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COMPARATIVE STUDY OF ETOMIDATE AND FENTANYL CITRATE WITH PROPOFOL (1%) AND FENTANYL CITRATE FOR TOTAL INTRAVENOUS ANESTHESIA IN COLONOSCOPY

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Abstract

Background: Total intravenous anesthesia (TIVA) combines induction agents, analgesics, and muscle relaxants, offering advantages over inhalational anesthesia. Commonly used induction agents include Etomidate, Propofol, Ketamine, Midazolam, and Fentanyl. This study compares Etomidate-Fentanyl citrate and Propofol-Fentanyl citrate combinations for colonoscopy, evaluating hemodynamic effects, onset, recovery, dosage, and adverse effects.

Patients and Methods: In this prospective randomized study, 60 patients undergoing colonoscopy were randomly allocated into two groups: Group E received Etomidate (0.3 mg/kg) IV and Group P received Propofol (1%) (2 mg/kg) IV. We recorded induction time, procedure duration, recovery time, vital signs (heart rate, blood pressure, respiratory rate, oxygen saturation), pain on injection, myoclonus, and side effects (nausea, vomiting, hypersensitivity reactions, hiccups).

Results: Group P showed increased heart rate at 1 minute post-induction, decreased MAP at 1-20 minutes, and decreased SpO2 at 1 minute. They also experienced more pain on injection, hypersensitivity reactions, longer induction times, and required more incremental doses, but had shorter recovery times. In contrast, Group E had higher rates of myoclonus, hiccups, and postoperative nausea-vomiting (PONV).

Conclusion: we concluded that Etomidate and Propofol both appear similarly safe for short procedure like Colonoscopy and should be individualize based on patient's unique characteristics and comorbidities. Etomidate is hemodynamically more stable, while Propofol provides earlier recovery with a lower incidence of postoperative nausea and vomiting (PONV).

KEYWORDS: Total intravenous anesthesia(TIVA), Colonoscopy, Etomidate, Propofol, Fentanyl.

INTRODUCTION

Colonoscopy is a common outpatient procedure for diagnosing and treating colorectal disorders, but it can cause pain, anxiety, and vasovagal reactions, requiring sedation and analgesia. Total intravenous anesthesia (TIVA) is a technique that combines induction agents, analgesics, and muscle relaxants to provide smooth induction, reliable maintenance, rapid emergence, and minimal side effects, while maintaining stage III surgical anesthesia. TIVA offers several advantages over inhalational anesthesia, including reduced operating room pollution, minimal cardiac depression, and decreased incidence of postoperative nausea and vomiting, making it a popular choice for many short surgical procedures.[1] Etomidate, Propofol, Ketamine, Midazolam and Fentanyl are commonly used induction agents in anesthesia, each with unique characteristics and side effects. Etomidate offers hemodynamic stability and cerebro-protective effects, but can cause reversible adrenocortical suppression and other adverse effects.[2] Propofol provides rapid and smooth induction, but can decrease blood pressure significantly and cause respiratory depression, while Fentanyl offers potent analgesia with minimal respiratory depression, making it a popular choice for pain management.[3,4] Propofol (1%) is usually used in patients with stable hemodynamic condition while Etomidate is used in patients with CVS problems, where its hemodynamic stability is desirable. Combining these drugs provides complete, balanced anesthesia and analgesia with high potency, lower dosages, and fewer side effects. The purpose of this study is to compare the Etomidate-Fentanyl citrate and Propofol-Fentanyl citrate combinations for colonoscopy in terms of their hemodynamic effects, onset of action, recovery time, total number of incremental doses, and adverse effects.

PATIENTS AND METHODS

A randomized, prospective trial was conducted at our institute in the Department of Anesthesiology from July 2022 to July 2024, involving 60 patients aged 18-60 years with ASA physical status I and II undergoing colonoscopy under total intravenous anesthesia. Patients of ASA grade > II, Allergic to any study drug, Pregnant women, cardiorespiratory disease like IHD, hypertension, bronchial asthma, MPG grade III and IV, Pathology of pharynx/larynx, H/o epilepsy/convulsion, drug, alcohol abuse were excluded from the study. Written informed consent was obtained from all patients.

A comprehensive pre-anesthetic evaluation was performed. Routine investigation was done. All patients were kept nil per orally for 6 hours prior to procedure.

