Tracheal Intubation with Different Doses of Propofol - Haemodynamic Changes

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ABSTRACT

BACKGROUND
Stress response to intubation produces marked hemodynamic changes during direct laryngoscopy using muscle relaxants. Since attenuation of hemodynamic response to laryngoscopy and tracheal intubation leads to better outcomes, a method for providing good intubating conditions rapidly without using muscle relaxants is being sought. The objective of the present study was to compare the hemodynamic changes occurring while intubating with 2 different doses of propofol.

METHODS
We compared heart rate, systolic blood pressure, diastolic pressure and mean arterial pressure changes during tracheal intubation with 2 different propofol doses without using muscle relaxants. Intravenous fentanyl inhibits the sympathetic nervous response to direct laryngoscopy and tracheal intubation in both groups of patients and acts as pre-emptive analgesia.

RESULTS
Comparison of the hemodynamic parameters revealed no statistically significant differences between the low dose propofol (PL) and high dose propofol (PH) groups with regard to heart rate or blood pressure changes at similar intervals post-intubation. Both patient groups showed blood pressure fall along with a reflex increase in heart rate at 1 minute to 5 minutes post-intubation, returning to near-baseline values 10 minutes post-intubation. None of these changes was either clinically detrimental or produced incidents of desaturation or arrhythmias in any study patient.

CONCLUSIONS
Low dose propofol may be useful in elderly or mildly hypovolemic patients, intolerant to a higher drug dosage whereas, the higher propofol dose may be particularly useful in the adult with a higher muscle mass in situations where muscle relaxant is to be restricted or avoided.

KEY WORDS
Tracheal Intubation, Hemodynamic Changes, Different Doses Propofol.
Airway manipulation by the anaesthesiologist during attempted endotracheal intubation of a patient produces inadvertent stimulation of pharyngeal and laryngotracheal nociceptors resulting in profound hemodynamic stress response. This is particularly deleterious to the patient with a poor cardiac reserve or with other comorbidities. Though modern muscle relaxants provide excellent intubating conditions, they do not produce a reduction in intubation stress response. Further, all of them have undesirable side effects: hypotension, dysrhythmias, bronchoconstriction, residual paralysis and long term muscle weakness, histamine release, allergic reactions, drug interactions etc. The use of a dedicated agent to attenuate the intubation stress response raises the issues of polypharmacy, drug interaction and hemodynamic disturbances produced by the said agent itself. Anaesthesiologists have for long tried to formulate a drug combination to intubate patients without coughing or bucking, in the absence of muscle relaxants. Keaveny JP & Knell PJ were among the first workers to propose this concept of tracheal intubation without muscle relaxants.1

Though endotracheal intubation is often facilitated by a depolarizing muscle relaxant like suxamethonium during anaesthetic induction with short-acting hypnotics, serious side effects like increased intraocular pressure, severe postoperative myalgia, prolonged paralysis (scoline apnea), hypokalemia2 etc are often associated. Also, suxamethonium can precipitate life-threatening masseter spasm, malignant hyperthermia, cardiovascular effects like nodal/ junctional rhythms, severe bradycardia or ventricular dysrhythmias, a raised intracranial tension and increased intragastric pressure, in turn leading to a higher risk of acid aspiration syndrome. Routine use of suxamethonium for elective tracheal intubation has, in effect, ceased in the developed world. Tracheal intubation with non-depolarising relaxants may be associated with undesirable side effects such as prolonged neuromuscular blockade or even the inability to reverse it in an unanticipated difficult airway wherein airway management via mask ventilation or tracheal intubation is virtually impossible. Problems with neuromuscular blocking agents also include anaphylaxis with the highest incidence for succinylcholine and rocuronium and residual neuromuscular blockade.3,4 Anaphylaxis has even been reported with the relatively safer cisatracurium.5 Addition of lignocaine only produces suppression of cough reflex and adds little to the ease of laryngoscopy or passage of a tracheal tube between the vocal cords.5 For these reasons, a method of providing acceptable intubating conditions rapidly, without muscle relaxants is being sought. Since the advent of short-acting potent opioids (good at suppressing airway reflexes) and newer intravenous anaesthetic agents, the possibility of intubation without muscle relaxant usage has been under evaluation.

