P2(87.2±16.8).

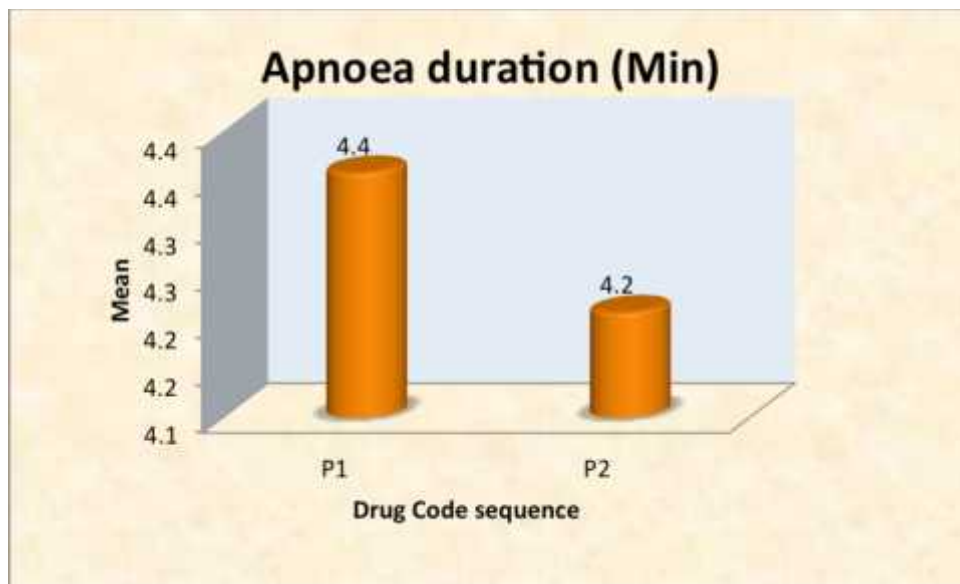
The MAP values in Group P2 were significantly lower than that of Group P1. ( $p=0.006$ )

**Table 31: Comparison of Mean Apnoea duration between study groups according to different time point**

Parameters	P1		P2		p value
	Mean	SD	Mean	SD	
Apnoea duration (Min)	4.4	0.5	4.2	0.6	0.281

Group P1 : Propofol 2mg/kg + Fentanyl 3µg/kg, Group P2 : Propofol 4mg/kg + Fentanyl 3µg/kg)

**Figure 10: Mean Apnoea duration between study groups according to different time point**



**APNOEA DURATION:**

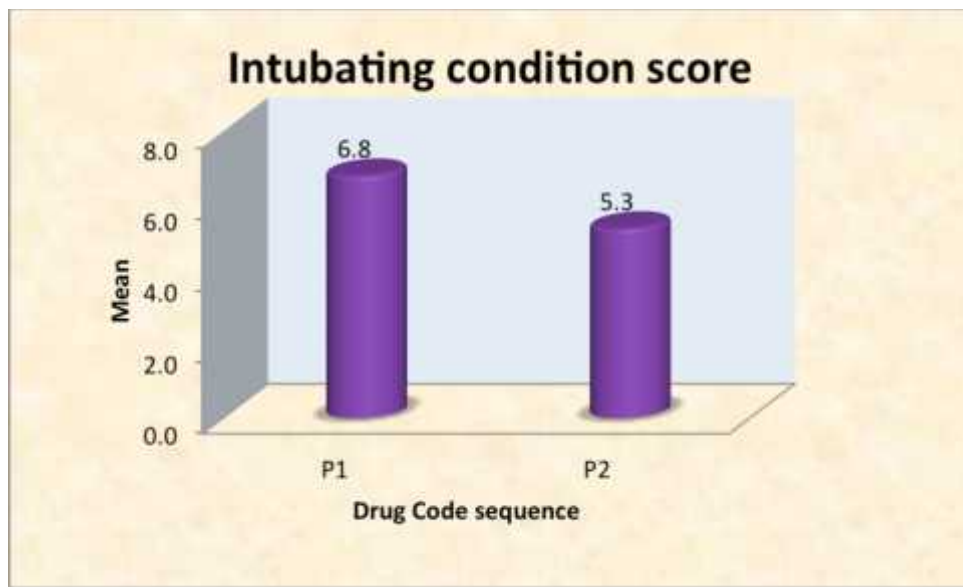
Duration of apnoea in both the groups was similar with no statistically significant difference ( p = 0.281) allowing successful endotracheal intubation in the first attempt.

**Table 32: Comparison of Mean Intubating condition score between study groups according to different time point**

Parameters	P1		P2		p value
	Mean	SD	Mean	SD	
<b>Intubating condition score</b>	6.8	2.2	5.3	1.0	<0.001(sig)

Group P1 : Propofol 2mg/kg + Fentanyl 3µg/kg, Group P2 : Propofol 4mg/kg + Fentanyl 3µg/kg)

**Figure 11: Comparison of Mean Intubating condition score between study groups according to different time point**



In our study, the intubating condition score of  $\leq 7$  was considered as an indicator of acceptable intubating conditions..

The intubating condition scores were

Group P1 (6.8) > Group P2 (5.3).