We randomly allocated 60 patients into two group equally. Group E (Etomidate) received Inj. Etomidate (0.3 mg/kg) IV. Group P (Propofol 1%) received Inj. Propofol (1%) (2 mg/kg) IV.

On the day of procedure 18 G intravenous (IV) cannula was secured in upper limb and inj. Ringer lactate infusion was started. Monitors like non-invasive blood pressure (NIBP), electrocardiogram (ECG) and pulse oximetry were attached and baseline hemodynamic parameters were recorded. Oxygen at 4 L/min by nasal cannula was administered throughout the procedure.

Patients received Inj. Glycopyrrolate 4 mcg/kg IV, Inj. Ranitidine 1 mg/kg IV, Inj. Ondansetron 0.1mg/kg IV, and Inj. Fentanyl citrate 1 mcg/kg IV 3 minutes prior to induction. Group E received Inj. Etomidate 0.3 mg/kg IV slowly, while Group P received Inj. Propofol (1%) 2 mg/kg IV slowly. Hemodynamic variables were recorded 1 minute post-induction, after confirming loss of consciousness via unresponsiveness to verbal commands and loss of eyelash and corneal reflex.

Anesthesia was maintained in Group E with intermittent boluses of Inj. Etomidate 0.1 mg/kg and in Group P with Propofol (1%) 0.5 mg/kg, administered as required. Incremental doses were given when patients showed signs of light anesthesia, such as changes in heart rate, blood pressure, respiratory rate, or limb movements.

If oxygen saturation dropped below 92% for more than 10 seconds or apnea persisted for over 20 seconds, a jaw thrust maneuver was performed, and ventilation was initiated with a bag and mask using 100% oxygen.

Vital signs, including heart rate, mean arterial blood pressure, respiratory rate, and oxygen saturation, were monitored and recorded at regular intervals (1, 5, 10, 15, 20, 30, and 45 minutes) after induction. Pain on injection was noted in both groups, with severity graded as: 0 (no pain), 1 (verbal complaint), 2 (arm withdrawal), or 3 (both verbal complaint and arm withdrawal).

Myoclonus was noted in both groups after induction, with severity graded as: 0 (no myoclonus), 1 (short movement of a body segment), 2 (slight movement of different muscles or muscle groups), or 3 (intense clonic movement in two or more muscle groups).

We recorded induction time and total duration of procedure in both groups. Recovery time was observed from the end of the procedure to the return of protective airway reflexes. We observed side effect like nausea, vomiting, hypersensitivity reactions, and hiccups etc in both groups. We also calculated total number of incremental dose and total dose of both drugs.

Statistical analysis

A power analysis determined that 27 patients per group were needed, assuming a 10% dropout rate, which increased the required number to 30 patients per group. Data were compared between groups using unpaired t-tests for continuous variables and chi-square or Fisher's exact tests for categorical variables.

The data was analysed using socialsciencestatistics.com and Microsoft Excel 2019.

Significant figures

1. SS- Statistically Significant (P: ≤ 0.05)
2. HS- Highly significant (P: ≤ 0.001)
3. NS- Not significant (P: > 0.05)

RESULTS

The study included 60 adult patients, aged 18-60 years, of both sexes, classified as ASA Class I and II, undergoing colonoscopy under total intravenous anesthesia.

The demographic data, including age, weight, and duration of procedures, as shown in Table 1, were comparable between the two groups and showed no statistically significant differences.

Table 1: Demographic data: Age, Weight and Duration of Procedures.

	Group E	**Group P**	**P Value**	**Significance**
Age (years)	42.80±13.26	43.1±12.03	0.463	NS
Weight (kg)	62.73±6.62	62.93±7.03	0.455	NS

Duration of procedure (min)	17.93±3.30	17.83±3.69	0.456	NS

Figure 1 illustrates that baseline heart rates were comparable between the two groups. However, Group P exhibited a statistically significant increase in heart rate at 1 minute post-induction, which later returned to non-significant differences.

FIGURE 1:CHANGES IN HEART RATE DURING THE PERIOPERATIVE PERIOD.

