

THE COMPARISON OF ETOMIDATE AND PROPOFOL FOR ATTENUATION OF HAEMODYNAMIC RESPONSE TO INDUCTION AND ENDOTRACHEAL INTUBATION

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Article Info: Received 11 February 2020; Accepted 10 March 2020

DOI: <https://doi.org/10.32553/ijmbs.v4i3.1036>

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Conflict of interest: No conflict of interest.

Abstract

Background: This study is designed to compare the degree of attenuation of hemodynamic response to induction, laryngoscopy and endotracheal intubation of etomidate with those of propofol in patients undergoing noncardiac surgical procedures.

Methods: The present study conducted in Non Cardiac Surgeries in the Department of Anaesthesiology, Jhalawar Medical College & Associated Hospitals, Jhalawar, Rajasthan. After institutional ethical committee's approval and written informed consent from the patient's attendant in the format as per proforma, the present study was conducted on 60 patients of ASA Grade I and II of either sex, aged 18 to 60 years, scheduled for a variety of non-cardiac surgical procedures requiring general anaesthesia.

Results: The findings of the study suggest that use of etomidate as inducing agent provides more hemodynamic stability as compared to propofol and can be preferred in patients prone to hemodynamic instability, cardiovascular abnormalities, hypovolemia, prone to renal failure due to hypotension. Propofol may be preferred for induction where hypertension is contraindicated or hypotension is preferred and myoclonus is to be avoided.

Conclusion: Etomidate provides a more stable hemodynamics during general anesthesia as compared to propofol.

Keyword:- Etomidate, Propofol, Hemodynamic.

Introduction

General anaesthesia (GA) or narcosis is a state of pharmacologically induced coma, temporary and reversible, which is characterized by the development of unconsciousness, analgesia, amnesia, myorelaxation and attenuation of autonomic response to painful stimulation. There are 3 phases of general anaesthetic procedures:- Induction, Maintenance and Emergence/Recovery. Various inhalational and intravenous agents are used for induction of GA which consists of the following stages: Stage 1 of analgesia, Stage 2 of delirium/excitement, Stage 3 of surgical anaesthesia and Stage 4 of medullary paralysis. Most of the surgical procedures are carried out in stage 3.

Propofol is an ultra-short-acting intravenous induction agent with some favourable properties like smooth induction, quick recovery and antiemetic properties. It is deemed not a suitable agent in patients with cardiovascular instability and shock as it decreases blood pressure, cardiac output and systemic vascular resistance due to inhibition of sympathetic vasoconstriction and impairment of baroreceptor reflex regulatory system. This effect may be exaggerated in hypovolemic and elderly

patients with compromised left ventricular function due to coronary artery disease. It produces dose dependent depression of ventilation. However, the adverse effects such as pain on injection, thrombophlebitis and myoclonus have been reduced by using reformulated lipofundin (lipuro) solution and pretreating with fentanyl, an opioid.

¹Etomidate is one of the induction agents which is claimed to be cardiostable and had gained lot of popularity in the past and fell out of use due to adrenocortical suppression. Further studies in the recent years on etomidate have yielded a promising results and it has regained its popularity as a safe anesthetic and more so in sepsis and critically ill patients who are haemodynamically unstable.² Although etomidate can cause adrenal insufficiency in these patients in postoperative period, clinical consequence of that is still unclear over its advantage to prevent hypotension at induction.³⁻⁵

Materials and Methods

The present study entitled "comparison of etomidate and propofol for attenuation of haemodynamic response to induction and endotracheal intubation" in Non Cardiac Surgeries was carried out in the Department of

Anaesthesiology, Jhalawar Medical College & Associated Hospitals, Jhalawar, Rajasthan.

Sample size determination:

Sample size was calculated using G Power Software (version 3.0.10). Based on the calculated effect size of 2.2 (assessed from similar study), 5% level of precision, 95% confidence level and 80% power of the study, minimum sample size was calculated as 57 which was rounded off to 60 (30 each group).

