ABSTRACT Background: Both inductions of anaesthesia and airway management are critical parts while conducting general anaesthesia. The common complications following injection of an induction agent, especially in hemodynamically unstable patients, ranges from hypotension to arrhythmias, subsequently leading to cardiovascular collapse. Conversely, during laryngoscopy and tracheal intubation, airway manipulation may cause arrhythmias, hypertension, myocardial injury, airway spasm, hypoxia, hypercapnia, and raised intracranial and intraocular pressure. Aims and Objective: To compare the hemodynamic response to laryngoscopy and tracheal intubation after induction of anaesthesia by Propofol and Etomidate. It is also to compare myoclonus incidence, oxygen saturation, and postoperative nausea and vomiting. Materials and methods: One hundred thirty American Society of Anaesthesiology grade I and II patients aged 18-50 years scheduled for the planned surgical procedure under general anaesthesia were randomly divided into two groups of 65, each is receiving Propofol 2 mg/kg and Etomidate 0.3 mg/kg as an induction agent. Vital parameters were measured at induction and after intubation for comparison. In addition, myoclonus and oxygen saturation was noted after induction. Results: Both groups are comparable in terms of demographic variables. The statistical evaluation showed that the decrease in blood pressure was statistically significant (p<0.05) in group P on induction. In contrast, there was a significant (p<0.05) increase in blood pressure and heart rate in group E after intubation. The incidence of myoclonus is significantly higher in the Etomidate group. There was no difference concerning oxygen saturation and postoperative nausea and vomiting. Conclusion: Etomidate is a more hemodynamically stable induction agent compared to Propofol but is less effective in preventing stress response to laryngoscopy and tracheal intubation with a higher incidence of myoclonus on induction if proper premedication is not used. Keywords Hemodynamic Response, Induction Agent, Laryngoscopy, Myoclonus, Tracheal Intubation
patients.[1] Conversely, airway management with direct laryngoscopy and tracheal intubation has adverse effects like hypertension, airway spasm, arrhythmias, myocardial injury, hypoxia, hypercapnia, increased intracranial pressure and intraocular pressure.[2,3]

Intravenous injection of a general anaesthetic agent is common to induce general anaesthesia. Injection of induction agent may decrease arterial blood pressure via myocardial depression, vasodilation and attenuation of autonomic nervous activity resulting in “alpine hemodynamic response”, leading to deleterious effects on maintaining the circulation to vital organs.[4]

At present, Propofol and Etomidate are commonly used, intravenous induction agents. Propofol (2,6 di-isopropanol) was discovered in 1970 and introduced in clinical practice in 1977. It has faster onset rapid recovery, causes potent attenuation of airway reflexes, provides an adequate depth of anaesthesia and has antiemetic property.[5] However, the main drawbacks are blood pressure, dose-dependent depression of ventilation and pain on injection.[1]

Etomidate is a carboxylated imidazole derivative synthesized in 1964 and introduced in clinical practice in 1972 in Europe and 1983 in the United States. Though it provides faster onset and rapid recovery with hemodynamic stability and minimal respiratory depression on induction, it is less effective in preventing stress response to laryngoscopy and intubation. Its use is associated with pain on injection, myoclonus and postoperative nausea and vomiting. Its use in clinical practice was declined due to reports of adrenocortical suppression.[5]; However, a single bolus injection blunts the hypothalamic-pituitary-adrenal axis for more than 24 h. This is not associated with an increased vasopressor requirement.[6]

Etomidate potentiates gamma-aminobutyric acid inhibitory action resulting in unacceptably high blood pressure and heart rate. Due to this unfavourable cardiovascular profile and myoclonus resulting in poor mask ventilation, Etomidate is not suitable for induction of anaesthesia unless supplemented by an opioid and/or benzodiazepine.[7]

One study has concluded that both (P vs E) groups showed a significant reduction in arterial pressure (30%-22%), systemic vascular resistance index (31%-23%) and left ventricular stroke work index (38%-32%) after induction of anaesthesia. Systemic vascular resistance index significantly increased in the Etomidate group after intubation.[8]

Another study has concluded that tracheal intubation produced a marked increase in arterial pressure in the Etomidate group, while such changes were absent in the Propofol group.[9] One study has shown that Propofol has more hemodynamic depressant effect during induction but resulted in less hypertension and tachycardia at and after intubation when compared to Etomidate.[10] Most of the above studies have focused on the hemodynamic changes either on induction of anaesthesia or after intubation, separately. Therefore, we chose this study to compare hemodynamic changes at induction and after intubation.

