International Journal of Basic & Clinical Pharmacology
Solanki KM et al. Int J Basic Clin Pharmacol. 2024 Jan;13(1):85-90
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20233897

Original Research Article

Comparison of etomidate and propofol as an induction agent to study hemodynamic effects and serum cortisol level following endotracheal intubation in hypertensive patients

Kinjal M. Solanki[1], Kinna G. Shah[2]*, Dipesh P. Shah[3], Jayshreeben M. Thakkar[1]

[1]Department of Anesthesia, Gujarat Cancer & Research Institute, B. J. Medical Collage, Ahmedabad, Gujarat, India
[2]Department of Anesthesia, Dr. M. K. Shah Medical College, Chandkheda, Ahmedabad, Gujarat, India
[3]Department of Anesthesia, S. V. P Hospital, N. H. L. Medical Collage, Ahmedabad, Gujarat, India

Received: 05 October 2023
Accepted: 07 November 2023

***Correspondence:**
Dr. Kinna G. Shah,
Email: kinnagaurang@gmail.com

ABSTRACT

Background: The present study aimed to compare hemodynamic parameters (heart rate, blood pressure) and adverse effects (injection pain, myoclonus, postoperative nausea/vomiting) between Etomidate and propofol groups.
Methods: Patients were divided into two groups: Etomidate Group E and a Propofol Group P. All hemodynamic data were measured during induction, intubation, and post-intubation up to 15 min. Intravenous cortisol levels were measured at baseline, just after induction and at 24 hours after induction.
Results: At 3 min and 5 min SBP was decreased by 22.04% and 18.39% in Group P. At 3 min there was fall in DBP by 20.13% in group P whereas there was an increase in group E by 0.13% which is statistically significant (p<0.001). At 1 min, 3 min and 5 min after intubation, fall in the MAP by 26.07%, 21.08% and 18.60% in group P and 0.77%, 0.42% and 1.30% in group E (p value <0.001). Serum cortisol level immediate after surgery was decrease (54%) in Group E (p value <0.001). In Group P, 40% of the patients and in group E 16.66 % of the patients complained of pain on injection (p value 0.046).
Conclusions: The cortisol suppression by Etomidate may be beneficial for intubation stress response. Etomidate is better for its hemodynamic stability over propofol.

Keywords: Intubation, Etomidate, Propofol, Myoclonus, Serum cortisol, Hemodynamic stability

INTRODUCTION

The vital aspect of patient induction forces medical science to concentrate on safer anesthetic techniques. Endotracheal intubation and laryngoscopy both activate the sympathetic nervous system, which results in considerable hemodynamic alterations. Healthy people can manage this, however those with concomitant disorders like hypertension or cardiovascular diseases have difficulties. Choosing an agent that is hemodynamically stable and has few side effects is therefore essential. Etomidate is a carboxylated imidazole, a hemodynamically stable induction agent with low respiratory depression and cerebral protective effects.[1] For cardiac patients, it is the strategy of preference. Adverse effects include pain on injection, thrombophlebitis, myoclonus, nausea, vomiting and rarely adrenocortical suppression.[2,3] Popular induction agent, Propofol ensures quick and smooth induction and recovery with little adverse effects. Through the suppression of sympathetic nerves, it lowers blood pressure, cardiac output, and systemic vascular resistance[4,5] through inhibition of sympathetic vasoconstriction and impairment of the baroreceptor reflex regulatory system.[1,6] The adverse

effects of both agents, such as pain on injection, thrombophlebitis, and myoclonus, are managed with pre-medication using the opioid fentanyl.[7] Etomidate inhibits the enzyme 11β-hydroxylase and resulting in decreased cortisol biosynthesis and mineralocorticoid production. It is a potent inhibitor of steroid synthesis than as a sedative hypnotic agent.[8,9] Estimation of serum cortisol levels after etomidate administration is done by collecting blood samples at different intervals. Limited studies suggest advantages of etomidate over propofol in terms of hemodynamic stability in hypertensive patients and the effect on serum cortisol levels. Therefore, the present study aimed to compare hemodynamic parameters (heart rate, blood pressure) and adverse effects (pain on injection, myoclonus, postoperative nausea/vomiting, requirement of Inj. Mephentermine) between etomidate and propofol groups. Adrenocortical suppression was also evaluated through blood samples collected at different intervals.

