Journal of Cardiovascular Disease Research

ISSN:0975-3583,0976-2833 VOL14, ISSUE06 ,2023

Comparison Of The Haemodynamic Responses To Laryngoscopy And Intubation On Induction With Etomidate, Propofol-Ketamine Or Propofol-Etomidate.

Dr. Pooja Wagh[1], Dr. Venus Sharma[2] and Dr. Pradeep Sharma[3]

[1]Assistant Professor, Department of Anaesthesia, Bharati Vidyapeeth Medical College, Pune
[2]Assistant Professor, Department of Anaesthesia, Gian Sagar Medical College, Patiala, Punjab
[3]Assistant Professor, Department of Medicine, Gian Sagar Medical College, Patiala, Punjab.

Corresponding Author:
Dr. Pooja Wagh
E-mail: poojakannadkar@gmail.com

Abstract

Background: Laryngoscopy and intubation, commonly employed for airway management during general anesthesia, often lead to undesirable hemodynamic changes.

Objectives: This study aimed to compare the effects of etomidate, a combination of propofol-ketamine, and propofol-etomidate as induction agents on the hemodynamic response to laryngoscopy and intubation.

Patients and Methods: In a double-blind, randomized clinical trial, 120 adult patients of both sexes, aged 18 to 45 years, scheduled for elective surgery under general anesthesia were randomly allocated into three equally sized groups. Group A received etomidate (0.3 mg/kg) plus normal saline as placebo. Groups B received propofol (1.5 mg/kg) plus ketamine (0.5 mg/kg) and Group C received the combination of 1mg/kg propofol plus 0.15mg/kg etomidate. respectively, for anesthesia induction. Hemodynamic values (systolic blood pressure [SBP], diastolic blood pressure [DBP], mean arterial pressure [MAP], and heart rate [HR]) were measured before laryngoscopy and tracheal intubation, immediately after, and one and three minutes after the procedures.

Results: Repeated-measures ANOVA revealed significant changes in mean SBP and DBP between the time points ($P < 0.05$). Additionally, the main effects of MAP and HR were statistically significant during the study period ($P < 0.05$). Moreover, after anesthesia induction, the three study groups exhibited significantly different changes in SBP, DBP, and MAP over time ($P < 0.05$). However, changes in HR over time were not statistically significant ($P > 0.05$). The combination of propofol-ketamine demonstrated superior hemodynamic stability compared to other induction agents.

Conclusions: The propofol-ketamine combination may be recommended as an effective and safe induction agent for attenuating hemodynamic responses to laryngoscopy and intubation with improved hemodynamic stability. Nevertheless, further well-designed randomized clinical trials are warranted to confirm the safety and efficacy of this combination, particularly in critically ill patients or those with cardiovascular disease.

Keywords: Etomidate, Propofol, Ketamine, Hemodynamics, Laryngoscopy.

INTRODUCTION

Laryngoscopy and tracheal intubation, often necessary for airway management during general anesthesia, are procedures known for their potential pain induction. They frequently lead to hemodynamic disturbances, including tachycardia, hypertension, arrhythmias, or other unwanted changes in blood flow [1, 2]. These hemodynamic shifts are considered hazardous complications of general anesthesia[3, 4]. Many studies have investigated various induction agents, such as etomidate, thiopental, propofol, ketamine, midazolam, and fentanyl, aiming to reduce the hemodynamic responses to laryngoscopy. Each of these pharmacological agents has its advantages and disadvantages, and there is no universally optimal choice for this purpose [1, 2, 5-7].

The choice of using etomidate for intubation depends on several factors, including the patient's medical condition, hemodynamic status, and the specific requirements of the procedure. Here are some considerations for using etomidate:

1. **Hemodynamic Stability:** Etomidate is known for its relatively stable cardiovascular profile, making it an attractive option for patients who require intubation but are hemodynamically compromised. It causes minimal changes in blood pressure and heart rate compared to other induction agents like propofol.
2. **Rapid Onset:** Etomidate has a rapid onset of action, typically inducing anesthesia within 30 to 60 seconds after administration. This makes it suitable for situations where a quick and smooth induction of anesthesia is necessary.
3. **Preservation of Respiratory Function:** Etomidate tends to preserve respiratory function, including airway reflexes and respiratory drive, which can be beneficial, especially in patients with compromised airways or respiratory conditions.