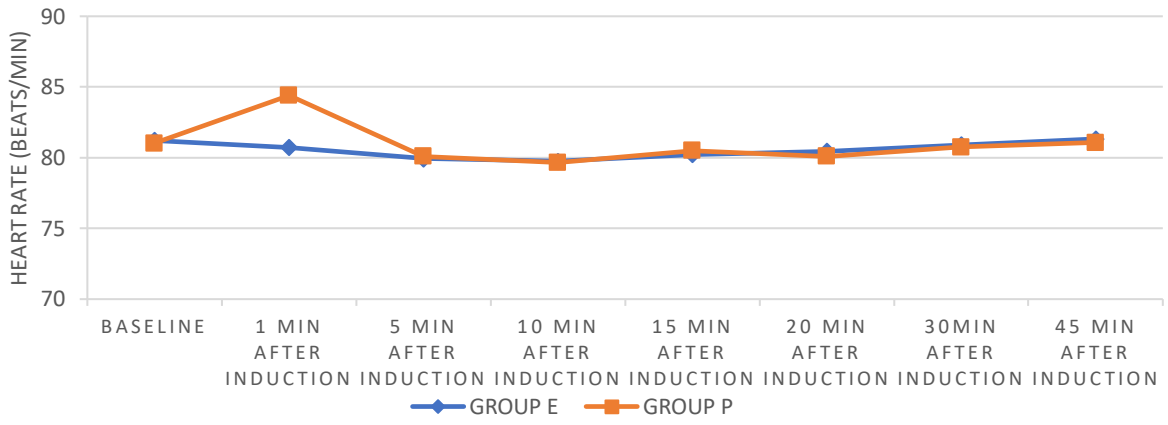


Figure 2 illustrates that baseline mean arterial pressure (MAP) was comparable between the two groups. However, Group P showed statistically significant fall in MAP at 1-20 minutes post-induction, which later returned to non-significant differences.

FIGURE 2: CHANGES IN MEAN ARTERIAL BLOOD PRESSURE DURING THE PERIOPERATIVE PERIOD

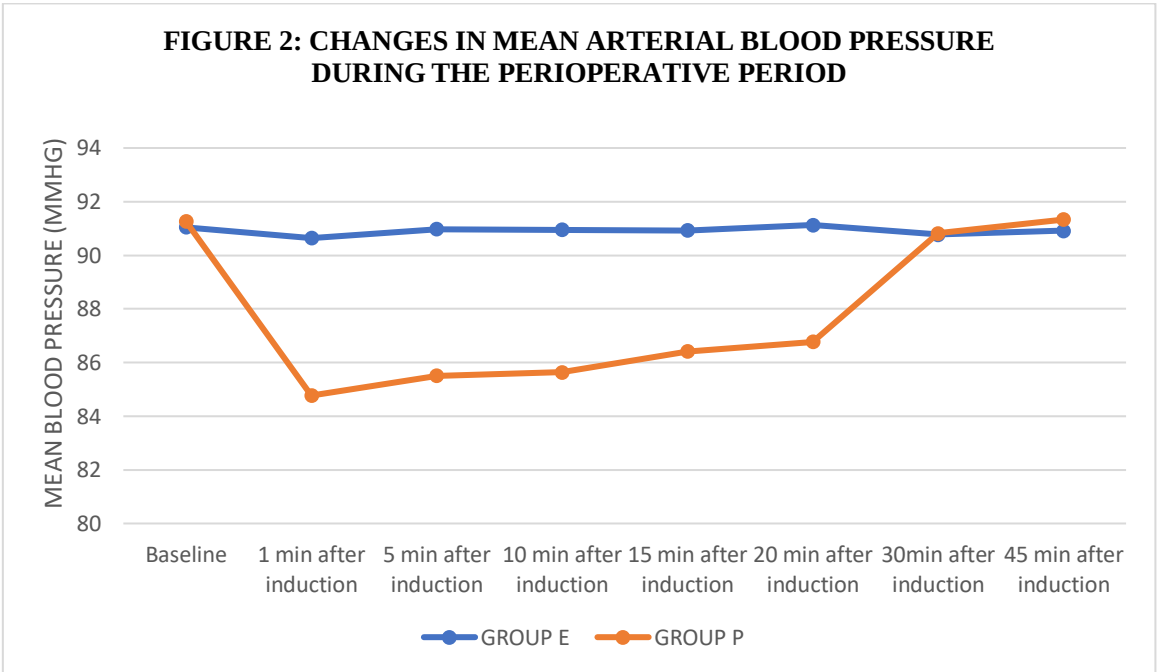


Figure 3 demonstrates that baseline SPO2 levels were comparable between the two groups. However, a transient, statistically significant decrease in SPO2 was observed in Group P at 1 minute post-induction, with no significant differences noted thereafter.