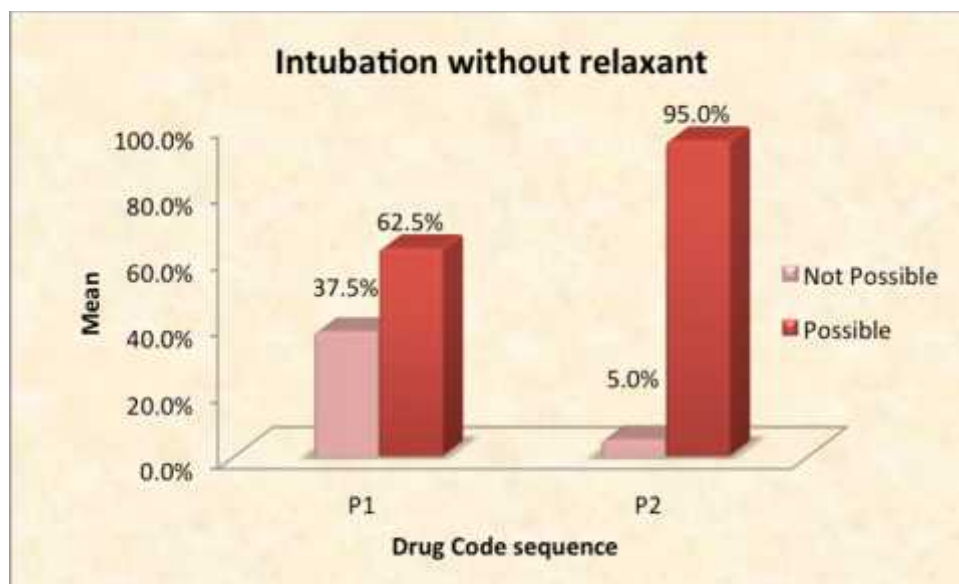
Intubating conditions scores in Group P2 group was lower than Group P1, the statistical difference being very highly significant (  $p < 0.001$  )

**Table 33: Distribution of cases between study groups according to Intubation without relaxant**

Intubation without relaxant	P1		P2		Total		p value
	N	%	N	%	N	%	
Not Possible	15	37.5%	2	5.0%	17	21.2%	<0.001(sig)
Possible	25	62.5%	38	95.0%	63	78.8%	
Total	40	100.0%	40	100.0%	80	100.0%	

Group P1 : Propofol 2mg/kg + Fentanyl 3µg/kg, Group P2 : Propofol 4mg/kg + Fentanyl 3µg/kg)

**Figure 12: Distribution of cases between study groups according to Intubation without relaxant**



The incidence of successful endotracheal intubation with Propofol alone was Group P2(95%) > Group P1(62.5%).

The difference in the incidence of successful intubation between Group P1(62.5%) and Group P2 (95%) is statistically highly significant. ( p <0.001 HS).



Hence we deduce that the difference in incidence of successful intubation between Group P1(62.5%) and Group P2(95%) is also highly significant.

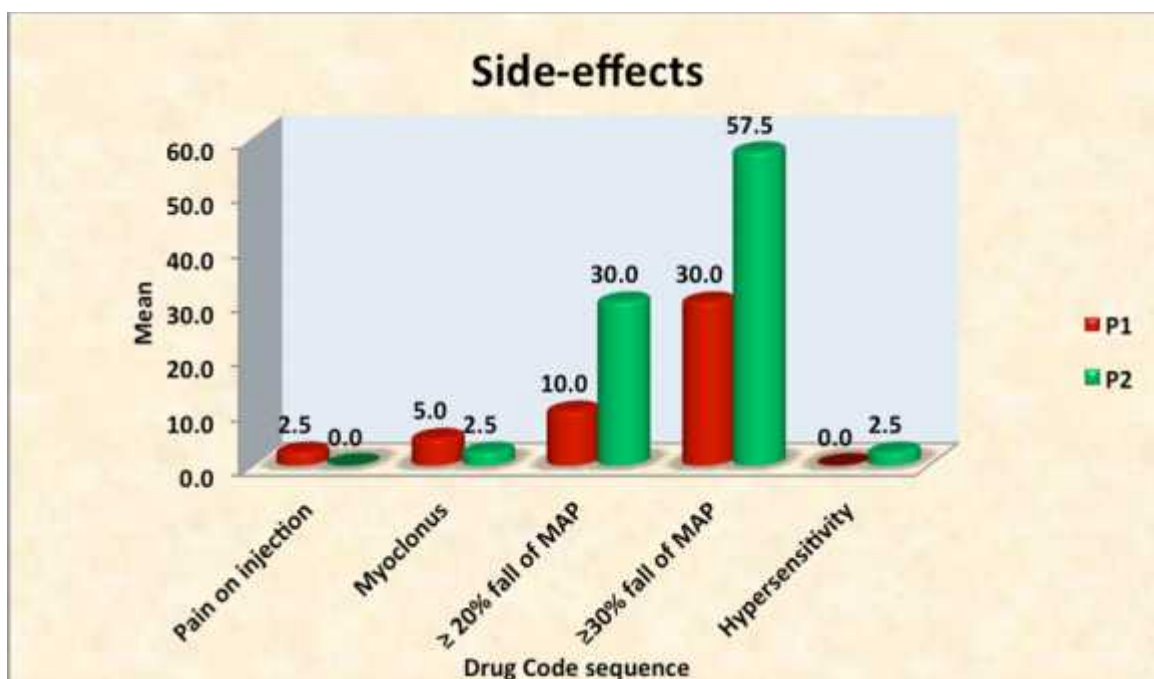
The success rate of endotracheal intubation is directly proportional to the dose of Propofol employed. Increasing the dose of Propofol from 2mg/kg to 4mg/kg increased the success rate of intubation by 34%.