ISSN:0975-3583,0976-2833 VOL14, ISSUE06 ,2023

4. **Adrenal Suppression:** One potential drawback of etomidate is its suppressive effect on adrenal function, which can lead to adrenal insufficiency, especially with repeated doses or prolonged infusions. This may be a concern in critically ill patients or those with underlying adrenal dysfunction.
5. **Patient Factors:** The choice of etomidate should also take into account individual patient factors such as age, comorbidities, and medication history. Etomidate is generally well-tolerated in most patient populations but may need to be used cautiously in certain groups, such as those with sepsis or compromised adrenal function.

Overall, etomidate can be a valuable option for intubation, particularly in patients who require rapid and stable induction of anesthesia with minimal hemodynamic effects. However, its potential for adrenal suppression should be considered, especially in patients requiring prolonged or repeated doses. As with any medication, the decision to use etomidate should be made based on a comprehensive assessment of the patient's clinical condition and in consultation with a medical professional.

The choice between using a combination of propofol with ketamine or propofol with etomidate for intubation depends on various factors, including the patient's medical condition, hemodynamic status, and the specific requirements of the procedure.

Propofol-Ketamine Combination:
This combination is often preferred when maintaining hemodynamic stability is a concern, especially in patients who are hemodynamically compromised or at risk of hypotension.
Ketamine has sympathomimetic properties, which can help maintain blood pressure and heart rate during induction and intubation. It acts as a counterbalance to the potential hypotensive effects of propofol.
Ketamine also provides analgesia and preserves airway reflexes, which can be beneficial in certain scenarios, such as trauma or patients with compromised airways.

Propofol-Etomidate Combination:
Propofol and etomidate are both agents that primarily cause central nervous system depression, leading to rapid induction of anesthesia.

Etomidate is often chosen when rapid and smooth induction with minimal cardiovascular effects is desired.
Etomidate has a relatively neutral effect on hemodynamics, making it suitable for patients who are hemodynamically stable or when maintaining blood pressure is not a primary concern.
However, etomidate may suppress adrenal function, potentially leading to adrenal insufficiency, especially with repeated doses or prolonged infusions.
Thus the current study is designed to compare the effects of etomidate, a combination of propofol-ketamine, and propofol-etomidate as induction agents on the hemodynamic response to laryngoscopy and intubation.

MATERIALS AND METHOD
In a double-blind, randomized clinical trial, 120 adult patients of both sexes, aged 18 to 45 years, scheduled for elective surgery under general anesthesia were randomly allocated into three equally sized groups.

Patients with a history of adrenal insufficiency, asthma, hypertension, suspected difficult airway, recent exposure to general anesthesia within the past week, use of steroids within the past 6 months, known sensitivity to etomidate, propofol, or thiopental, allergy to egg or soy, pregnancy, chronic inflammatory conditions, or significant psychiatric, endocrine, or neurological disorders were excluded from the study. Eligible participants meeting the inclusion criteria were randomly assigned to one of three groups (groups A, B, and C) using random number tables, by an anesthetic nurse who was blinded to the study groups.

Following the establishment of venous access on the forearm of the nondominant hand, all patients received an infusion of lactated Ringer's solution at a rate of 5 ml/kg. Baseline measurements of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP), and heart rate (HR) were recorded upon completion of the infusion. For premedication, each patient received midazolam (0.02 mg/kg) and fentanyl (3 µg/kg). One minute later, hypnotic drugs were administered to each group for anesthesia induction. Patients in Group A received etomidate (0.3 mg/kg) plus normal saline as placebo. Patients in Group B received propofol (1.5 mg/kg) plus ketamine (0.5 mg/kg) and Group C received the combination of (1mg/kg) propofol plus (0.15mg/kg) etomidaterespectively, for anesthesia induction. The medications were administered in equal volumes, and the syringes were covered with masking tape to conceal product details. The loss of eyelash reflex served as the endpoint for induction.