Material and Methods
This prospective randomized, double-blind comparative study is conducted on 130 American Society of Anaesthesiology (ASA) grade I and II patients between 18 and 50 years of either gender, undergoing elective surgical procedures under general anaesthesia with tracheal intubation. After approval from the institutional ethical and scientific committee, written informed consent was obtained from all the patients. The total 130 patients were randomly divided into two groups of 65 patients using computer-generated randomization.

- Group P (n=65): received Inj. Propofol 1% (2 mg/kg body weight)
- Group E (n=65): received Inj. Etomidate (0.3 mg/ kg body weight)

Patients with a history of allergy to study drugs, seizure disorder history, steroid deficiency/on steroid medication, history of hyper/hypotension, patients with anticipated difficult intubation, and more than one intubation attempt were excluded from the study.

All patients were premedicated with tablet Alprazolam 0.5 mg and Ranitidine 150mg night before surgery and instructed for the fasting of 8 hours. On arrival at the operation theatre, the monitor was attached to the patient to monitor Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), Heart Rate (HR), peripheral oxygen saturation (SpO2) and electrocardiogram. An 18 G intravenous (IV) cannula was secured, and ringer lactate 10 ml/kg/h was started. Patients were preoxygenated with 100% oxygen using a face mask for 3 minutes before induction of anaesthesia. The syringes containing the study drugs were prepared by a resident to ensure proper blinding. The coded syringes (P or E) contained either Propofol 10 mg/ml or Etomidate 2 mg/ml, respectively. Syringes were prefilled to contain 20 ml opaque white liquid for blinding purposes so that no visual difference could be detected between syringes. The residents who injected the drugs and the person who collected the data were different. Therefore, no premedication is given immediately before induction.

After preoxygenation, patients were induced by drugs contained in prefilled syringes as per body weight. Propofol and Etomidate group received induction doses of 2 mg/kg and 0.3 mg/kg body weight, respectively. Both drugs were injected slowly in ringer lactate flow using an 18 G IV cannula.

Patients were observed for myoclonic movements after injection and noted if present. After checking mask ventilation, IV Succinylcholine 1.5 mg/kg was given. Intubation was performed using an appropriate size endotracheal tube (ETT) after 60 seconds of Succinylcholine administration by an experienced anaesthetist using a rigid laryngoscope. ETT was secured after confirming the correct position and positive pressure ventilation started. Further anaesthesia was maintained with oxygen and N2O (30:70) in sevoflurane; IV Atracurium 0.5 mg/kg followed by a maintenance dose of 0.1 mg/kg. After recording the hemodynamic parameters, IV Fentanyl 2 microgram/ kg and Glycopyrrolate 0.004 mg/kg were given. At the end of the surgery, the residual neuromuscular block was antagonized with IV Neostigmine 0.5 mg/kg and Glycopyrrolate 0.01 mg/kg, and extubation was done after achieving adequate tidal volume. SBP, DBP, MAP, HR and SpO2 were recorded before induction (T0), at the end of induction (T1) and 1 (T2), 3 (T3), 5 (T4) and 10 (T5) minutes after intubation. The incidence and intensity of myoclonic movements were recorded as follows: 0 = no myoclonus, 1 = mild myoclonus, 2 = moderate myoclonus, and 3 = severe myoclonus.

Statistical Methods
Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0. Continuous variables are presented as mean ± SD, and categorical variables...
are presented as absolute numbers and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student’s t-test. In addition, nominal categorical data between the groups were compared using the Chi-squared test as appropriate. P<0.05 was considered statistically significant.

Results

Total 145 patients were assessed for eligibility from March 2017 to March 2018, out of which 15 patients were excluded from the study due to hypertension (8) and more than one attempt at intubation(7). 130 patients completed the study after random allocation into two groups (Fig.1).