**Table 34: Distribution of cases between study groups according to Side effects**

Side-effect	P1		P2		p value
	N	%(out of 40 cases)	N	%(out of 40 cases)	
Pain on injection	1	2.5	0	0.0	0.314
Myoclonus	2	5.0	1	2.5	0.556
20% fall of MAP	4	10.0	12	30.0	0.025 (Sig)
30% fall of MAP	12	30.0	23	57.5	0.013 (Sig)
Hypersensitivity	0	0.0	1	2.5	0.314
Incidence of total side effect (%)	47.5		92.5		<0.001 (Sig)

Group P1 : Propofol 2mg/kg + Fentanyl 3µg/kg, Group P2 : Propofol 4mg/kg + Fentanyl 3µg/kg)

**Figure 13: Distribution of cases between study groups according to Side effects**



The incidence of total side effects appears to be related to the dose of Propofol Group P2(92.5 %) > Group P1(47.5%).

Pain on injection: Wincing facial movement of the patient in response to the injection of study drugs was taken as indicator of pain.

In Group P2, there was no pain on injection and incidence of pain on injection in the study groups - Group P1 is (2.5%) and is statistically insignificant. 2. Myoclonus:

Incidence of myoclonus in fingers of upper limb was -

Group P1(5%)> Group P2(2.5%)

The difference in incidence of myoclonus among the study groups was statistically insignificant.

### **3. Hypersensitivity:**

Hypersensitivity was observed in 1/40 (2.5%) patients of Group P2.

The patient developed cutaneous erythematous rashes along the course of the cannulated vein coupled with bronchospasm .

Histamine release (probably Propofol formulation induced) could be the cause of rashes and bronchospasm.

The patient responded to deepening the plane of anaesthesia and injection Dexamethasone 8mg i.v. In this patient haemodynamics was maintained within normal limits.

No anaphylactic reaction causing life threatening haemodynamic decompensation was observed.

#### **4. Hypotension:**

The incidence of Hypotension was

Group P2 (87.5%) > Group P1 (40%).

In all these patients, hypotension was the sole clinical manifestation without concomitant clinical findings in other systems.

The incidence of mild Hypotension (up to 20 % fall in MAP ) was statistically significant (p = 0.025 )

Group P2 (30 %) > Group P1(10%)

Fast crystalloid administration counteracted the hypotension.

The incidence of severe hypotension (30% fall in MAP) was significantly higher (p = 0.013).

Group P 2(57.5%) > Group P1 (30%).

Fast crystalloid infusion coupled with incremental doses of vasopressor, mephentermine titrated to response restored blood pressure to normal levels.

We have not encountered any case of cardiovascular collapse in our entire study series.

## DISCUSSION

Endotracheal intubation which is an integral part of general anaesthesia is commonly facilitated by the administration of muscle relaxants following intravenous induction agent. Suxamethonium produces ideal condition for elective as well as rapid sequence endotracheal intubations. Hence it is the gold standard against which other alternatives to facilitate endotracheal intubation are compared. But the side effects like myalgia, hyperkalemia, bradycardia /asystole, increased intraocular and intracranial pressures and sometimes life threatening malignant hyperthermia limits the use of Suxamethonium . Use of nondepolarising muscle relaxants to facilitate endotracheal intubation has limitations such as prolonged neuromuscular blockade or the inability to reverse the paralysis quickly if tracheal intubation is not possible or when the surgery is of short duration but intubation is mandatory<sup>19</sup>.

Hence some investigators attempted to carry out endotracheal intubation without using muscle relaxants. The advantages being preservation of spontaneous respiration and the avoidance of the complications of muscle relaxant use, misuse and their antagonism. Endotracheal intubation under topical anaesthesia was safe but aesthetically unacceptable to some patients. Intubation under volatile anaesthetics preserved spontaneous respiration but had disadvantages like Laryngospasm, Short intubation time and Myocardial depression.

Propofol depresses pharyngeal and laryngeal tone making insertion of supraglottic airways easier. Propofol in certain doses depresses the laryngeal reflexes enabling laryngoscopy, abducts and immobilizes the vocal cords<sup>11</sup> . These unique airway properties of Propofol made some authors attempt endotracheal intubation under Propofol alone

without the use of muscle relaxants in adults<sup>8</sup> and children<sup>10</sup>. In these studies, intubating conditions under Propofol alone ranged from- Impossible/ unacceptable. Acceptable but not -as ideal as produced by Succinylcholine.

### **NEED OF OUR STUDY:**

Above mentioned conflicting conclusions regarding intubating conditions with Propofol without muscle relaxants prompted us to undertake this prospective randomized triple blind comparative study to evaluate the feasibility/ nonfeasibility of endotracheal intubation using arbitrarily chosen prefixed doses of Propofol 2mg/kg or 4mg/kg bodyweight without the use of muscle relaxants. Study of available literature reveals that supplementation of Propofol with opioid-Alfentanil further improved the intubating conditions<sup>8</sup>. In our study, we supplemented Propofol with 3µg/kg Fentanyl because of a) Easy availability in our setup b) lack of studies on Fentanyl pretreatment in available literature.

### **CASE SELECTION:**

Induction doses of Propofol causes hypotension and myocardial depression in a dose dependent manner. So we chose ASA Grade I patients for our study. Further we selected young adults patients with favourable airway anatomy (Mallampati class I view) because in these patients the feasibility / nonfeasibility of endotracheal intubation probably is solely determined by study drugs. We have excluded Mallampati class II ,III and IV from our study since in addition to the study drugs, the pre existent anatomical and or pathological airway abnormalities could also affect the intubating conditions.