METHODS

After institutional ethics committee approval and informed consent, 60 ASA II and III patients listed for Gastrointestinal, Gynecological, Urological, Head & Neck surgeries who requires oral endotracheal intubation were selected in a randomized fashion. This study followed a prospective, randomized, double blind design and the study was done during October 2019 to December 2020 in Gujarat Cancer & Research institute, Civil hospital, Ahmedabad. The patients were systematically allocated to ensure equal number of patients in each group.

Inclusion and exclusion criteria

Patients with American Society of Anesthesiologist grade I-II, Surgery done under general anesthesia, Age from 20 to 70 years, Controlled blood pressure with anti-hypertensive drugs except beta blockers (BP <150/90 mmHg), BP ≤ 140/90 mmHg and Modified Mallam Patigrade 1 and 2 were included. Excluded patients with MPG 3 & 4, Emergency surgeries, known primary or secondary adrenal insufficiency, a history of steroid supplementation in the previous 6 months or prolonged steroid medication, patients having anticipated difficult intubation, history of difficult intubation, patients having asthma, epilepsy, COPD, Allergic to any study drug.

Hypertensive patients were controlled either by Tab. Amlodipine alone 5mg (7/60) or 10mg (17/60) or combination Tab. Amlodipine (5 mg) and Tab. Telmisartan 40 mg (36/60).

Pre-operative preparation

All the patients were fasted for 10 hours and received Tab. Lorazepam 1 mg a night before surgery. Demographic data including age, sex, height, weight was plotted. Venous access was established with large bore cannula and an infusion of normal saline 6 mg/kg was started. Patients were connected to a multipara meter monitor and base line values of heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and oxygen saturation were recorded and blood sample for serum cortisol was taken. The syringes containing Etomidate 2mg/ml or Propofol 10mg/ml were prepared by an independent anesthesiologist (Not involved in the study) to ensure a proper blinding procedure. The syringes were filled with normal saline up to 15 ml for blinding purpose.

Pre oxygenation and premedication

Patient was pre oxygenated with 5 l/min of oxygen for 3 mins and premedicated with Inj. Glycopyrrolate 0.005 mg/kg IV, Inj. Ranitidine 1 mg/kg IV, Inj. Ondansetron 0.1 mg/kg IV, Inj. Lignocaine 2% 1.5 mg/kg and respective antibiotics.

Group allocation

Group-P: Inj. Fentanyl 2 µg/kg followed by inj. Propofol 2 mg/kg IV over 15 seconds**.** Group-E: Inj. Fentanyl 2 µg/kg followed by inj. Etomidate 0.3 mg/kg IV over 15 seconds**.** Patients of both the groups were asked for pain on injection. Grading of pain on injection was done (Grade 0=No pain, 1=Mild, 2=Moderate, 3=Severe or hand withdrawal to pain). After infusion of the drug, occurrence of myoclonus was noted. Inj. Succinylcholine in a dose of 1.5 mg/kg was given for intubation and mask ventilation for 60 seconds done and patients were intubated with appropriate sixed endotracheal tube, cuff inflated and after confirming ETCO2 and bilateral air entry ET tube was fixed. Anesthesia was maintained with oxygen and nitrous oxide in a ratio of 1:1 and sevoflurane in a dial concentration of 1-3% and vecuronium as muscle relaxant and patient is put on volume or pressure control mode of ventilation with Tidal volume 6-8 mg/kg, frequency 12-14 bpm, I:E ratio 1:2, PEEP 5 cmH2O, PINSP 15-25 cmH2O throughout the surgery. Intravenous paracetamol infusion of 100 mg was given.