Selection of patients

After institutional ethical committee's approval and written informed consent from the patient's attendant in the format as per proforma, the present study was conducted on patients of ASA Grade I and II of either sex, aged 18 to 60 years, scheduled for a variety of non-cardiac surgical procedures requiring general anaesthesia. Study period was 9 months.

Exclusion criteria

1. Patients refusal
2. Bradycardia pulse rate / heart rate <60
3. Emergency surgery
4. Patient known cardiovascular disease like ischaemic heart disease or have hypertension.
5. Bronchial asthma
6. Neuromuscular disorder,
7. Impaired liver and kidney function,
8. History of hypersensitivity to any of the drugs going to be used or its contents,
9. Patients with anticipated difficult intubation, mouth opening <2 cm, mallampatti grade 3-4, considerable pathology in pharynx or larynx.
10. Hereditary disorder of haemoglobin synthesis,
11. Adrenocortical dysfunction,
12. Sepsis
13. Pts. on verapamil, neuroleptics, opiates, sedatives, droperidol was excluded from surgery.
14. Patient with GERD

Pre anesthesia assessment

All patients in this study was subjected to detailed pre anaesthetic evaluation which includes - Present complaints, drug allergy history, past history of surgical procedure under general anaesthesia, history of nausea, retching or vomiting within preceding 24 hours, any major medical illness and drug history. Complete general physical examination and ASA grading was done. Routine blood investigations, urine analysis, ECG, Chest-X-ray and other lab investigations was done as protocol of the required procedure.

Tablet Alprazolam 0.5mg night before surgery was given and Tablet Ranitidine and Tablet Metaclopramide in morning on day of surgery were advised.

Monitoring

The following parameters will be monitored:

1. Pulse rate
2. Blood pressure (systolic, diastolic, and mean arterial blood pressure) at different time intervals.
3. Pulse oxymetry (SpO₂).
4. Continuous ECG monitoring.
5. Et. CO₂.
6. Complications like nausea, vomiting, bradycardia, and hypotension will be noted.

Procedure

On arrival to the operating room, the patients was examined to confirm the finding of pre-anaesthetic check-up and was enquired about the fasting status. An IV line was secured. Standard monitoring was applied using multiparameter monitor for heart rate, NIBP, pulse oximetry, ECG recording.

All patients were premedicated intravenously with inj. Glycopyrrolate 0.004 mg/kg im, inj. 45min. before surgery Midazolam 0.015mg/kg, inj fentanyl citrate 1.5 µg/kg i.v. before induction.

Induction of anaesthesia was randomly selected for different groups as follows after double blinding :-

Group A received Etomidate 0.3mg/Kg for induction

Group B received Propofol 2mg/Kg for induction

After loss of eye reflexes and consciousness Succinylcholine 1.0 mg/kg intravenously was administered to facilitate endotracheal intubation. After injection of succinylcholine, laryngoscopy and intubation was performed. Patients requiring laryngoscopy and intubation for more than 15 seconds or requiring second attempt for intubation were excluded from study.

After assuring the proper placement of endotracheal tube, anaesthesia was maintained with 66% nitrous oxide in oxygen, 0.5-3.5% sevoflurane and inj. Vecuronium 0.08 to 0.1mg/kg intravenously loading and 0.01 to 0.015 mg/kg for maintenance and patients was mechanically ventilated to maintain EtCO₂ 35 to 40 mm of Hg.

After completion of surgery, neuromuscular blockade was reversed with inj. Neostigmine 0.05mg/kg and Glycopyrrolate 0.008 mg/kg, intravenously.

Pulse rate, pulse oxymetry (SpO₂) and blood pressure (systolic, diastolic and mean arterial blood pressure) was recorded as baseline, after preanaesthetic medication, after induction, after laryngoscopy and intubation, at 1,2,3,

5, 10 minutes after laryngoscopy and intubation. Vitals were monitored throughout the procedure. After the operation the patients were monitored in recovery room for 1 hour and then in post operative ward for next 24 hours. Complications like nausea, vomiting, dizziness, bradycardia, hypotension, myoclonus if any, were recorded.