## SCORING SYSTEM FOR INTUBATING CONDITIONS:

Many scoring systems to evaluate intubating conditions are available. Based on study done by S. Grant *et al*<sup>15</sup>, J.M.Blair *et al*<sup>21</sup> and Gupta A *et al*<sup>22</sup>, we chose Modified Helbo Hansen's scoring system as it is more descriptive including 5 parameters, each parameter assessed and graded individually. We preferred Modified Helbo Hansen scoring system over the other scoring systems where all the variables were clubbed together and assessed in the same plane without assigning individual scoring to each of the variable. In practice, all the variables need not be in the same plane at a given time of assessment.

We considered 4(out of 5) variables - Jaw relaxation, Ease of laryngoscopy, Position of vocal cords and Coughing as the factors likely to influence the feasibility of endotracheal intubation. Hence score  $\leq 7$  was considered as Acceptable intubating condition score.

We have not further graded the quality of tracheal intubation as good or excellent. We have not taken purposeful limb movements scoring into consideration as it may have been a somatic reaction unlikely to influence either the feasibility or the intubating conditions. Here we differ from the study of S.Grant *et al*<sup>15</sup> who considered all the variables including the limb movements of Modified Helbo Hansen's scoring system to assess the intubating conditions. In our study, the incidence and intensity of purposeful /gross limb movements, (Propofol 2mg/kg + Fentanyl 3 $\mu$ g/kg group only) at the time of Laryngoscopy, was minimal and we were still able to intubate in first attempt.. This conclusion is in agreement with the study of Dr. Srivastava *et al*<sup>19</sup>.

## **OUR STUDY V/S CORROBORATIVE STUDIES:**

### **Propofol 2mg/kg + Fentanyl 3µg/kg :**

Our intubation success rate (62.5%) with Propofol 2mg/kg + Fentanyl 3µg/kg is almost similar to the success rate (67%) in Mark S.Scheller *et al*<sup>10</sup> and Tsuda A *et al*<sup>20</sup> study. Our intubation success rate (62.5%) with Propofol 2mg/kg + Fentanyl 3µg/kg in patients is marginally lesser than that of Mangesh S Gore and Kalpana D Harnagale<sup>26</sup> (66.7%) in patients. Mangesh S Gore and Kalpana D Harnagale used i.v. Lignocaine 1.5mg/kg bolus after induction with Propofol. Lignocaine has been reported to be a useful adjunct to facilitate tracheal intubation in the doses of 1-2/kg.

A decrease in heart rate by 5% in our study post injection of study drugs agrees with a similar reduction ( 4%) in the heart rate observed in the study of S.Grant *et al*<sup>15</sup> .

In our study total incidence of hypotension was 40%. 19% fall in MAP (from preinduction to 1minute after induction) is almost similar to the MAP fall in the studies of R. Alexander *et al*<sup>16</sup> ( 21-22%) and James B Stevens and La Dona Wheatley<sup>14</sup> (16 -20%).

### **Propofol 4mg/kg + Fentanyl 3µg/kg:**

Our intubation success rate (95%) with Propofol 4mg/kg + Fentanyl 3µg/kg is almost similar to the success rate (95%) in studies done by Olmos *et al*<sup>3</sup> , Striebel *et al*<sup>4</sup> and (93%) J.M. Morgan *et al*<sup>23</sup> . Decrease in heart rate by 10 % in our study post injection of study drugs is slightly different when compared to the heart rate



change ( 13%) observed in the study of Dr. Uma Srivastava *et al*<sup>19</sup> .

In our study, the incidence (83%) and magnitude of fall in MAP ( 27% mmHg) in response to the injection of the study drugs was observed. We are unable to quote any corroborative study.

### **SAFETY OF STUDY DRUGS:**

We have taken into account the two side effects observed-

- 1) Hypotension
- 2) Histamine related phenomenon, for evaluating the safety of the study drugs in our series.

#### **1. HYPOTENSION:**

Young adult ASA grade I patients without any co morbid cardiac illnesses even after preloading were observed to have hypotension post injection of study drugs. The incidence and magnitude of hypotension was found to be related to the dose of Propofol. In some patients hypotension ( $\leq 30\%$  , incidence Group P1 10% and Group P2 57.5 %) was counteracted successfully by rapid infusion of crystalloids while in rest ( $\geq 30\%$  incidence Group P1 30% and Group P2 57.5%) incremental doses of vasopressor titrated to the blood pressure in addition to the fluid infusion restored the blood pressure to acceptable levels.

#### **2. HISTAMINE RELATED SIDE EFFECTS:**

2.5% incidence of histamine related side effects- bronchospasm coupled with cutaneous erythematous rashes was observed in Group P2 only while no such side effects were observed in the Group P2 study group. Histamine release could have

been due to Propofol formulation since Fentanyl is unlikely to release histamine. Since amount of histamine release is related to the dose of triggering agent, we thought that histamine related side effects were observed in Propofol 4mg/kg + Fentanyl 3 $\mu$ g /kg study group only. We have not encountered massive histamine release causing life threatening anaphylactic cardiovascular collapse in our entire study.

We infer based on our study findings that combination of Fentanyl 3 $\mu$ g /kg + Propofol 2 or 4mg /kg administered intravenously is reasonably safe.

## **CONCLUSION:**

We conclude that endotracheal intubation is possible in premedicated adult ASA Grade I patients with receiving 3 µg /kg Fentanyl + 2 or 4 mg/kg Propofol for induction without muscle relaxants and the intubating conditions are acceptable. The success of endotracheal intubation , the cardiovascular effects and the side effects are dose related . This technique is an alternative to the use of muscle relaxants on an individualized basis. We feel that Propofol 4mg/kg + Fentanyl 3µg/kg is the optimal dose required for intubation without the use of muscle relaxants.