Intra operative monitoring

Hemodynamic parameters like Heart rate (HR), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP) were noted at different time intervals i.e. Before induction (baseline), Induction, at the time of intubation then at 1 min, 3 min, 5 min, 7 min, 10 min, 15 min and no surgical stimuli were applied for 15 min. Any hypotension was managed by intravenous fluid bolus and or 3 -6 mg Inj. Mephentermine IV each time till MAP < 60 mmHg reached within normal limits. Heart Rate <50 beats per min was managed by IV Atropine 0.6 mg. After operation, residual neuromuscular block was reversed with Inj. Neostigmine 0.07 mg/kg and Inj. Glycopyrrolate 0.005 mg/kg. Extubation is to be performed after the patient is fully awake. Incidence of post-operative nausea vomiting was noted in all the cases. All the patients were then sent to post anesthetic care unit. Collected blood samples of all the patients were sent at

completion of operation and 24 hours after the induction for measurement of serum cortisol. Here, serum cortisol is in nmol/l and calculated by ECLIA method with ECL technique by using Roche Cobas Pro instrument. In the postoperative ward, analgesia is provided by giving Inj. Paracetamol 15mg/ kg, Inj. Tramadol 1 mg/kg, Inj. Diclofenac 75 mg.

Statistical analysis

All the data were presented and entered in the Microsoft Excel 2020 as Mean±Standard deviation (SD). Categorical data were described as number of patients (N). Physical characteristics, heart rates, systolic blood pressure, diastolic blood pressure, mean arterial pressures and serum cortisol level were analyzed using unpaired t-test. All categorical data including pain on injection, myoclonus, post-operative nausea vomiting, requirement of Inj. Mephentermine/Inj. Atropine was compared using Chi-square test. All differences were considered significant at $p<0.05$. Statistical analysis was done using GraphPad.

RESULTS

All demographic data are equal in both the groups. PONV was seen in 26.66% of the patients in propofol group and 33.33% in etomidate group with p=0.57.

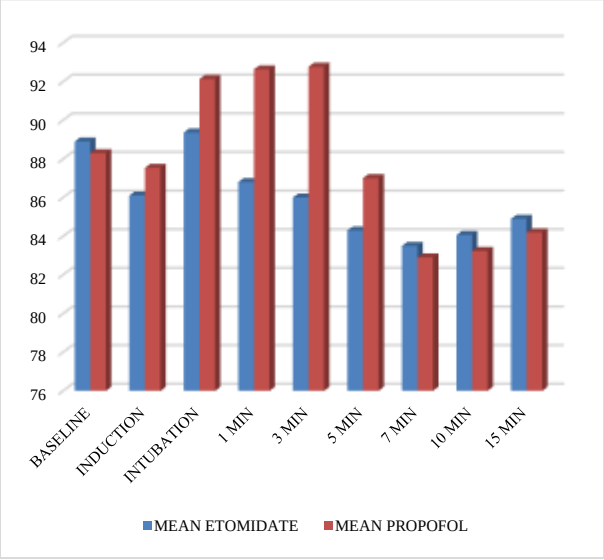

Figure 1: Changes in mean heart rate.

The Changes in the heart rate from the baseline was compared between the two groups at 1, 3, 5, 7, 10 and 15 min following induction. At 1 & 3 min after intubation, increase in heart rate in Group P (p value 0.01).

There was statistically significant change in mean systolic blood pressure throughout anesthetic procedure. One min following intubation, there was fall in systolic blood pressure by 29.13% in Group P and increase in SBP by 1.23% in group E ($p<0.001$).

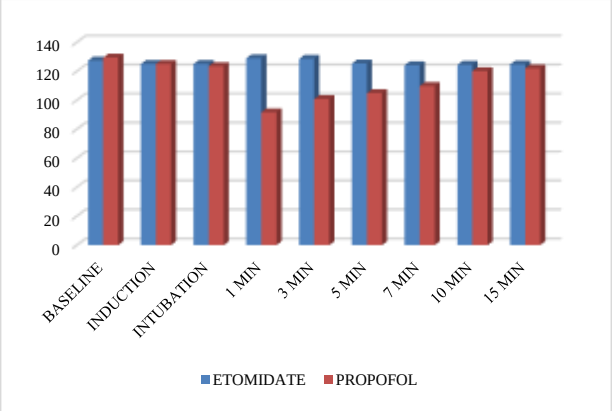

Figure 2: Changes in mean systolic blood pressure.