OBSERVATIONS AND RESULTS

Data of 60 patients were evaluated in two groups of 30 each. Group A received (etomidate 0.3 mg/kg) and Group B received (propofol 2 mg/kg).

Table 1: Age wise Distribution

	Group A		Group B		p-value
	Mean	SD	Mean	SD	
Mean±SD	37.60	10.77	35.37	11.48	0.448
Male : female	20:10		21:9		0.99

The age distribution of patients amongst both the groups. The mean age of group A was 37.60±10.77 years and of group B was 35.37±11.48 years. The difference in the age & sex group was not significant (p value > 0.05).

Table 2: Comparison of Pulse Rate (bpm) among two groups

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	80.13	13.44	80.97	16.58	0.831
Pre Medication	82.87	16.28	81.63	11.75	0.737
After induction	94.70	19.73	90.27	14.65	0.327
After Intubation	111.80	18.07	110.93	18.81	0.856
1 min	104.00	16.86	107.70	13.53	0.352
3 min	100.53	14.17	99.13	18.47	0.743
5 min	99.40	17.30	96.30	19.63	0.519
10 min	98.90	19.99	90.80	17.85	0.103

Mean pulse rate was compared among different groups at different intervals, none of the group showed significant differences in mean pulse rate as (p>0.05).

Table 3: Comparison of Systolic Blood Pressure among two groups

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	130.23	11.36	122.23	10.57	0.006
Pre Medication	127.70	14.70	121.07	12.78	0.067
After induction	125.13	22.58	111.47	12.92	0.005
After Intubation	152.23	24.45	138.93	30.53	0.067
1 min	143.67	22.71	132.97	27.38	0.104
3 min	127.90	20.65	118.07	14.86	0.038
5 min	115.43	17.42	112.60	14.89	0.500
10 min	119.77	23.26	113.40	17.33	0.234

Group wise comparison of systolic blood pressure of study population at different intervals. When mean systolic blood pressure was compared among different groups at different intervals. Group comparison of SBP revealed significant differences in mean systolic blood pressure as

(p<0.05) at time of induction and 3 minute after intubation. which shows significance decrease in mean systolic blood pressure in group B receiving propofol after induction which increased after intubation but the mean systolic blood pressure had a significant (p<0.05) fall from baseline after 3 minute of intubation.

Table 4: Comparison of Diastolic Blood Pressure among two groups

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	81.60	10.48	79.10	8.44	0.313
Pre Medication	79.57	10.86	75.43	11.34	0.154
After induction	73.30	13.38	70.60	12.46	0.421
After Intubation	95.97	16.84	86.40	18.32	0.039
1 min	87.93	15.62	80.53	12.66	0.048
3 min	76.43	17.33	74.37	13.93	0.061
5 min	69.23	14.64	70.70	15.61	0.708
10 min	72.57	16.79	72.67	14.79	0.980

Groupwise comparison of diastolic blood pressure of study population at different intervals. When mean diastolic blood pressure was compared among different groups at different intervals. Group comparison of DBP revealed significant differences in mean diastolic blood pressure as (p<0.05) at time of intubation and 1 minute among both the groups.

Table 5: Comparison of Mean Arterial Pressure among two groups

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	101.40	9.66	96.53	7.50	0.033
Pre Medication	99.30	12.17	91.20	13.07	0.015
After induction	94.33	14.95	85.53	13.69	0.020
After Intubation	122.17	21.59	104.73	20.65	0.002
1 min	109.53	17.68	99.80	16.33	0.030
3 min	96.77	17.67	93.30	13.30	0.394
5 min	88.47	16.64	90.13	15.30	0.687
10 min	94.97	21.03	89.70	17.65	0.297

Groupwise comparison of mean arterial blood pressure of study population at different intervals. When mean arterial blood pressure was compared among different groups at different intervals. Group comparison of MAP revealed significant differences in mean arterial blood pressure as (p<0.05) at time of induction, after intubation and at 1 minute among both the groups.