Both groups were comparable in terms of demographic characteristics with no statistically significant differences (p>0.05) (Table 1, Figure 2). Baseline hemodynamic parameters were comparable in both groups with no statistically significant differences (p>0.05). There was a significant decrease in mean SBP, DBP and MAP from baseline in Propofol than Etomidate group at induction (p<0.05). In contrast, a significant increase in mean SBP, DBP, MAP and HR was seen in the Etomidate group, especially 1 minute after intubation (Table 2, 3, 4, 5 and Figure 3, 4, 5, 6). Incidence of myoclonus was higher in the Etomidate group compared to the Propofol group (64.6% vs 3.1%) with a statistically significant difference (p<0.05) (Table 6, Figure 7). There were no statistically significant differences in SpO2 and PONV between the two groups.

Discussion

Induction of general anaesthesia by injecting an IV induction agent and securing the airway with the help of a direct laryngoscope and ETT is an important part of achieving controlled ventilation in the conduct of general anaesthesia. During these steps, hemodynamic fluctuation is common and inevitable. Both hypo- and hypertensive effects bear clinical significance in patient management. Sudden hypotension on induction compromises cellular perfusion of vital organs. In contrast, tachycardia and hypertension have deleterious effects in patients with uncontrolled hypertension, coronary heart disease, valvular heart disease, and raised intracranial pressure. Therefore, it is important to choose a safe induction agent.

In this study, we have compared the haemodynamic response to induction of anaesthesia and tracheal intubation following induction with Propofol and Etomidate.

In our study, demographic variables are comparable in both groups. The baseline parameters such as mean SBP, mean DBP, mean MAP and mean HR were comparable in both groups (p>0.05) before induction.
Table 1 Demographic characteristics of patients (p>0.05).

| Variable         | Group P | Group E | P value |
|------------------|---------|---------|---------|
| Sex (female: male) | 39:26   | 41:24   | 0.718   |
| Age (years) mean+/- SD | 33.37 +/- 9.07 | 33.83 +/- 8.35 | 0.763   |
| Weight (kg)      | 60.45 +/- 8.42 | 58.58 +/- 8.91 | 0.233   |
| Height (m)       | 1.55 +/- 0.03  | 1.55 +/- 0.03  | 0.101   |
| BMI              | 25.61 +/- 3.37 | 25.01 +/- 3.54 | 0.324   |

Table 2 Comparison of mean SBP at different time points.

| SBP   | Propofol Mean ± SD | Etomidate Mean ± SD | P value |
|-------|---------------------|----------------------|---------|
| T0    | 124.88 ± 9.65       | 127.60 ± 8.47        | 0.090   |
| T1    | 110.71 ± 13.65      | 137.97 ± 24.49       | <0.001  |
| T2    | 130.09 ± 22.13      | 154.75 ± 27.16       | <0.001  |
| T3    | 110.95 ± 15.18      | 128.63 ± 19.86       | <0.001  |
| T4    | 110.89 ± 15.02      | 118.63 ± 18.52       | <0.001  |
| T5    | 114.29 ± 15.02      | 119.69 ± 18.10       | 0.066   |

Table 3 Comparison of mean DBP at different time points.

| DBP   | Propofol Mean ± SD | Etomidate Mean ± SD | P value |
|-------|---------------------|----------------------|---------|
| T0    | 74.55 ± 8.10        | 76.57 ± 8.45         | 0.367   |
| T1    | 64.6 ± 9.72         | 84.03 ± 17.49        | <0.001  |
| T2    | 78.66 ± 17.09       | 91.37 ± 19.09        | <0.001  |
| T3    | 64.06 ± 12.29       | 72.94 ± 14.79        | <0.001  |
| T4    | 65.82 ± 13.6        | 68.14 ± 12.27        | 0.308   |
| T5    | 68.38 ± 11.07       | 71.48 ± 14.10        | 0.167   |

Table 4 Comparison of mean MAP at different point times.