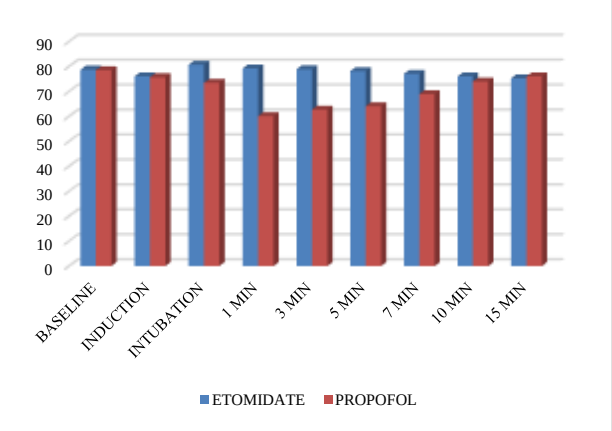

Figure 3: Changes in mean diastolic blood pressure.

One min after induction there was fall in the DBP by 23.40 % in group P and by 12.91% in group E with p value of <0.001. At 3 min there was fall in DBP by 20.13 % in group P whereas there was an increase in group E by 0.13% which is statistically significant ($p<0.001$).

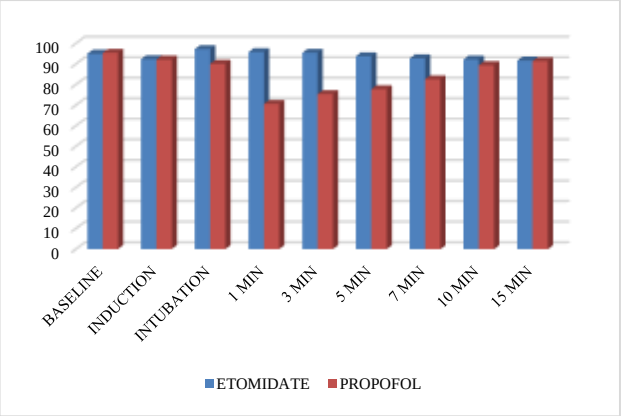

Figure 4: Changes in mean arterial blood pressure.

It was observed that at 1, 3 and 5 min following intubation there was fall in the MAP by 26.07 %, 21.08% and 18.60% in group P and 0.77 %, 0.42 % and 1.30 % in group E with $p<0.001$. At 10 min MAP was less than the baseline in

group P and MAP increased by 2.98 % in group E which were statistically significant with p=0.032.

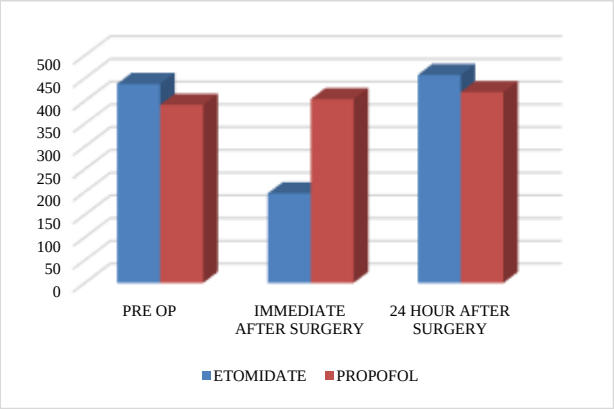

Figure 5: Serum cortisol level measurement.