FIGURE 3: CHANGES IN OXYGEN SATURATION (SPO_2) DURING THE PERIOPERATIVE PERIOD

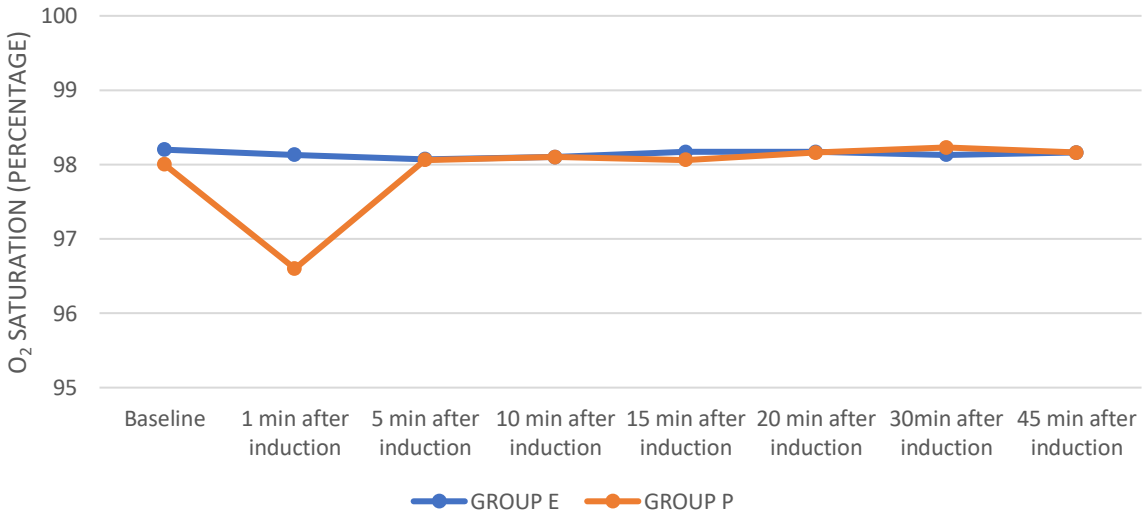


Figure 4 reveals that Group P had a significantly higher incidence of pain on injection, affecting 40% of patients, compared to Group E, where only 10% of patients experienced pain on injection.

FIGURE 4: INCIDENCE & GRADING OF PAIN ON INJECTION

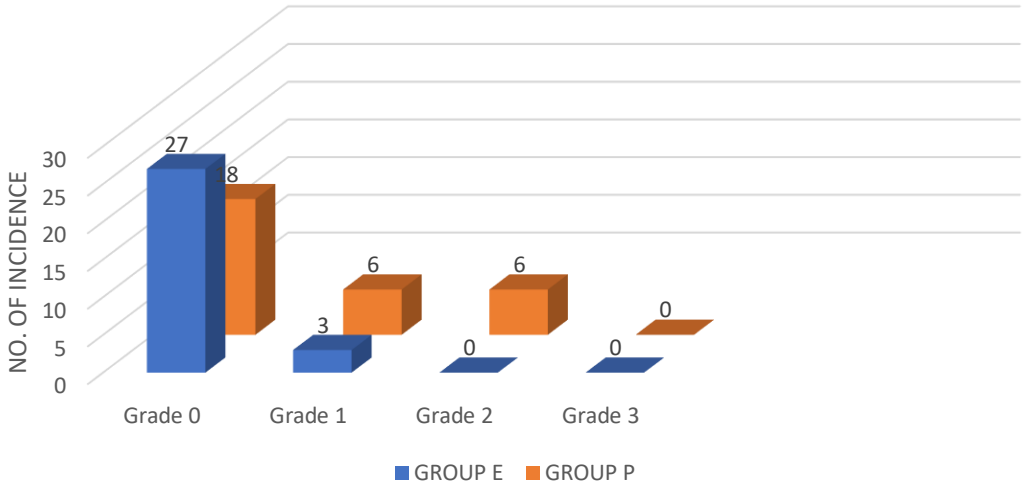
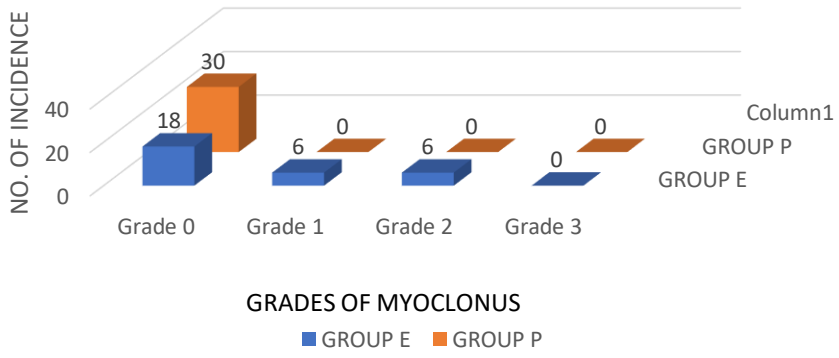