In 1988, McKeating, Bali IM, Dundee JW compared IV thiopentone sodium (4.5 mg/kg) and propofol (2.5 mg/kg) to assess suppression of airway reflexes and found out the latter to be a better hypnotic.7 Lateron Steven JB, Vescova MV, Harris KC & others found that intubating conditions of IV etomidate with alfentanil were comparable to those with propofol and alfentanil and in fact, better than with IV thiopentone and alfentanil8 since propofol has been reported to possess some characteristics that provide adequate intubation conditions in combination with fentanyl.9,10,11 Due to its profound suppression of airway reflexes, propofol is the most favoured agent in this regard.12,13,14 A study by Saarnivara L et al. only achieved a very low success rate of 16% with IV 2 mg/kg propofol and 30 µg/kg alfentanil. However, Saarnivara L, Klemola VM could achieve 89% success in intubation with 2.5 mg/kg IV propofol with 30 µg/kg alfentanil without muscle relaxants.15,16,17 Another study that compared tracheal intubation with 2.5 mg/kg IV propofol with and without 1.5 mg/kg lignocaine without using opioids or muscle relaxants found that the dose of IV propofol was sufficient to intubate the trachea without muscle relaxants and that adding 1.5 mg/kg IV lignocaine well attenuated the stress response to intubation.18,19,20 Most previous studies on tracheal intubation without muscle relaxants were conducted using propofol along with short-acting strong opioids like alfentanil, sufentanil and remifentanil.21,22,23 In view of these studies, higher doses of IV propofol (2.5 mg/kg and 3 mg/kg body weight) were selected in our study for better results.

The objective of the present study was to compare the hemodynamic changes occurring while intubating with 2 different doses of propofol.

**METHODS**

A prospective study comparing the heart rate, systolic blood pressure, diastolic and mean arterial blood pressure changed during intubation with varying doses of propofol without using muscle relaxants.

**Study Design**

The sample size was calculated using the formula

\[
N = \frac{(\sigma_1^2 + \sigma_2^2)(Z_{1-α/2} + Z_{1-β})^2}{d^2}
\]

Where,

\[
n\quad\text{Sample size, } \sigma_1, \sigma_2 \quad \text{standard deviation of samples, } d = \text{the difference between means, } Z_{1-α/2} = \text{table value for significance level } α \quad \text{&} \quad Z_{1-β} = \text{table value corresponding to power (1-β).}
\]

Considering heart rate and mean arterial pressure values at 1 minute after intubation from the reference study,24 minimum sample size required (n) was calculated as 26. α = 0.05; β = type 2 error (20%) and expected 13% drop-out rate, hence decided to take a sample size of 30 in each group.

After acquiring approval from our hospital ethics committee, ASA (PS) I and II patients, 20 – 65 years of either sex of Mallampatti Class I and II airway were included in the study. The study period was 18 months from April 2014 to September 2015. The body mass index for all selected subjects was < 28 kg/m². Pregnant patients, patients with documented difficult airways, those with unstable hemodynamics or allergy to propofol, those on beta-blocker medication and those with systemic illnesses like systemic
hypertension, type 2 diabetes mellitus or bronchial asthma were all excluded. Patients were selected from the elective cases posted for abdominal, orthopaedic and ENT surgeries by consecutive sampling at Government Medical College, Thrissur and assessed pre-operatively. Written informed consent was obtained for the study.