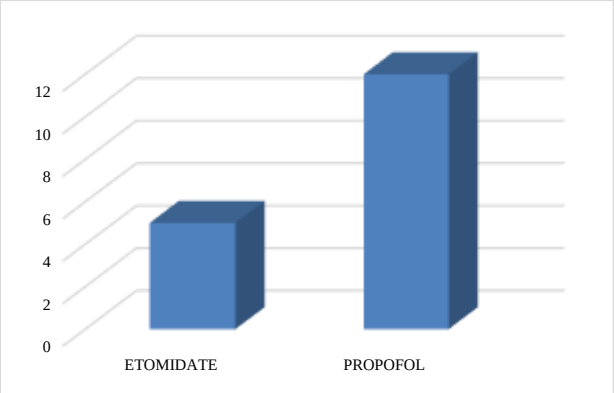

Figure 6: Pain on injection.

In our study, there is no significant difference found in the pre-op and 24 hours after surgery in both the group. But there is significant difference found in serum cortisol level taken immediate after surgery with p<0.001 suggestive of drastic decrease (54%) in serum cortisol level in Group E whereas in 3.27% increase in Group P. In Group P 40% of the patients and in group E 16.66% of the patients complained of pain on injection. This is statical significant with the p value 0.046.

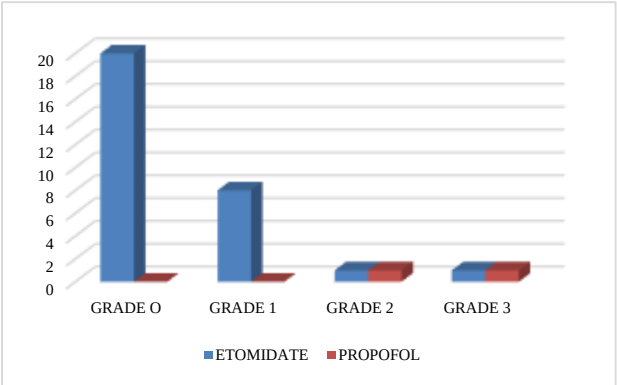

Figure 7: Myoclonus.

In Group P, only 2 patients developed myoclonus grade 2 & 3. Whereas in Group E, 26.66%, 3.33%, 3.33% patients showed Grade 1, 2 and 3 grade myoclonus which is statical significant with p value 0.0105.

DISCUSSION

Induction of anaesthesia can cause mild to moderate hemodynamic variations, with propofol showing more significant hypotension and tachycardia than etomidate. This is especially important for comorbid patients, especially those with multiple drugs, who are post-operatively more likely to experience nausea and myoclonus. Etomidate, on the other hand, is preferred due to its stable hemodynamic state but may cause adrenal suppression and adverse effects. The study found no significant difference in the heart rate during induction, intubation, or post-intubation, but significant changes in heart rate after endotracheal intubation. Etomidate provides more stable hemodynamic parameters at all time intervals except 1 min after intubation compared to propofol. Masoudifoar et al, Pandey et al, Skinner et al, Ko et al and Ye et al studies have shown that etomidate provides more stable parameters when used for induction of anaesthesia, making it a preferred choice for general anaesthesia.[10-14] Studies have also shown that systolic and diastolic blood pressure are substantially stable with etomidate, but the SBP remains lower in the propofol group.[15] Harris et al found a significant decrease in arterial blood pressure after propofol.[16] Shah et al compared the hemodynamic effects of intravenous etomidate versus propofol during induction and intubation using entropy guided hypnosis levels. It shows fall in arterial pressure following induction was 30% and 32% in group P at 1 and 3 min following induction, while increase by 11.4% at laryngoscopy.[17] In our results, Systolic pressure fall by 29.13% and 22.04% in group P, while in group E, it fall by 1.23% and 0.92% at 1 and 3 min following induction. In the study of Moller et al there was no change in MAP before intubation.[18] After intubation up to 7 min MAP was significantly higher in group E with p=0.019. In our study, MAP was significantly higher in group E after intubation, but no significant fall in MAP after third min of intubation. There was 7.16% Hypotension was observed up to 10 min of propofol induction, which was in line with another study Kaushal et al that found propofol significantly decreased blood pressure after induction.[19] Local side effects, such as pain on injection, were more severe in group P (40%) compared to group E (16.30%). Pain was due to the addition of propylene glycol diluent in the etomidate, which can be minimized by administering etomidate with prior use of lignocaine or opioid through a large vein with a rapid intravenous injection rate.[20]

