Original Article

Effect of etomidate and propofol on airway mechanics during induction – A prospective randomized trial

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Abstract

Background and Aims: Intravenous induction agents like propofol and etomidate change the airway mechanics and thus influence mask ventilation. These changes have an impact on the administration of muscle relaxant in a difficult mask ventilation scenario. The difference in dynamics of airway after administration of two different intravenous agents has been assessed in this study.

Material and Methods: After formal registry in clinical trials, patients undergoing general anesthesia were recruited and randomized into group P and E. Patients were induced with either of the intravenous agents, and mask ventilation was performed with a ventilator. After 60 s, rocuronium was administered and ventilation continued. Measurements of tidal volume, peak airway pressure, and compliance were taken from the anesthesia ventilator at different time points – induction, relaxant, and intubation.

Results: There was no statistically significant difference between the two groups with respect to demographics, airway parameters, and airway mechanics, as measured by tidal volume, peak airway pressure, and lung compliance. There was an improvement in the tidal volume and compliance following induction with propofol, with a *P* value of 0.007 and 0.032, respectively, obtained in within-group comparison.

Conclusion: Propofol and etomidate were comparable in airway mechanics, but compliance and tidal volumes improved with propofol, which facilitated face mask ventilation.

Keywords: Airway, etomidate, induction, propofol, ventilation

Introduction

The primary objective of general anesthesia includes securing airway for oxygenation by maneuvers like mask ventilation (MV), supraglottic airway, or endotracheal tube intubation. Several studies have focused on assessing and predicting the difficulty in intubation or supraglottic airway placement, but the emphasis on MV is less.

MV is the most basic and essential skill in airway management. It is the primary technique of ventilation before tracheal intubation or insertion of any airway device. There are lot of controversies about giving neuromuscular blockers in cases of difficult MV after induction of anesthesia. Whether or not routine administration of neuromuscular blocker before testing the operator's ability to ventilate the patient is helpful is debatable.[1]

Certain studies argue that presence of residual neuromuscular activity after intravenous induction results in resistance to MV, which is therefore interpreted as difficult MV.[2-5] The variation in airway mechanics following intravenous induction agents during MV has been less well studied.

Propofol and etomidate are rapidly acting, safe, and popular induction agents with different characteristics. Propofol is

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popular for its rapid and smooth induction characteristics along with recovery. Propofol has cardiorespiratory depressant effect and apnea in both adult and pediatric induction. The duration of apnea may be more than 30 s, which is increased by premedication with opioid just before induction.

Etomidate is unique due to its rapidity of induction and hemodynamic stability. It has the effect of sedation and hypnosis, rather than analgesia and muscle relaxation. Induction with etomidate produces brief periods of hyperventilation, sometimes followed by apnea. The common side effect of etomidate is spontaneous movement and myoclonic activity.[6,7] We suspected this might have some hindrance in MV and airway dynamics.

Thus, the primary aim of the study is to assess the change in compliance during induction with etomidate and propofol. The secondary aim is to assess the changes in tidal volume, peak airway pressure, effect of neuromuscular block on airway dynamics, and side effects of etomidate and propofol.

Material and Methods

This prospective, randomized trial was conducted in a tertiary care center after obtaining ethics committee approval and informed consent from the patients. Trial recruitment was started following the approval of clinical trial registry (CTRI/2019/03/018197). Sixty-five patients of age between 18 and 60 years, belonging to American Society of Anesthesiologists (ASA) grade 1–3, posted for elective surgery under general anesthesia were recruited for the study. Patients who were pregnant or those with diaphragmatic hernia, gastric outlet obstruction, or anticipated difficult MV and intubation were excluded from the study. Patients were allocated to two groups by computer-generated simple randomization.

During preoperative assessment, features of difficult MV and intubation were assessed in the patients (like large tongue/epiglottis, tonsillar hyperplasia, airway edema, edentulous, presence of beard, upper or lower airway tumors, extrinsic compression of airway, foreign bodies, pneumothorax, bronchopleural fistula, chest wall deformity, previous neck irradiation, laryngospasm, bronchospasm, and obesity- body mass index [BMI] >30 kg/m^2) and if present, they were excluded.