Figure 5 illustrates that myoclonus occurred exclusively in Group E, with 20% of patients experiencing grade 1 severity and 20% experiencing grade 2 severity, resulting in a statistically significant difference between the two groups.

FIGURE 5: INCIDENCE & GRADING OF MYOCLONUS



Group E had a statistically significant shorter induction time (0.818 ± 0.148 minutes) and required fewer incremental doses (1.433 ± 1.104) compared to Group P, which had a longer induction time (1.24 ± 0.303 minutes) and required more incremental doses (2.2 ± 1.156). However, Group E had a statistically significant longer recovery time (6.3 ± 1.087 minutes) compared to Group P (5.36 ± 1.37 minutes). Additionally, Group E experienced higher rates of PONV (20%) and hiccups (10%), while Group P had a higher incidence of hypersensitivity reactions (10%).

DISCUSSION

Total Intravenous Anesthesia (TIVA) has garnered significant interest among anesthesiologists, with ongoing efforts to optimize drug combinations for rapid induction, smooth maintenance, and swift recovery, addressing limitations of single-drug approaches.[5] By combining multiple agents, TIVA aims to provide a balanced anesthetic technique, minimizing side effects and maximizing patient comfort, while also facilitating efficient surgical workflows.[6] Combining hypnotics like Propofol with analgesics like Fentanyl in Total Intravenous Anesthesia (TIVA) provides hemodynamic stability, reduces respiratory depression, and creates a synergistic interaction that minimizes side effects and drug accumulation.[7,8]

We studied 60 adult patients undergoing colonoscopy under Total Intravenous Anesthesia, randomly allocated into two groups: Group E (Etomidate plus Fentanyl citrate) and Group P (Propofol plus Fentanyl citrate). Demographically, both groups were comparable in terms of age, weight, and procedure duration (Table 1), with no statistically significant differences ($p>0.05$). The procedure duration was 17.93±3.30 minutes in Group E and 17.83±3.69 minutes in Group P (Table 1). We observed all patients peri-operatively for one hour post-induction and again after four hours before discharge, if the procedure was on a daycare basis. Pre-induction vital signs, including heart rate, mean arterial pressure, oxygen saturation, and respiratory rate, were comparable between both groups, with no statistically significant differences ($p>0.05$).

Regarding hemodynamic parameters, Group E maintained stable heart rates throughout the induction, maintenance, and recovery periods, closely mirroring baseline values. In contrast, Group P experienced a transient increase in heart rate immediately after induction, which was statistically significant at 1 minute post-induction ($p < 0.05$). However, heart rates in Group P returned to near-baseline levels thereafter, becoming comparable to Group E's rates for the remainder of the procedure ($p > 0.05$) (Figure 1).