The rate of injection also influences the likelihood of pain on injection. In our study, the incidence of pain on injection was 40% in propofol, which is lesser in the etomidate group. It might be due to fentanyl in dose of 2 mcg/kg IV was given. However, 16.66% incidence of pain was higher in etomidate group, because propylene glycol

was used as a solvent with etomidate in our study. In the study of Kaur et al they found pain on injection in 26.7% of the patients in group P and 6.7% in group E. In other study values were 28% and 8% respectively in both the cases incidence of pain on injection was significantly higher in group P which can tally with our data.[21] It is known that myoclonus is dose dependent. The incidence of myoclonus with etomidate induction is 50-80% in general and decrease to 16.7% using fentanyl or remifentanil as premedicates. In our etomidate group incidence is 33%.[21] Reason could be that they have used etomidate 0.2 mg/kg body weight compared to 0.3 mg/kg etomidate in our study. Myoclonus was found to be higher in the etomidate group, possibly due to the use of 0.2 mg/kg body weight etomidate compared to 0.3 mg/kg etomidate. Pre-medication with benzodiazepines and opioids have been shown to reduce myoclonus. In our study, higher incidence of pain on injection and myoclonus was seen assuming oncological patients with a history of previous chemotherapy and difficult venous access, which may have affected the results. In our study, patients in both the groups experienced nausea but no vomiting. Wu et al found that in the propofol group PONV was 2.5%, whereas in etomidate group was 50%.[22] Ultimately proving that incidence of PONV is higher with etomidate compared to propofol, which can be attributed to antiemetic property of propofol. In our study, cortisol levels were reduced after etomidate administration, but remained within the physiological range after 12 hours of induction. The study also observed more decrease in SBP and DBP till 5 min post-induction with Group P compare to Group E, suggesting that etomidate is more stable hemodynamic during the post-induction phase of anaesthesia. This might be due to temporary fall in cortisol after etomidate injection. This pharmacological effect of etomidate is much beneficial to attenuate stress induced hypertension and tachycardia during first 5 min of induction. The serum cortisol level at 24 hours was higher as compared to baseline values in both the groups. In the etomidate group the serum cortisol returned to lower levels which was however almost twice the baseline value. In the propofol group the serum cortisol levels remained high and were almost three times the base line values.[11] In our study, average cortisol value was reduced by almost 54% in the etomidate group, while it increased by 3.27% in the propofol group immediately after surgery. Serum cortisol levels were higher at 24 hours, but no adverse effects were observed. None of the patients had any adverse effects that could be attributed to cortisol suppression.