Patients were premedicated orally with alprazolam 0.5 mg and rantidine 150 mg on the night before and the morning of surgery. The anesthetic machine (Datex Ohmeda S5 Avance; GE Healthcare, Madison, WI, USA) was checked before use on every patient. On arrival into the operating room, patients were monitored using standard monitors like pulse oximetry, noninvasive blood pressure, and electrocardiogram. All the patients were premedicated with intravenous fentanyl 2 μg/kg and preoxygenated using anatomical face mask appropriate for the patient. The head and neck position was standardized by using similar single-head pillow for all patients and sniffing the morning air. Induction was performed using propofol 2 mg/kg in group P and etomidate 0.3 mg/kg in group E. Adequacy of induction was checked by loss of verbal response to commands, and lungs were ventilated with volume control mode, tidal volume of 8 ml/kg, respiratory rate of 14/min, and inspiratory to expiratory ratio of 1:2.

MV was graded as described by Han *et al.* [Table 1].[8] If required, adjustments like optimum jaw thrust, two-handed mask holding, or insertion of oropharyngeal airway were performed at the discretion of the anesthesiologist (either Dr. KJ or Dr. IG). Anesthesia was maintained by air, oxygen, and sevoflurane. At the end of 60 s, the muscle relaxant rocuronium 1 mg/kg was given to assess the effect of induction agent given.[9] Ventilation was continued in the same manner following relaxant, and trachea was intubated using standard laryngoscope with McIntosh blade 90 s later. The study ended 5 min after intubation. Post inclusion, the exclusion criteria were life-threatening conditions like severe hemodynamic instability, bronchospasm, and pulmonary aspiration, since these situations warrant different management, which can alter the airway mechanics.

Parameters studied were expired tidal volume, peak expiratory pressure, and compliance during MV and up to 5 min following intubation. Hemodynamics was maintained within normal range (20% of baseline values) by administration of ephedrine for hypotension and 2% lignocaine in case of tachycardia or hypertension. The time taken for intubation was measured by the time from mask removal to the time for appearance of end-tidal carbon dioxide curve. Intubation difficulty score was assessed for the easiness of intubation.[10] Adverse events like myoclonus and hemodynamic changes which required additional drug administration were noted.

Statistical analysis was performed using IBM Statistical Package for the Social Sciences (SPSS, version 20; IBM, Illinois, USA). The descriptive analysis of normally distributed

Table 1: Han scale of mask ventilation

Classification	Description/definition
Grade 0	Ventilation by mask not attempted
Grade 1	Ventilated by mask
Grade 2	Ventilated by mask with oral airway or another adjuvant
Grade 3	Difficult mask ventilation (inadequate, unstable, or requiring two practitioners)
Grade 4	Unable to mask ventilate

continuous variables was expressed as mean with standard deviation (SD). The categorical variables were expressed as frequencies with percentages. The ordered categorical variables were expressed as median with interquartile range (IQR). The statistical analysis for comparison of continuous variables between the groups was performed using independent samples *t*-test, and paired *t*-test was used for within-groups comparison. The comparison of categorical variables between the groups was performed using Chi-square test or Fisher exact test when the expected cell values were <5. A two-tailed *P* value of <0.05 was considered as a significant difference between the groups. The primary outcome of the study was airway dynamics as assessed by ventilatory parameters. With a pilot study conducted in 12 patients, we expected a mean difference (SD) in compliance of 10(15) ml/cm of H_2O following induction between the two groups. To detect such difference, with at least 80% power at one-sided significance of 5%, a total of 56 patients were required. Considering the dropout rate, 65 patients were recruited in the study.

Results

A total of 65 patients scheduled for elective surgery were enrolled in the study. Two patients in the propofol group and two patients in the etomidate group were excluded. In the final analysis, 61 patients were included, as explained in the CONSORT diagram [Figure 1]. Patients were statistically comparable demographically, as given in Table 2.