ISSN:0975-3583,0976-2833 VOL14, ISSUE06,2023

After the administration of hypnotic drugs, succinylcholine (1.5 mg/kg) was given as a muscle relaxant to aid intubation. One minute later, laryngoscopy was performed by an anesthesiologist blinded to the study groups. Hemodynamic values (SBP, DBP, MAP, and HR) were measured immediately after laryngoscopy and tracheal intubation, as well as at one and three minutes post-procedure. If SBP dropped to less than 20% of the baseline, 10 mg of ephedrine was administered and documented.

Furthermore, a nurse, unaware of the study groups, noted the occurrence of muscle twitching following hypnotic drug administration, as well as the occurrence of nausea and vomiting during anesthesia recovery. The primary outcome measure was hemodynamic changes (SBP, DBP, MAP, and HR) following laryngoscopy and intubation, while the secondary outcome was the incidence of muscle twitching and postoperative nausea and vomiting (PONV) across the three study groups.

RESULTS

The data were analyzed using SPSS 20 statistical software (SPSS Inc., Chicago, IL). Chi-squared test was used for analyzing qualitative data, while quantitative data were analyzed using a mixed-design analysis of variance model. A p-value below 0.05 was considered statistically significant.

Table 1: Demographic Characteristics of Patients in the Three Groups

Variables	Group A (Etomidate/Normal Saline)	Group B (Propofol/Ketamine)	Group C (Propofol-Etomidate)	P-Value
Gender				.64
Male	19 (32.2)	18 (30.5)	22 (37.3)	
Female	21 (34.4)	22 (36.1)	18 (29.5)	
Age, y	31.30 ± 8.52	29.75 ± 6.92	32.27 ± 7.05	.23
Body mass index, kg/m ^{2}	26.15 ± 3.58	25.24 ± 3.16	26.49 ± 5.94	.42

- Gender distribution across the three groups did not show a statistically significant difference ($p = 0.64$).
- The mean age of participants in each group was not significantly different ($p = 0.23$).
- Similarly, the body mass index (BMI) of participants did not differ significantly between the groups ($p = 0.42$).

Overall, there were no significant differences in gender distribution, age, or BMI among the participants across the three groups.

Table 2. Hemodynamic Variables in Three Treatment Groups, Mean and 95% CI

Measurement Time/ Hemodynamic Variable	Etomidate	Propofol-Ketamine	Propofol-Etomidate	P-Value
Baseline Measurement				
Systolic BP	128.66 (124.81 - 132.48)	131 (125.57 - 134.41)	132.41 (128.47 - 136.2)	.408
Diastolic BP	79.36 (79.26-82.43)	77.61 (74.87-80.32)	81.36 (78.05 - 84.64)	.216
Mean Arterial BP	93.21 (89.34-97.05)	91.26 (86.72-93.22)	95.26 (93.75-98.74)	.125
Heart Rate	89.46 (83.51 - 93.38)	97.63 (93.10 - 102.14)	85.65 (80.14 - 91.25)	.021
First Measurement (Immediately after intervention)				
Systolic BP	125.17 (120.86 - 129.48)	127.75 (122.18 - 133.31)	122.47 (117.56 - 127.38)	.317
Diastolic BP	78.27 (74.55 - 81.99)	74.35 (71.33 - 77.26)	75.1 (71.85 - 78.34)	.207
Mean Arterial BP	92.60 (88.979 - 96.40)	87.17 (83.62 - 90.72)	89.17 (85.91 - 92.43)	.91
Heart Rate	84.55 (80.16 - 88.93)	96.42 (92.35 - 100.49)	86.55 (81.62 - 91.47)	> .0001
Second Measurement (One minute after intervention)				