## SUMMARY

The present study entitled “**EFFICACY OF DIFFERENT DOSES OF PROPOFOL FOR ENDOTRACHEAL INTUBATION – A RANDOMISED CLINICAL TRIAL**” was carried out at BLDE UNIVERSITY Shri.B.M.Patil Medical College, Hospital And Research Centre, Vijayapur, from December 2014 to June 2016.

Patients of either sex were randomly allocated into group P1 and group P2.

1. Group P1 received 2mg/kg Propofol +3µg/kg Fentanyl.
2. Group P2 received 4mg/kg Propofol+ 3µg/kg Fentanyl.

The demographic changes such as Age, Sex, Weight, BMI were comparable in all the groups.

The success rate of endotracheal intubation was 62.5% and 95% in Propofol 2mg/kg + Fentanyl 3µg /kg and Propofol 4mg/kg + Fentanyl 3µg /kg respectively.

The total incidence of hypotension was 40% and 83% in Propofol 2mg/kg + Fentanyl 3 µg /kg and Propofol 4mg/kg + Fentanyl 3µg /kg respectively. The incidence of hypersensitivity was noted only in Propofol 4mg/kg + Fentanyl 3 µg /kg group and was 2.5%.

Propofol 4mg/kg + Fentanyl 3µg/kg is reasonably safe for smooth intubation without the use of muscle relaxants.

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## ANNEXURE - I



**E.L.D.E. UNIVERSITY'S**  
**SHRI B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103**  
**INSTITUTIONAL ETHICAL COMMITTEE**


**INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE**

The Ethical Committee of this college met on 22.11.2014 at 3-20 pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title efficacy of different doses of propofol for endotracheal intubation - A randomised clinical trial,

Name of P.G. student Dr. Aman Sai Guntreddy  
Dept of Anaesthesiology

Name of Guide/Co-investigator Dr. R.R. Kusurkar  
Associate professor of Anaesthesiology

  
**DR. TEJASWINI VALLABHA**  
**CHAIRMAN**  
**INSTITUTIONAL ETHICAL COMMITTEE**  
**BLDEU'S, SHRI B.M.PATIL**  
**MEDICAL COLLEGE, BIJAPUR.**

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.

## ANNEXURE – II

**TITLE OF THE PROJECT** : **“EFFICACY OF DIFFERENT DOSES OF PROPOFOL FOR TRACHEAL INTUBATION-A RANDOMISED CLINICAL TRIAL”**

**PRINCIPAL INVESTIGATOR** : Dr. AMAN SAI GUNTREDDY

Department of Anaesthesiology

Email: amansai4 @gmail.com

**PG GUIDE** : Dr.R.R.KUSUGAL

Associate Professor, Dept of Anaesthesiology

B.L.D.E. University’s Shri B.M. Patil

Medical College Hospital & Research

Centre, Sholapur Road BIJAPUR-03

### **PURPOSE OF RESEARCH:**

I have been informed that this study is **“EFFICACY OF DIFFERENT DOSES OF PROPOFOL FOR TRACHEAL INTUBATION-A RANDOMISED CLINICAL TRIAL ”** I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have also been given free choice for either being included or not in the study.

### **PROCEDURE:**

I understand that I will be doing: **“EFFICACY OF DIFFERENT DOSES OF PROPOFOL FOR TRACHEAL INTUBATION-A RANDOMISED CLINICAL TRIAL”**.

**RISKS AND DISCOMFORTS:**

I understand that I/my ward may experience some pain while intubating and I understand that necessary measures will be taken to reduce these complications as and when they arise.

**BENEFITS:**

**I understand that my/my wards participation in this study will help in finding out: “EFFICACY OF DIFFERENT DOSES OF PROPOFOL FOR TRACHEAL INTUBATION-A RANDOMISED CLINICAL TRIAL”**

**CONFIDENTIALITY:**

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records, but will be stored in the investigator’s research file and identified only by a code number. The code key connecting name to numbers will be kept in a separate secure location.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

**REQUEST FOR MORE INFORMATION:**

I understand that I may ask more questions about the study at any time. Dr. Aman Sai Guntreddy is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study,

which might influence my continued participation.

If during this study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me.

And that a copy of this consent form will be given to me for keep for careful reading.

**REFUSAL OR WITHDRAWAL OF PARTICIPATION:**

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that Dr.Aman Sai Guntreddy will terminate my participation in this study at any time after he has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist, if this is appropriate

**INJURY STATEMENT:**

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have explained to \_\_\_\_\_ the purpose of this research, the procedures required and the possible risks and benefits, to the best of my ability in patient's own language.

Date:

Dr. R.R.Kusugal  
(Guide)

Dr. Aman Sai Guntreddy  
(Investigator)

**STUDY SUBJECT CONSENT STATEMENT:**

I confirm that **Dr. AMAN SAI GUNTREDDY** has explained to me the purpose of this research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

---

(Participant)

---

Date

---

(Witness to above signature)

---

Date



**ANNEXURE – III**

**PROFORMA**

**STUDY: “EFFICACY OF DIFFERENT DOSES OF PROPOFOL FOR  
TRACHEAL INTUBATION-A RANDOMISED CLINICAL TRIAL”**

Patient Name :	I.P. No:
Age :	Weight:
Height :	Gender:
Date of Operation:	Occupation:
Address :	Anaesthesiologist:

**Preanaesthetic evaluation**

**Chief Complaints**

**Past History**

- a. HTN / DM / Asthma / Epilepsy / Drug allergy
  
- b. Drug therapy
  
- c. Previous exposure to anaesthesia

**Family history**

**General Physical Examination**

Pallor / Icterus / Clubbing / Lymphadenopathy / Odema

BP:

PR :

RR :

**Musculoskeletal disorders**

Jaw movements

Teeth:

Airway assessment:

Spine:

**Systemic examination**

R.S.