The difference in the airway parameters assessed in patients during the perioperative period were not statistically significant between the groups [Table 2].

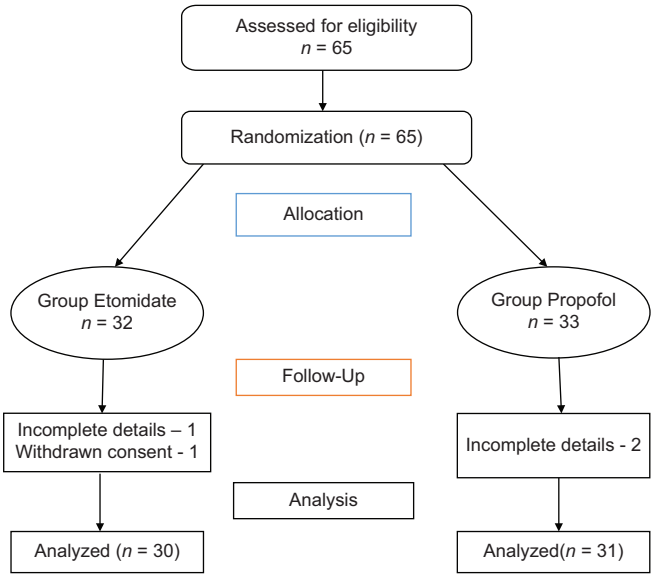

Figure 1: CONSORT (Consolidated Standards of Reporting Trials) diagram – flow chart of the study

Nine patients in group E and 10 patients in group P required two-handed MVs, who were also included in grade 1 of the Hans MV grading. Oral airway insertion was necessary for one patient in group E and two patients in group P and they belonged to grade 2. This grading of MV was statistically comparable between the groups, as given in Table 2. The Cormack Lehne grading, time taken for intubation, and the intubation difficulty scores were statistically comparable between the groups [Table 2].

The mean of ventilatory parameters was considered for comparison between the groups. This was taken for ventilatory breaths after the loss of verbal response as induction, following relaxant as relaxation and all breaths for a minute following intubation as intubation. There was no significant difference in airway dynamics between the two groups when the tidal volume, peak pressure, and compliance were compared at these time intervals [Figures 2-4].

When tested within the groups, there was no change in airway dynamics in the etomidate group, but significant changes were present in the propofol group. Tidal volume in group P was significantly different between induction with relaxant and with intubation groups (0.007, 0.005). Compliance in group P was significantly different between the induction and relaxant, relaxant and intubation (0.032, 0.004, respectively). Peak pressure was significantly different between the relaxant and intubation (0.000).

The incidence of adverse events in terms of myoclonus was higher in the etomidate group compared to the propofol group, as shown in Table 2.

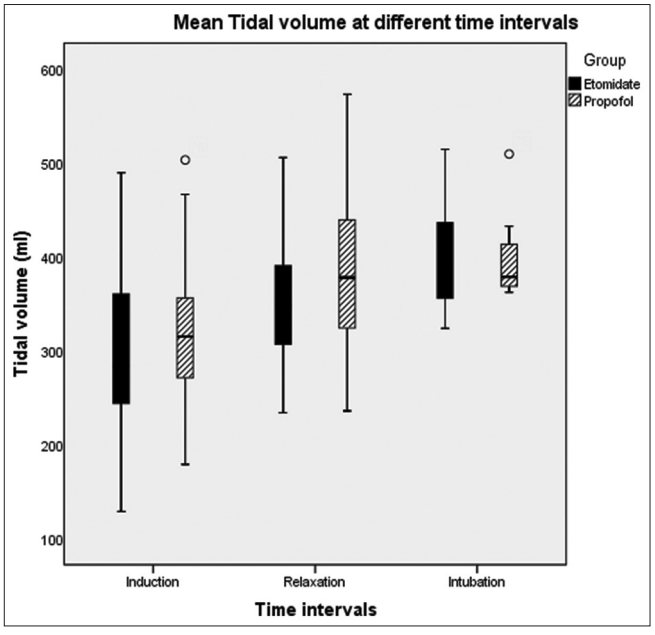

Figure 2: Graphical representation of the mean tidal volume at different time intervals between the two groups