| MAP   | Propofol Mean ± SD | Etomidate Mean ± SD | P value |
|-------|--------------------|----------------------|---------|
| T0    | 90.95 ± 7.76       | 93.23 ± 7.78         | 0.097   |
| T1    | 79.58 ± 10.08      | 101.69 ± 19.08       | <0.001  |
| T2    | 95.46 ± 17.9       | 112.38 ± 21.02       | <0.001  |
| T3    | 79.4 ± 12.56       | 91.26 ± 15.47        | <0.001  |
| T4    | 80.4 ± 14.32       | 84.57 ± 13.65        | 0.092   |
| T5    | 83.38 ± 11.35      | 87.22 ± 14.78        | 0.100   |
Table 5 Comparison of mean HR at different time points.

| HR  | Propofol          | Etomidate         | P value |
|-----|-------------------|-------------------|---------|
|     | Mean ± SD         | Mean ± SD         |         |
| T0  | 85.18 ± 16.44     | 86.35 ± 17.52     | 0.695   |
| T1  | 86.29 ± 12.31     | 91.48 ± 19.86     | 0.076   |
| T2  | 91.03 ± 14.33     | 98.38 ± 16.77     | 0.008   |
| T3  | 82.15 ± 14.93     | 83.65 ± 16.47     | 0.589   |
| T4  | 78.23 ± 16.03     | 78.91 ± 15.14     | 0.805   |
| T5  | 77.11 ± 14.71     | 80.09 ± 15.06     | 0.255   |

Table 6 Comparison of myoclonus between two groups (A = Absent, P = Present)

| Myoclonus | Propofol | Etomidate | P value |
|-----------|----------|-----------|---------|
|           | Frequency | %         | Frequency | %       |         |
| A         | 63       | 96.9%     | 23        | 35.4%   | <0.001  |
| P         | 2        | 3.1%      | 42        | 64.6%   |         |
| Total     | 65       | 100%      | 65        | 100%    |         |

Figure 6 Comparison of mean HR at different time points

Figure 7 Showing presence (P) and absence (A) of myoclonus in between two groups

Postinduction in the Propofol group, there was a fall in mean SBP by 14.17 mmHg, whereas mean SBP increased by 10.37 mmHg in the Etomidate group from baseline. Muzi et al. 11 and Hoka S et al. 12 also increased hypotension after induction with Propofol, similar to our findings. This may be due to Propofol mediated sympatholytic actions causing vasodilation or its direct effects on vascular smooth muscles.

Masoudifar M et al. 2 and Aggarwal S at el 1 had conducted similar studies comparing hemodynamic response following induction with Propofol and Etomidate. They reported similar findings with Etomidate as more hemodynamically stable than Propofol. This could be due to the preservation of both sympathetic outflow and autonomic reflexes by Etomidate.

After induction, there was a statistically significant rise in mean SBP and DBP in the Etomidate group, whereas, in the Propofol group, there was a fall in mean SBP and DBP. Similarly, the mean MAP increased in the Etomidate group by 19.15 mmHg, but MAP in the Propofol group reduced further. Hence, the above finding suggests that Etomidate is a more hemodynamically stable agent.

However, after the intubation, statistically significant rise in HR, SBP, DBP, and MAP were found in the Etomidate group compared to the Propofol group. Similar findings were observed by Petrun AM et al. 10 and Singh R et al. 13. Harris CE at al. 14 also concluded with significant increase in arterial pressure following intubation in patients induced with Etomidate alone. Hence, the above finding suggests that Etomidate is less effective in minimizing stress response to intubation.

In our study, myoclonic movements were seen in 42 out of 65 patients on induction in the Etomidate group, whereas in the Propofol group, it was seen in only 2 out of 65 patients. Luan HF et al. 15, Saricaoglu F et al. 16 and Döenick A et al. 17 also reported a higher incidence of myoclonus between 50% and 80% in patients induced with Etomidate without premedication. However, in other studies conducted by Aggarwal S at el 1, Kaur S at el 18, Srivastava S at el 19 and Hueter L at el 20, the incidence of myoclonus after Etomidate was less in the patients who were premedicated with benzodiazepine or opioids. Unlike in our study, no premedication was given.

There was no statistical difference in PONV and SpO2 of patients in the two groups at all times (p>0.05).

Limitation: In our study, we did not measure the drug level in blood and plasma cortisol level.
Conclusion

Etomidate is a more hemodynamically stable induction agent compared to Propofol but is less effective in preventing stress response to laryngoscopy and tracheal intubation with a higher incidence of myoclonus on induction if proper premedication is not used.

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