Momin AG et al [1] compared etomidate and fentanyl citrate with propofol (1%) and fentanyl citrate for total intravenous anesthesia in short surgical procedures, revealing notable tachycardia and hypotension following induction with propofol (1%) and fentanyl citrate, whereas induction with etomidate and fentanyl citrate demonstrated consistent cardiovascular stability throughout the procedure and recovery phase. Shah SB et al [9] found that propofol caused a sustained heart rate increase during induction and intubation, whereas etomidate maintained stable heart rates. Li Li, et al [10] found that combining etomidate and propofol for pediatric anesthesia improved heart rate recovery compared to using either medication alone. Masoudifar M et al [11] found no significant difference in heart rate between propofol and etomidate groups during laryngoscopy and tracheal intubation. Results are also concordant with the study conducted by Banihashem N et al [12], Aggarwal S et al. [13]

Etomidate is an induction agent with minimal cardiovascular depression, making it suitable for hemodynamically unstable patients and those requiring rapid sequence induction. Unlike Thiopental or Propofol (1%), Etomidate has

negligible effects on heart rate, systemic vascular resistance, and cardiac output in healthy individuals or those with mild cardiovascular disease. Propofol (1%) can cause tachycardia due to hypotension or pain on injection, in this study, there was significant increase in heart rate. Overall, Etomidate's unique characteristics make it an ideal choice for patients with cardiovascular instability or those undergoing short surgical procedures.

The mean arterial blood pressure (MAP) was comparable in both groups before induction ($p > 0.05$). However, Group P experienced a significant drop in MAP at 1 minute post-induction, which gradually returned to pre-induction levels during maintenance and recovery. In contrast, Group E maintained stable MAP throughout the procedure. The difference in MAP between groups was statistically significant until 20 minutes post-induction ($p < 0.05$) (Figure 2). The Propofol (1%) group experienced more hypotension, while the Etomidate group maintained more stable blood pressure. No patients required treatment for hypotension or had adverse effects, likely due to intravenous fluid administration prescribed by their primary consultant.

Momin AG et al [1], Shah SB et al [9], Masoudifar M et al [11], Aggarwal S et al [13] concluded that Etomidate preserves hemodynamic stability during anaesthesia. Several studies, including those by Li Li, et al [10], Rathore VS et al [14], Meena K et al [15], and Li Yun, et al [16], found that combining etomidate and propofol resulted in significantly better hemodynamic outcomes compared to using either agent alone. However, Banihashem N et al [12] reported no significant difference in hemodynamic changes between the two groups.

The hemodynamic stability of Etomidate is attributed to its minimal impact on the sympathetic nervous system and baroreceptor function, as well as its ability to stimulate peripheral alpha-2B adrenergic receptors, leading to vasoconstriction.[17]

Hypotension with Propofol (1%) is primarily caused by reduced sympathetic activity, leading to vasodilation, or its direct effect on vascular smooth muscles. [18] The severity of the decrease in mean arterial pressure (MAP) is dependent on both vasodilation and myocardial depression. [19] This sudden hypotension and tachycardia can compromise perfusion to vital organs in patients with uncontrolled hypertension, coronary artery disease, valvular stenosis, and shock. Ramdev B et al [20] found a notable drop in blood pressure one minute after induction in the Propofol-fentanyl group.

Oxygen saturation (SPO2) remained stable in Group E, but significantly dropped in Group P, particularly at 1 minute post-induction ($p < 0.05$) (Figure 3). In Group P, 20% of patients (6/30) experienced a fall in SPO2 below 90% after induction with Propofol (1%) and Fentanyl citrate. Four patients required jaw thrust maneuver, and two needed bag and mask ventilation with 100% O2. Saturation returned to baseline within 2-3 minutes, and no patients experienced significant respiratory depression during recovery.

Studies by Momin AG et al [1] and Masoudifar M et al [11] found comparable oxygen saturation (SPO2) and respiratory rates between Etomidate and Propofol groups. However, Ramdev B et al [20] observed a significant drop in respiratory rate in the Propofol-Fentanyl group, particularly at 1 minute post-induction. Propofol (1%) is known for its potent respiratory depressant effects, often causing apnea, especially when combined with opioids. [21]

Pain on injection was a significant issue in both groups, but more prevalent in Group P (40%, 12/30) compared to Group E (10%, 3/30), with a statistically significant difference ($p < 0.05$). The severity of pain was also greater in Group P (Figure 4). The Etomidate formulation's propylene glycol solvent, with high osmolality (4,900 mOsm/L), contributes to pain on injection and venous irritation. Studies by Momin AG et al [1], Li Yun, et al [16], Aggarwal S et al [13], and Rathore VS et al [14] found that pain on injection was more frequent in the Propofol group. A study by Kosarek L, et al [22] found that faster injection rates (15 seconds) reduced pain on injection compared to slower rates (30 seconds) in the Etomidate group (14% vs. 27%). Also reduced contact time between propofol and the endothelium, minimizing mediator release and pain on injection.[23] Pain on injection with Propofol can be reduced by various methods, including slow injection into a carrier fluid or large vein, prior administration of Xylocaine 2% IV, analgesics, or opioids. In this study, Inj. Fentanyl 2 mcg/kg IV was given before induction.