CNS

CVS

GIT

**Investigations**

Hb%:

Total count:

Differential count:

Bleeding time:

Clotting time:

PT:

aPTT:

INR:

Urine routine

Any others

**Preoperative physical status:**

ASA Grade I II III IV V

**Diagnosis:**

**Proposed surgery:**

**Monitors attached**

Pulse oximeter

Non invasive blood pressure:

ECG

PREMEDICATION: TAB. DIAZEPAM (0.01mg/kg) 2hrs preoperatively

INDUCTION SEQUENCE GROUP- STUDY GROUP

TIME	SPO2	HR	MAP
PREINDUCTION-(A)			
SOON AFTER INDUCTION- (B)			
1 MIN POST INTUBATION-(C)			
3 MIN POST INTUBATION -			

	HR	MAP	SPO2
<b>A≈B</b>			
<b>A≈C</b>			

TIME AT WHICH MUSCLE RELAXANTS GIVEN:

MODIFIED HELBO-HANSEN'S SCORING SYSTEM OF INTUBATING  
CONDITIONS

Variable	1	2	3	4
Jaw relaxation	Complete	Slight tone	Stiff	Rigid
Laryngoscopy	Easy	Fair	Difficult	Impossible
Vocal cords	Open	Moving	Closing	Closed
Coughing	None	1-2 bouts	3-4 bouts	>4 bouts,persistent
Limb movements	None	Slight	Moderate	Severe

INTUBATING CONDITIONS SCORE = (a+b+c+d) =

4-7 acceptable

>=8 unacceptable

(Limb movements ( e) scoring is not considered.)

TRACHEAL INTUBATION POSSIBLE

- a) WITHOUT Succinyl Choline
- b) AFTER 2mg/kg Succinyl Choline

## ANNEXURE – IV

### KEY TO MASTER CHART

Group P1 - Propofol 2 mg/kg + Fentanyl 3µg/kg

Group P2 - Propofol 4mg/kg + Fentanyl 3µg/kg

P - Possible

NP - Not Possible

- Pain on injection
- Myoclonus
- 20% fall of MAP
- 30% fall of MAP
- Bronchospasm
- Hypersensitivity (Angioneurotic oedema of eyelid)