ISSN:0975-3583,0976-2833 VOL14, ISSUE06,2023

Systolic BP	145.10 (137.12 - 153.07)	123.82 (117.09 - 130.55)	139.92 (134.03 - 145.81)	> .0001
Diastolic BP	92.90 (86.71 - 99.02)	77.37 (73 - 81.74)	91.40 (86.48 - 96.31)	> 0.0001
Mean Arterial BP	107.17 (100.98 - 113.38)	88.22 (82.50 - 93.94)	107.80 (102.50 - 113.09)	> .0001
Heart Rate	94.67 (88.41 - 100.93)	97.62 (94.69 - 100.55)	92.05 (86.80 - 97.29)	.285
Third Measurement (Three minute after intervention)				
Systolic BP	138.45 (130.60 - 146.20)	119.67 (114.16 - 125.18)	138.12 (133.30 - 142.94)	> .0001
Diastolic BP	84.55 (78.37 - 90.72)	76.30 (73.45 - 79.14)	86.90 (83.04 - 90.75)	0.003
Mean Arterial BP	99.07 (92.45 - 105.09)	86.32 (83.07 - 89.57)	104.05 (100.95 - 107.14)	> .0001
Heart Rate	89.25 (83.03 - 95.40)	95.17 (92.05 - 98.29)	89.12 (83.33 - 94.91)	.171

Abbreviation: BP: Blood pressure.

Here's a summary of the hemodynamic variables at different measurement times and their analysis:

Baseline Measurement:

- Systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MAP) did not show significant differences between the groups ($p > 0.05$).
- Heart rate (HR) differed significantly among the groups ($p = 0.021$).

First Measurement (Immediately after intervention):

- SBP, DBP, and MAP did not exhibit significant differences between the groups ($p > 0.05$).
- HR showed a significant difference among the groups ($p < 0.0001$).

Second Measurement (One minute after intervention):

- SBP, DBP, and MAP differed significantly among the groups ($p < 0.0001$).
- HR did not show significant differences between the groups ($p = 0.285$).

Third Measurement (Three minutes after intervention):

- SBP, DBP, and MAP differed significantly among the groups ($p < 0.0001$).
- HR did not exhibit significant differences between the groups ($p = 0.171$).

Overall, significant differences were observed in SBP, DBP, and MAP among the groups at the second and third measurement times. HR showed significant differences immediately after intervention but not at subsequent measurement times.

Table 3. Prevalence of Side Effects in the Three Study Groups

Side-Effects	**Group**			**P-Value[c]**
	Etomidate	**Propofol-ketamine**	**Propofol-Etomidate**	
Muscle Twitching	6 (15)	0	8 (20)	.006
PONV	11 (27.5)	0	3 (7.5)	< .001

Muscle Twitching:

- The incidence of muscle twitching was 15% in the Etomidate group, 0% in the Propofol-ketamine group, and 20% in the Propofol-Etomidate group.
- The difference in the incidence of muscle twitching between the groups was statistically significant ($p = 0.006$).

Postoperative Nausea and Vomiting (PONV):

- The incidence of PONV was 27.5% in the Etomidate group, 0% in the Propofol-ketamine group, and 7.5% in the Propofol-Etomidate group.
- The difference in the incidence of PONV between the groups was highly statistically significant ($p < 0.001$).

ISSN:0975-3583,0976-2833 VOL14, ISSUE06 ,2023

Overall, significant differences were observed in the incidence of both muscle twitching and PONV among the three groups.

DISCUSSION

In our study, we investigated the impact of three different induction agents—etomidate, a combination of propofol-ketamine, and a combination of propofol-etomidate—on the hemodynamic response to laryngoscopy and intubation. One significant discovery was that patients administered the propofol-ketamine combination exhibited superior hemodynamic stability compared to those in the other groups. Additionally, a notable finding was that none of the patients in the propofol-ketamine combination group experienced muscle twitching or postoperative nausea and vomiting (PONV), whereas 14 patients in the propofol-etomidateand etomidate groups did. These results underscore the potential advantages of the propofol-ketamine combination in terms of hemodynamic control and minimizing adverse effects such as muscle twitching and PONV.