Etomidate-induced myoclonus is thought to result from disinhibition of subcortical structures that normally suppress extrapyramidal motor activity [24]. In this study, no patients in Group P exhibited myoclonic movements, whereas 40% (12/30) of patients in Group E did, a statistically significant difference ($p < 0.05$). The severity was evenly split, with 20% (6/30) of patients experiencing Grade 1 and 20% (6/30) experiencing Grade 2 myoclonus (Figure 5). No patients required immediate treatment or experienced recurrence during post-observation. Studies by Momin AG et al [1], Li Yun, et al [16], Aggarwal S et al [13], Rathore VS et al [14], and Saricoaglu et al [25] also found a higher incidence of myoclonus in the Etomidate group compared to the Propofol (1%) group.

An ideal induction agent should provide rapid induction without side effects. In this study, Group E (Etomidate) had a significantly shorter induction time (0.81±0.14 min) compared to Group P (Propofol) (1.24±0.30 min) ($p < 0.001$). Etomidate also required fewer incremental doses (1.43±1.104) than Propofol (2.2±1.15) ($p < 0.05$). However, Propofol's longer half-life reduced the amount of drug needed in subsequent doses, whereas Etomidate showed little cumulation with repeated doses. Momin AG et al [1] found that Etomidate required fewer incremental doses compared to Propofol (1%) in short surgical procedures. Both Etomidate and Propofol (1%) have rapid induction times and short durations of action. Etomidate 0.3 mg/kg induces sedation in 30-50 seconds, lasting 5-10 minutes, with incremental doses of 0.1

mg/kg needed every 5-8 minutes. Propofol (1%) has an onset of 45-90 seconds, with effects resolving in 3-5 minutes by redistribution, and incremental doses of 0.5 mg/kg needed every 3-5 minutes.
Recovery time was significantly longer in Group E (6.3±1.08 min) compared to Group P (5.36±1.37 min) ($p < 0.05$). Momin AG et al [1] and Banihashem N et al [12] also found longer recovery times in the Etomidate group compared to the Propofol (1%) group. Our study showed that patients receiving Propofol (1%) took longer to respond to verbal commands and regain protective airway reflexes compared to those receiving Etomidate. Both drugs provided smooth and rapid recovery without prolonged sedation.
Colonoscopy was successful with adequate sedation and analgesia in all patients, except for 2 patients in each group, who required a rescue dose of Inj. Sodium thiopentone 5-7 mg/kg for adequate amnesia and sedation.
Post-operative nausea and vomiting were significantly higher in Group E (20%, 6/30) compared to Group P (10%, 3/30). Pre-treatment with histamine receptor 2 antagonists and ondansetron reduced the incidence in both groups. Propofol (1%) showed superior antiemetic effects, likely due to its modulation of subcortical pathways or direct depressant effect on the vomiting centre [24]. Hiccups occurred in 10% (3/30) of Group E patients, while Group P had no cases. Hypersensitivity reactions were seen in 10% (3/30) of Group P patients, with no cases in Group E.

CONCLUSION

we concluded that Both Etomidate–Fentanyl citrate and Propofol (1%)–Fentanyl citrate combinations offer smooth induction, easy maintenance, and rapid recovery with minimal hemodynamic changes, making them ideal options for total intravenous anesthesia (TIVA) technique. Etomidate is preferred over Propofol (1%) for patients who are hemodynamically unstable due to its minimal effects on the cardiovascular and respiratory systems. Propofol (1%) is associated with a higher incidence of hypotension, pain on injection, and hypersensitivity reactions, whereas Etomidate is more commonly linked to myoclonus, hiccups, nausea, and vomiting. Hence, we concluded that Etomidate and Propofol both appear similarly safe for short procedure like Colonoscopy and should be individualize based on patient's unique characteristics and comorbidities.

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Conflicts of interest
There are no conflicts of interest.

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