**ANNEXURE-IV**

Sl. No.	IP No.	Age (in years)	Sex	Wt. (in Kg)	BMI	ASA GRADE	Drug Code sequence	Pre induction (A)				1 minute after induction(B)				1 minute post intubation (C)				3 minutes post intubation (D)				A-B		A-C		Intubating condition score	Intubation w ithout relaxant (P/NP)	Apnoea duration (in minutes)	side effects
								HR	Systolic	Diastolic	M AP	HR	Systolic	Diastolic	M AP	HR	Systolic	Diastolic	M AP	HR	Systolic	Diastolic	M AP	HR%	M AP%	HR%	M AP%				
1	37020	36	F	43	19.1	I	P1	109	132	76	95	90	110	64	79	96	107	76	86	97	99	70	80	17	17	12	9	7	P	5	
2	1360	24	F	50	20.8	I	P1	100	131	84	100	94	112	64	80	104	134	95	108	96	124	76	92	6	20	4	8	9	NP		
3	3258	28	M	65	23	I	P1	85	140	97	111	87	88	60	69	83	107	72	84	82	117	86	96	2	38	2	24	6	P	5	
4	13923	23	M	56	20.3	I	P1	75	145	91	109	82	122	94	103	99	225	147	173	110	199	131	154	9	5	32	59	11	NP		
5	12944	33	F	42	18.7	I	P1	85	172	101	125	81	163	93	116	109	219	133	162	110	191	118	142	5	7	28	23	9	NP		
6	16370	37	F	50	19	I	P1	124	142	185	104	87	127	75	92	100	140	88	105	97	140	80	100	30	11	19	1	RJ	NP		
7	24124	34	M	64	21.1	I	P1	104	128	94	105	82	92	53	66	85	106	70	82	78	106	61	76	21	37	18	22	5	P	4	
8	31652	38	M	57	19.3	I	P1	77	113	75	88	84	101	71	81	89	133	97	109	91	138	85	103	9	8	16	24	7	P	4	
9	35340	29	F	52	18.6	I	P1	75	128	83	98	95	133	76	95	94	137	74	95	93	131	71	91	27	3	25	3	11	NP		
10	38604	25	M	61	22.1	I	P1	67	123	81	95	58	99	63	75	73	103	63	76	61	102	62	75	13	21	9	20	4	P	5	
11	37279	40	F	43	18.9	I	P1	110	154	97	114	115	136	77	97	129	130	74	93	127	129	78	95	4	16	17	21	7	P	4	
12	596	31	M	47	19.6	I	P1	50	208	120	149	67	138	88	105	54	109	77	87	53	114	77	89	34	29	8	42	4	P	5	
13	7127	40	M	56	19.4	I	P1	99	111	64	80	89	83	48	60	134	127	80	96	136	111	63	79	10	25	35	22	9	NP		
14	9126	34	F	41	18.7	I	P1	98	140	90	107	92	104	53	70	87	167	132	144	102	238	204	215	6	34	11	34	6	P	4	
15	11440	35	M	56	19.8	I	P1	102	154	93	113	100	129	70	90	102	135	80	98	98	132	73	93	2	20		13	4	P	5	
16	14029	35	F	48	19.2	I	P1	109	117	73	88	94	91	52	65	115	150	95	113	123	128	94	105	14	26	5	28	9	NP		
17	20945	23	M	60	19.4	I	P1	80	127	84	98	61	118	75	89	74	143	89	107	79	133	83	100	24	9	7	9	9	NP		
18	25796	30	M	62	19.1	I	P1	104	136	91	106	105	147	101	116	115	165	132	142	107	175	117	136	1	9	10	35	5	P	4	
19	32089	30	F	56	20.3	I	P1	122	190	110	137	96	150	90	110	94	150	110	123	96	150	100	113	21	20	23	10	5	P	4	
20	40956	28	M	58	20.6	I	P1	96	180	113	135	83	113	65	81	90	170	109	129	96	159	112	128	13	14	6	4	6	P	4	
21	40100	24	F	51	19.9	I	P1	77	146	78	101	83	137	71	93	73	146	71	96	92	158	84	109	8	8	5	5	6	P	4	
22	7523	22	F	59	23	I	P1	85	111	68	82	76	94	51	65	85	126	82	97	77	125	73	90	11	21		18	9	NP		
23	11160	28	F	48	21.3	I	P1	91	130	80	97	90	110	70	83	105	160	90	113	114	150	90	110	1	14	15	16	9	NP		
24	12563	23	F	42	19	I	P1	117	135	83	100	97	109	66	80	111	146	82	103	110	128	84	99	17	20	5	3	9	NP		
25	17716	38	M	59	20	I	P1	100	130	96	107	93	90	60	70	98	100	96	84	85	106	70	82	7	35	2	21	5	P	4	
26	15997	24	M	52	18.6	I	P1	75	130	96	107	82	90	60	70	88	100	96	84	90	106	70	82	9	35	2	21	5	P	4	
27	20582	28	F	48	18.6	I	P1	75	110	76	107	82	100	72	83	88	130	98	105	90	134	95	108	9	22	17	2	6	P	4	
28	17114	33	M	59	20.4	I	P1	78	142	75	97	85	136	71	93	96	146	78	101	94	54	82	106	9	4	23	4	6	P	4	
29	39555	30	M	56	19	I	P1	103	126	92	103	98	95	61	72	86	105	72	83	79	107	80	89	5	30	16	19	5	P	4	
30	10773	27	M	62	22.5	I	P1	78	115	60	78	85	100	71	81	90	128	97	107	96	133	98	110	9	4	15	37	5	P	4	
31	7127	40	M	63	23.7	I	P1	66	124	80	95	57	104	60	75	72	105	61	76	60	106	59	75	13	21	9	20	4	P	5	
32	9773	39	F	40	18.9	I	P1	108	152	95	114	113	136	78	97	127	132	74	93	125	130	77	95	4	16	18	20	7	P	4	
33	19810	38	M	58	20.3	I	P1	74	132	81	98	94	126	80	95	94	124	79	95	93	132	71	91	27	3	25	3	11	NP		
34	3439	40	F	44	19.4	I	P1	104	134	90	105	82	92	53	66	85	108	69	82	78	106	61	76	21	37	18	22	5	P	4	
35	24709	35	F	48	19.7	I	P1	100	136	82	100	94	115	62	80	104	137	94	108	96	124	76	92	6	20	4	8	9	NP		
36	37528	35	F	50	20.3	I	P1	98	124	83	97	90	90	55	67	97	104	69	101	88	100	64	76	8	31	1	4	4	P	4	
37	22052	22	M	54	20.1	I	P1	72	124	79	94	97	122	72	89	101	142	87	105	99	136	91	106	35	5	40	12	6	P	4	
38	6831	23	F	56	21.3	I	P1	76	132	86	101	70	95	57	70	66	100	62	75	78	105	70	82	8	31	13	27	5	P	5	
39	9468	35	M	60	19.6	I	P1	96	129	71	90	86	110	56	74	88	134	90	105	89	127	77	94	10	18	8	17	9	NP		
40	8381	29	F	48	18.7	I	P1	94	148	88	102	85	104	53	70	99	142	93	109	97	137	85	102	10	35	5	1	9	NP		