CONCLUSION

Etomidate is a good induction agent for controlled hypertensive patients. The suppression of the intubation stress response in the form of cortisol suppression by etomidate may be beneficial, as seen in our study where the serum cortisol levels decreased. Etomidate is better for its hemodynamic stability over propofol along with less incidence of pain on injection. Only drawback was high incidence of myoclonus.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Steingraber A, Simon C. Hiller. Pharmacology and physiology in anesthetic practice. 4th ed. Philadelphia: Lippincott Williams and Wilkins Publishers; 2006:159-60.
2. Longnecker DE. Stress free: to be or not to be?. Anesthesiology. 1984;61:643.
3. Owen H, Spence AA. Etomidate. Br J Anaesth. 1984; 56:555.
4. Larsen R, Rathgeber J, Bagdahn A. Effects of Propofol oncardiovascular dynamics andcoronary blood flow in geriatric patients; A comparison with Etomidate. Anaesthesia. 1988;43:25-31.
5. Van-Aken H, Meinshausen E, Prien T. The influence of fentanyl andtracheal intubation on thehemodynamic effects of anesthesia inductionwith Propofol/N2O in humans. Anesthesiology. 1988;68: 157-63.
6. Stoelting, Roberta L. Hinges, Katherine E. Marschall. Stoelting'sAnesthesia and Co- existing Disease. 5th ed. Philadelphia: Churchill Livingstone; 2009.
7. Carlos R, Innerarity S. Effect of Premedication on Etomidate Anaesthesia. Br J Anaesth.1979;51:1159.
8. Fragen RJ. Clinical pharmacology of propofol. Anesthesiology. 1987;66:839.
9. Diago MC. Ose of etomidate. Anaesthesia. 1988; 43:644.
10. Masoudifar M, Beheshtian E. Comparison of cardiovascular response tolaryngoscopy andtracheal intubation after induction of anaesthesia by Propofol and Etomidate. J Res Med Sci. 2013;18(10):870-4
11. Etomidate and propofol. Available at: https://www.The_Effects_of_Etomidate_and_Propofol_Indcion_on_Hemodynamic_and_Endocrine_Response_in_Patients_Undergoing_Coronary_Artery_Bypass_Graft_Surgery_on_Cardiopulmonary_Bypass. Accessed on 20 February 2023.
12. Skinner HJ, Biswas A, Mahajan RP. Evaluation of intubating conditionswith rocuronium andeither propofol or etomidate for rapid sequenceinduction. Anaesthesia. 1998;53(7):702-6
13. Ko YK, Kim YH, Park S, Chung WS, Noh C, Lee JU. Comparison ofetomidate and propofol on intubating conditions and the onset time associated with cisatracurium administration. Korean J Anesthesiol. 2015;68(2):136-40.
14. Ye L, Xiao X, Zhu L. Comparison of etomidate and propofol anesthesiain patients undergoing gastrointestinal endoscopy: a systematic reviewand meta-analysis. Surg Laparosc Endosc Percutan Tech. 2017;27(1):1-7.
15. Aggarwal S, Goyal VK, Chaturvedi SK, Mathur V, Baj B, Kumar A. A comparative study between propofol and etomidate in patients under general

anesthesia. Braz J Anesthesiol. 2016;66(3):237-41.
16. Harris CE, Murray M, Anderson AM, Grounds RM, Morgan M. Effectsof thiopentone and propofol on the hemodynamic response to trachealintubation. Anaesthesia. 1988;43:32-6.
17. Shah S, Chowdhury I, Bhargava A, Sabbharwal B. Comparison ofhemodynamic effects of intravenous etomidate versus propofol duringinduction and intubation using entropy guided hypnosis levels. J Anaesthesiol Clin Pharmacol. 2015;31(2):180.
18. Petrun MPA, Kameni K. Bispectral index-guided induction ofgeneral anaesthesia in patients undergoing major abdominal surgery usingpropofol or etomidate: a double-blind, randomized, clinical trial. Br J Anaesth. 2013;110(30):388-96.
19. Kaushal RP, Vatal A, Pathak R. Effect of etomidate and propofolinduction on hemodynamic and endocrine response in patients undergoingcoronary artery bypass grafting/mitral valve and aortic valve replacementsurgery on cardiopulmonary bypass. Ann Cardiac Anaesthes. 2015;18(2):172.
20. Mayer M, Doenicke A, Nebauer AE, Hepting L. Propofol and etomidate-Lipuro for induction of general anesthesia. Hemodynamics, vascular compatibility, subjective findings and postoperative nausea. Anaesthesist. 1996;45(11):1082-4.
21. Kaur S, Kataria AP, Kaur G, Kaur M, Attri JP, Mohan B. Comparison of induction characteristics of propofol-lipuro and etomidate-lipuro in cardiac patients in non-cardiac Surgery. Int J Sci Stud. 2014; 2(6):66-72.
22. Wu J, Yao S, Wu Z, Wu Z, Chu S, Xia G, et al. A comparison ofanesthetic regimens using etomidate and propofol in patients undergoingfirst-trimester abortions: double-blind, randomized clinical trial of safety andefficacy. Contraception. 2013;87(1):55-62.

Cite this article as: Solanki KM, Shah KG, Shah DP, Thakkar JM. Comparison of etomidate and propofol as an induction agent to study hemodynamic effects and serum cortisol level following endotracheal intubation in hypertensive patients. Int J Basic Clin Pharmacol 2024;13:85-90.