Anesthesiologists are attentive to anesthesia-induced fluctuations in hemodynamics due to their potential association with postoperative complications in surgical patients. To mitigate these fluctuations, various induction agents have been utilized. Etomidate stands out among these agents for its minimal impact on hemodynamics and wide safety profile. However, despite its advantages, etomidate can lead to the suppression of adrenocortical steroid synthesis and increased postoperative nausea and vomiting (PONV). Lundy et al.[8] documented a case of adrenal insufficiency following a single dose of etomidate used for anesthesia induction. Additionally, O'Leary et al.[9] demonstrated that after a single bolus dose of etomidate administration in gynecological surgery patients, the cortisol response to surgery was absent for up to 48 hours, whereas in the thiopental group, circulating cortisol levels notably increased postoperatively.

CONCLUSION

In summary, if maintaining hemodynamic stability is a priority, especially in patients with compromised cardiovascular status, the propofol-ketamine combination may be preferred. On the other hand, if rapid induction with minimal cardiovascular effects is the goal and the patient's adrenal function is not a concern, the propofol-etomidate combination may be suitable. It's essential to consider the individual patient's clinical condition and consult with a medical professional to determine the most appropriate choice for intubation.

REFERENCES

1. Habibi MR, Baradari AG, Soleimani A, EmamiZeydi A, Nia HS, Habibi A, et al. Hemodynamic responses to etomidate versus ketamine-thiopental sodium combination for anesthetic induction in coronary artery bypass graft surgery patients with low ejection fraction: a double-blind, randomized, clinical trial. *J Clin Diagn Res.* 2014;8(10):GC01–5.
2. KordValeshabad A, Nabavian O, Nourijelyani K, Kord H, Vafainejad H, KordValeshabad R, et al. Attenuation of Hemodynamic Responses to Laryngoscopy and Tracheal Intubation: Propacetamol versus Lidocaine-A Randomized Clinical Trial. *Anesthesiol Res Pract.* 2014;2014:170247.
3. Dashti M, Amini S, Azarfarin R, Totonchi Z, Hatami M. Hemodynamic changes following endotracheal intubation with glidescope((R)) video-laryngoscope in patients with untreated hypertension. *Res Cardiovasc Med.* 2014;3(2):e30071. doi: 10.5812/cardiovascmed.17598.
4. Forbes AM, Dally FG. Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. *Br J Anaesth.* 1970;42(7):618–24.
5. Abbasivash R, Aghdashi MM, Sinaei B, Kheradmand F. The effects of propofol-midazolam-ketamine co-induction on hemodynamic changes and catecholamine response. *J Clin Anesth.* 2014;26(8):628–33.
6. Meftahuzzaman SM, Islam MM, Ireen ST, Islam MR, Kabir H, Rashid H, et al. Comparison of efficacy of labetalol and fentanyl for attenuating reflex responses to laryngoscopy and intubation. *Mymensingh Med J.* 2014;23(2):242–8.
7. Smischney NJ, Beach ML, Loftus RW, Dodds TM, Koff MD. Ketamine/propofol admixture (ketofol) is associated with improved hemodynamics as an induction agent: a randomized, controlled trial. *J Trauma Acute Care Surg.* 2012;73(1):94–101.
8. Lundy JB, Slane ML, Frizzi JD. Acute adrenal insufficiency after a single dose of etomidate. *J Intensive Care Med.* 2007;22(2):111–7.
9. O'Leary E, Lam Y, Bryant AE, Burrin JM, Hall GM. Etomidate and the osteocalcin response to gynaecological surgery. *Br J Anaesth.* 1999;83(3):461–3.