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								HR	Systolic	Diastolic	M AP	HR	Systolic	Diastolic	M AP	HR	Systolic	Diastolic	M AP	HR	Systolic	Diastolic	M AP	HR%	M AP%	HR%	M AP%				
1	37327	35	M	56	22	I	P2	106	122	82	95	100	100	64	76	98	132	93	106	98	105	72	83	6	20	7	11	5	P	3	
2	39874	35	F	44	19	I	P2	120	131	77	95	98	103	57	72	97	121	63	82	92	101	46	73	18	24	19	14	5	P	5	
3	2402	29	M	62	22.5	I	P2	106	136	82	100	84	94	53	67	77	114	70	85	79	102	61	75	21	33	27	15	5	P	3	
4	457	37	F	56	19.6	I	P2	101	129	91	104	77	91	59	70	79	100	63	75	70	91	57	68	24	33	22	28	5	P	5	
5	8245	32	M	58	21.7	I	P2	86	171	92	118	75	129	74	92	100	128	91	103	104	153	96	115	13	22	14	13	5	P	4	
6	9106	27	M	64	20.2	I	P2	88	128	83	98	84	90	53	65	81	89	48	62	82	89	51	64	4	34	8	37	5	P	5	
7	7325	29	M	62	21	I	P2	119	129	84	99	93	98	59	72	93	120	87	98	91	98	58	71	22	27	22		5	P	4	
8	12070	40	F	48	19.7	I	P2	81	147	91	110	95	122	79	94	92	117	87	97	88	150	97	115	17	14	14	12	5	P	5	
9	5089	34	F	44	18.6	I	P2	89	118	77	91	109	155	111	126	139	163	103	123	139	149	100	116	22	38	56	35	5	P	3	
10	16088	30	F	54	19.8	I	P2	93	133	88	103	80	94	45	61	101	122	82	95	100	118	70	86	14	40	9	8	7	P	5	
11	13555	30	F	48	18.7	I	P2	97	147	82	104	86	101	60	74	87	126	74	91	87	124	73	90	11	29	10	12	5	P	5	
12	7445	35	M	62	22	I	P2	115	137	84	102	99	105	53	70	110	132	85	101	108	128	84	99	14	31	4	1	9	NP		
13	9929	21	F	50	18.8	I	P2	81	122	71	88	83	110	54	73	98	122	75	91	93	132	64	87	2	17	21	3	6	P	4	
14	18657	24	M	58	20.1	I	P2	116	124	70	88	83	106	46	66	115	105	57	73	122	111	60	77	28	25	1	17	5	P	4	
15	38450	37	F	48	18.6	I	P2	91	175	104	128	96	97	54	68	100	136	83	101	99	121	74	90	5	47	9	21	6	P	4	
16	16090	32	M	50	19.5	I	P2	87	123	76	92	86	88	45	59	87	115	83	112	90	106	59	75	1	36		22	5	P	4	
17	8207	38	M	56	19.8	I	P2	82	151	99	116	75	101	64	76	81	180	100	127	77	150	100	117	8	34	1	9	5	P	4	
18	36902	25	M	54	18.7	I	P2	69	166	94	118	64	108	55	73	117	81	93	89	123	71	84	80	7	38	69	24	5	P	4	
19	12192	30	M	60	20.1	I	P2	86	148	100	116	88	75	59	71	72	108	71	83	75	119	77	91	2	39	16	28	4	P	4	
20	20961	38	M	49	18.7	I	P2	113	142	91	108	106	105	54	71	95	126	82	97	90	110	62	78	6	34	16	10	5	P	4	
21	5685	25	M	56	19.4	I	P2	120	120	79	93	84	103	54	70	92	104	58	73	94	113	66	82	30	25	23	21	4	P	4	
22	41164	21	F	48	18.7	I	P2	106	155	93	114	86	98	61	73	80	153	82	106	85	117	72	87	19	36	24	7	5	P	4	
23	14529	25	F	50	19.1	I	P2	119	191	133	152	109	141	98	112	94	140	93	109	110	125	77	93	8	26	21	28	6	P	4	
24	38790	22	M	59	19.7	I	P2	110	121	81	94	85	88	50	63	113	118	77	91	98	111	71	84	23	33	3	3	5	P	4	
25	21679	25	F	54	19.6	I	P2	96	130	60	83	81	103	44	64	106	114	67	83	109	109	54	72	16	23	10	S	5	P	4	
26	11790	26	F	42	18.7	I	P2	75	156	87	110	78	107	54	72	92	118	70	86	104	115	64	81	4	34	23	22	5	P	4	
27	3619	28	F	48	19.2	I	P2	99	157	93	114	85	109	68	82	95	95	74	81	93	117	72	87	14	28	4	29	5	P	4	
28	3362	35	F	50	18.8	I	P2	115	130	86	101	95	90	61	71	98	120	84	96	92	98	58	71	17	30	15	5	5	P	4	
29	2407	36	M	54	19.4	I	P2	85	140	86	104	93	90	71	77	80	100	76	84	82	120	77	91	9	26	6	19	4	P	4	
30	457	37	F	48	18.7	I	P2	114	146	91	109	109	103	62	76	94	133	84	100	90	110	67	81	5	30	18	8	5	P	5	
31	18426	25	F	50	19.8	I	P2	86	125	75	92	85	87	44	59	87	102	60	74	90	111	57	75	1	36		17	5	P	4	
32	31157	28	M	52	20.1	I	P2	82	151	98	116	75	103	62	76	81	166	108	127	77	148	102	117	8	34	1	9	5	P	4	
33	6657	32	F	53	19.2	I	P2	82	131	81	98	80	94	50	65	81	88	49	62	82	91	50	64	2	34	8	37	5	P	5	
34	14227	33	M	58	20.1	I	P2	120	130	84	99	92	100	58	72	93	130	82	98	90	100	56	71	23	27	22		5	P	4	
35	10065	22	F	54	21.1	I	P2	80	152	89	110	94	127	76	93	92	122	81	95	88	150	94	113	17	15	15	13	5	P	5	
36	31652	38	M	58	19.4	I	P2	58	154	92	113	70	112	57	75	79	149	68	95	72	129	67	88	21	34	36	16	6	P	4	
37	37400	40	M	49	18.9	I	P2	66	116	64	81	96	111	72	85	104	127	89	102	102	104	70	81	45	5	58	26	6	P	4	
38	32251	35	F	54	19.6	I	P2	84	148	98	115	77	96	62	73	103	161	108	126	107	152	127	135	8	36	23	10	9	NP		
39	35340	29	F	56	20.8	I	P2	98	145	107	120	88	104	59	74	95	123	69	87	94	126	69	88	10	38	3	27	5	P	5	
40	10965	29	M	60	19.4	I	P2	106	131	76	94	102	91	50	64	110	110	74	86	101	101	62	75	4	32	4	8	5	P	5	