A well-equipped operation room with central oxygen supply, working suction, and anaesthetic work-stations with suitable vaporizers filled adequately and checked. Anaesthetic breathing circuits, assorted airways & masks were kept ready. Emergency trolley with all necessary drugs and equipments, sufficient quantities of all drugs for GA induction, maintenance and reversal including opioids, benzodiazepines, succinylcholine, thiopentone sodium and propofol were also kept. Multichannel monitors with a defibrillator, blood pressure cuffs, suitable probes for pulse oximetry and capnography, intravenous cannulae of various gauges, central venous catheters, arterial and venous extension lines, Foley’s urinary catheter and any other appropriate equipment required were kept ready in the OR. ASA Class I & II patients undergoing elective abdominal, orthopaedics and ENT surgeries requiring general anaesthesia who met the inclusion criteria, were included in 2 groups of 30 each and weighed pre-operatively to accurately calculate drug dosages. An appropriate free-flowing intravenous line was established as soon as the patient was brought into the OR. On the table, a 5-lead ECG monitor, pulse oximeter and properly fixed BP cuff were attached to the patient. All patients were given 10 ml/kg Ringer Lactate IV infusion 10 minutes pre-induction and pre-medicated with IV glycopyrrolate 5 µg/kg, IV ranitidine 0.3 mg/kg, IV ondansetron 100 µg/kg, IV midazolam 0.02 mg/kg and IV fentanyl 2 µg/kg as slow bolus in the same order. After giving inj. fentanyl, patients were watched for apnoea, oxygen saturation and given 100 % oxygen support by mask.

As it takes 5-7 minutes for the plasma concentration of fentanyl to equilibrate with that of the brain, 5 minutes were given following inj. fentanyl. Lignocaine 1.5 mg/kg as IV bolus followed by propofol in pre-calculated amounts (2.5 or 3 mg/kg), were given slowly intravenously over 10 seconds to each patient by the attendant anaesthesiologist as per his/her pre-anaesthetic assessment of the individual patient and grouped accordingly. IV propofol and lignocaine were administered in such a manner as to do laryngoscopy and intubation at 7 minutes after IV fentanyl. The attending anaesthesiologist was the final authority in deciding to include a particular patient in the low dose or high dose propofol group. The investigator (s)/ observer(s) had no say at all in this matter. Patients were watched for apnoea or fall in O2 saturation & if required, ventilated bag-mask with 100 % oxygen was given.

Laryngoscopy and intubation were done 90 seconds after completion of propofol injection since good to excellent intubating conditions were obtained 90 seconds after a hypnotic dose of propofol as per various studies. Only one attempt at laryngoscopy and intubation was considered for the study. All male patients were intubated with Portex cuffed endotracheal tube ID 8.5 mm and female patients ID 7.5 mm. Hemodynamic responses (Heart rate, Systolic Blood Pressure, Diastolic Blood Pressure & Mean Arterial Pressure) were recorded at the following stages:- baseline value, just after giving propofol & lignocaine, 1-minute post-intubation and then 3, 5 & 10 minutes after intubation. If intubation was not possible, patients were given a muscle relaxant to facilitate intubation and excluded from the study. Following intubation, anaesthesia was maintained at the discretion of the attending anaesthesiologist.

Collected data were analyzed using SPSS software. Quantitative data were analyzed using mean +/- standard deviation and independent sample t-test. Qualitative data were analyzed using the proportions & the chi-square test. The patients were grouped into 2 based on the dosage of propofol used – a low dose group, PL and a high dose group, PH. Both groups were comparable with respect to age, sex and ASA physical status of patients. The maximum number of patients in both groups was in the 50- 64 years age range, followed by equal numbers in 20 – 34 years & 35 – 49 years age bracket.
Comparison of the hemodynamic parameters revealed no statistically significant differences between the low dose propofol (PL) and high dose propofol (PH) groups. Even though heart rate was found to increase at 3 to 10 minutes post-intubation, very similar changes were found in both groups. Statistically, significant change was seen only in heart rate values at 1-minute post-intubation. Also, the blood pressure values showed similar trends of initial decrease (albeit statistically insignificant) followed by a subsequent increase at 1 minute to 10 minutes post-intubation. In premedicated healthy patients with favourable airway anatomy, tracheal intubation was comfortably achieved with a combination of IV 2 µg/kg fentanyl and IV 2.5 mg/kg or 3 mg/kg propofol. This technique is valued in select patients as muscle relaxant administration is associated with quite a few undesirable effects. No significant incidents of desaturation or arrhythmias occurred in any patient during the course of this study. No statistically significant difference in heart rate, systolic blood pressure, mean arterial pressure or diastolic blood pressure between PL & PH groups was noted before intervention. No statistically significant difference seen in hemodynamic values in PL & PH groups just after IV propofol and lignocaine administration at 1, 3, 5 or 10 minutes post-intubation.