Table 2: Demographic data, airway parameters, and intraoperative findings

Variable	Etomidate group	Propofol group	Probability
Age (years)	40.86 (14.617)	39.53 (15.496)	0.815
Gender (male/female)	14/16	15/16	0.297
BMI	24.40 (1.96)	23.34 (2.35)	0.244
ASA (I/II/III)	18/9/3	17/12/2	0.475
Airway parameters			
Mouth opening	4.786 (0.6112)	4.567 (0.4952)	0.297
MHD	6.036 (0.7712)	5.867 (0.6673)	0.532
TMD	7.643 (0.9288)	7.567 (0.6510)	0.799
SMD	14.536 (0.970)	14.533 (1.26)	0.995
NC	34.929 (2.6736)	34.700 (2.102)	0.782
Neck movements (normal/ restricted extension)	28/2 19/10/1/0	28/3 17/13/1/0	0.932 0.238
Mallampati (1/2/3/4)	16/5/4/4/1	12/6/6/5/3	0.760
Intubation parameters	19.57±7.61	21.14±15.64	0.380
CL grades (1/2a/2b/3a/3b)	1.60±1.68	2.00±1.839	0.974
Time taken for intubation			
Intubation difficulty scores			
Intraoperative findings			
Mask ventilation grades (1/2/3/4)	29/1/0/0	29/2/0/0	0.607
Adverse effects	7	0	0.052
Myoclonus			

ASA=American Society of Anesthesiologists, BMI=body mass index, MHD=Mentohyoid distance, TMD=Thyromental distance, SMD=Sternomental distance, NC=Neck circumference, CL=Cormack Lehane grade

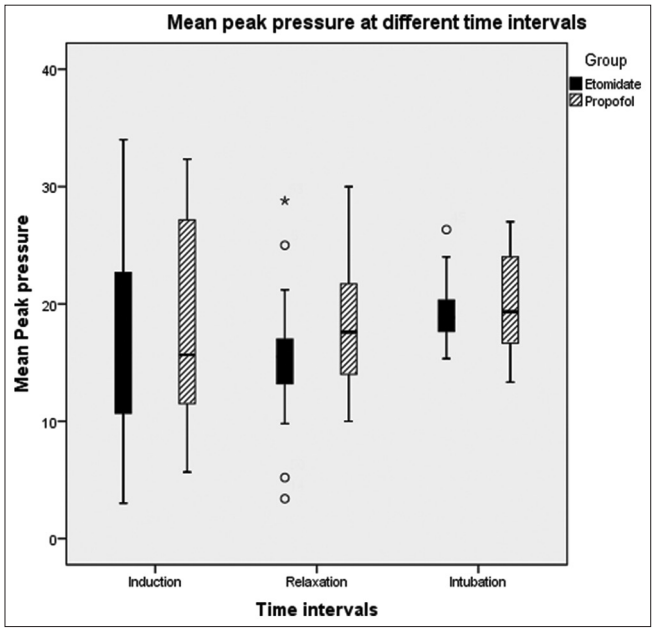

Figure 3: Graphical representation of the mean peak pressure at different time intervals between the two groups