**DISCUSSION**

A method for providing good intubation conditions safely, effectively and rapidly without the use of muscle relaxants has been long sought after. This is primarily due to the side-effect profile of the commonly used non-depolarizing and depolarizing muscle relaxants. The present study was thus conducted in 60 ASA (PS) I and II patients included in two groups of 30 each; the first group being PL – Propofol lower dose and the second group, PH – Propofol higher dose who were posted to undergo general surgical, orthopaedic or ENT procedures at Government Medical College, Thrisur to verify the ease of intubation with 2 different induction doses of propofol without the use of any muscle relaxant and to compare the hemodynamic effects therein. Consecutive sampling was used in this study. Group PL received 2.5 mg/kg IV propofol and PH group received 3 mg/kg IV propofol. In addition, both the groups were given 2µg/kg IV fentanyl as pre-medication 7 minutes prior to intubation. Heart rates, systolic blood pressure, mean arterial pressure, and diastolic blood pressures were recorded at the onset (baseline value) of the procedure, just after IV propofol and lignocaine 1.5 mg/kg IV and at 1, 3, 5 minutes and 10 minutes post-intubation. Comparing the hemodynamic parameters revealed no differences of

**Table 8. Comparison of Hemodynamic Parameters – Baseline & at 10 Minutes Post-Intubation**

| Parameters | Baseline | 1 Minute Post- Intubation | Mean Difference | P Value |
|------------|----------|--------------------------|----------------|--------|
| HR         | 80.5 ± 9.2 | 81.1 ± 6.8               | 0.6            | 0.87   |
| Systolic BP| 135.6 ± 10.6 | 135.1 ± 9.7               | 0.5            | 0.98   |
| MAP        | 83.0 ± 6.7 | 83.5 ± 6.2               | 0.5            | 0.87   |

No statistically significant heart rate or BP changes were noted at 10 minutes post-intubation.
Patients in group PL (propofol low dose) and PH (propofol high dose) had adequate and comparable intubating conditions with similar changes in hemodynamic parameters like heart rate, systolic blood pressure, mean arterial pressure and diastolic blood pressure during intubation through 1, 3, 5 and 10 minutes afterwards. There was no significant statistical difference between groups PL and PH regarding changes in heart rate & blood pressure at similar intervals. After intubation, though both groups of patients saw a decrease in blood pressure values along with a reflex increase in heart rate at 1 minute to 5 minutes post-intubation, it returned to near-baseline values by 10 minutes post-intubation. None of the changes noted was clinically detrimental to the patients. It can thus be safely concluded that both doses of IV propofol used in the study with prior administration of IV fentanyl, 7 minutes before intubation, provide good intubating conditions without the use of muscle relaxants. The lower dose propofol used in the PL group may be more useful in elderly or mildly hypovolemic patient groups while the higher dose used in the PH group is helpful in the healthy adults with a higher muscle mass in clinical situations where muscle relaxant usage is to be restricted or altogether avoided.

Limitations
They include varied drug doses dependent on patients’ weight which can have some effect on final results. Also, as laryngoscopy and intubation were performed by different anaesthesiologists, the degree of difficulty in intubation could not be accurately compared and assessed. As only a single attempt at intubation was permitted in the study, many faulty laryngoscopes and intubation techniques may have counted out as difficult airways, being excluded from the study altogether.

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