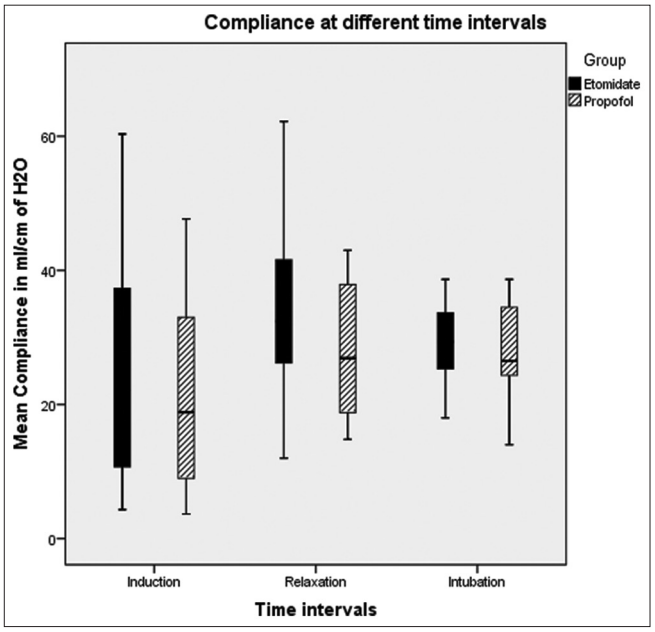

Figure 4: Graphical representation of compliance at different time intervals between the two groups

Discussion

We examined the effect of induction agents etomidate and propofol on airway dynamics and also the variation following muscle relaxant rocuronium. There was no difference in airway dynamics when both the groups were compared with respect to tidal volume, peak airway pressure, or compliance. As per our study, there was an improvement in MV in terms of tidal volume and peak airway pressures predominantly in patients who received propofol, whereas no such change was observed with etomidate at different time points.

Following intravenous induction, it is mandatory to support ventilation to prevent airway obstruction. This is essential because of the variation in anesthesia depth, consciousness, change in the upper airway patency, and airway reflexes

following induction.[1] These variations in airway mechanics have a direct effect on MV and are less studied. Several studies have assessed the influence of MV by neuromuscular blocking agents and propofol, but none of them have compared the induction agents. The practice of assessing MV following induction has been questioned by many studies. This is predominantly observed in patients who are obese and have sleep-disordered breathing, which is attributed to pharyngeal collapse and increased chest wall rigidity following opioid administration.[11,12]

Etomidate, being a non-barbiturate intravenous anesthetic, acts predominantly on gamma amino butyric acid (GABA) receptors. It has an effect on sedation and hypnosis compared to analgesia and muscle relaxation. This along with transient myoclonus which occurs in 30%–60% of patients during induction might affect the MV. But our study had proved that no such detrimental effects were caused following administration of etomidate.[7,13] Propofol provided better ventilatory parameters during MV before muscle relaxant administration when compared to etomidate. Administration of muscle relaxant had improved the airway dynamics following induction by both propofol and etomidate, which is similar to other studies.[9,14,15]

Propofol induction doses produce respiratory depression for 8–11 min, which might help in better ventilatory conditions than that of etomidate.[16,17] Opioids, even in small doses, negatively affects the upper airway patency and may contribute to difficult MV. As per the National Audit Project of Royal College of Surgeons and the Difficult Airway Society, when the facemask or laryngeal MV is complicated, the anesthesia is deepened and neuromuscular blocker can be administered.[18] The choice of induction agent in these cases would be propofol as per our study, rather than etomidate.

A smaller study done by Ikeda *et al.*[1] compared the effects of suxamethonium and rocuronium on MV. They concluded that rocuronium did not worsen MV while suxamethonium improved it when they had used propofol for induction. The variation in our results was because we had used rocuronium and compared two induction agents. In another study, Sachdeva *et al.*[19] reported improvement in tidal volumes following administration of rocuronium in 125 patients and the average tidal volumes increased from 525 (116) ml to 586 (129) ml ($P < 0.001$). In this trial, propofol was used as an induction agent, and the propofol group of our trial showed similar changes.

In our study, we had assessed the depth of anesthesia clinically before initiating MV, without using any specific monitor. This is because there may be a variation between bispectral index and entropy at the point of loss of consciousness following etomidate injection.[20] So, we cannot exclude the possibility of variation in airway dynamics due to suboptimal depth of monitoring. Also, operator-induced adjustments in airway positioning for adequate MV had not been excluded in our study. We had excluded patients with features of difficult MV, extrapolating these results to that scenario is impossible.

Conclusion

Propofol and etomidate were comparable with respect to airway mechanics, but compliance and tidal volumes improved following administration of propofol than prior facilitated better facemask ventilation. Airway dynamics improved following administration of rocuronium when any induction agent was used.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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