Table 6: Comparison of SPO₂ among two groups

	Group A		Group B		P value
	Mean	SD	Mean	SD	
Baseline	99.93	0.25	99.43	0.94	0.006
Pre Medication	99.90	0.55	99.87	0.51	0.807
After induction	99.97	0.18	99.73	0.69	0.079
After Intubation	99.97	0.18	99.83	0.53	0.198
1 min	99.83	0.65	99.83	0.53	-
3 min	99.87	0.51	99.80	0.61	0.647
5 min	99.87	0.73	99.83	0.53	0.840
10 min	99.87	0.73	99.83	0.53	0.840

Group wise comparison of SpO₂ of study population at different intervals. There was no significant difference in both the groups (p value > 0.05).

Discussion

Aim of this study is to compare hemodynamic effects of etomidate (group A) with that of propofol (group B) at different time intervals i.e. at baseline, after premedication, after induction, after intubation, at 1,3,5,10 minutes after intubation. As evident from the results of the present study significant differences were observed in Systolic, Diastolic and Mean Arterial Blood Pressure after induction, intubation and 1 and 3 minutes after intubation.

Similar findings were observed in a study conducted by **Dorantes-Mendez**⁶ showed a significant decrease in the mean values of SBP, DBP, MBP during propofol induction and after the intubation was obtained with respect to awake period, mainly due to the vasodilator effect of the anesthetic agent, this finding is consistent with the results of present study. These results suggested that propofol induction may reduce sympathetic nervous modulation on peripheral vasculature, and this was consistent with the results reported by **Ogawa**⁷ and with the attenuation in peripheral sympathetic outflow reported by **Sellgren**.⁸

In a study by Muriel et al.⁹, a comparison was made of propofol (2 mg/kg), thiopental (5 mg/kg) and etomidate (0.3 mg/kg) in anesthesia induction. A statistically significant increase was determined in systolic and diastolic arterial pressure and HR in the etomidate and thiopental group after intubation and the highest rate of complication was reported in etomidate group.

Harris et al.¹⁰ compared the hemodynamic response to tracheal intubation in 303 patients in whom anesthesia was induced with either thiopentone 4 mg/kg, etomidate 0.3 mg/kg or propofol 2.5 mg/kg with or without fentanyl 2 µg/kg. after propofol alone, there was a significant decrease in arterial blood pressure, which did not increase above control value after intubation. Significant increase in arterial pressure followed intubation in patients induced with thiopentone or etomidate alone. Increases in heart rate occurred with all agents after laryngoscopy and intubation. The use of fentanyl resulted in arterial pressure lower than those after the induction agent alone and in an attenuation, but not abolition, of responses to laryngoscopy and intubation. We got similar results in our study with significant decrease in arterial blood pressure, after induction with propofol which did not increase above baseline value after intubation, while, with etomidate, there was significant increase in arterial pressure following intubation. Also, increase in heart rate occurred with all agents after laryngoscopy and intubation

Schmidt et al.¹¹ found in their study that, hypotension caused by propofol is due to the reduction of heart's preload and afterload which are not synchronized with heart's compensatory responses such as increased cardiac output and increased HR. This hemodynamic drop would be intensified by high doses of the drug and high speed injection of the drug. In our study we got similar results in group B that is after induction with propofol there was hypotension and not synchronized with increased HR.

Mehrdadet al.¹² conducted a study including patients of 18-45 years of age that were admitted for elective orthopedic surgeries. patients were divided in two groups, their cardiovascular responses including: systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), and O₂ saturation (O₂ saturation) were measured before the laryngoscopy, during the anesthesia induction with Etomidate (0.3 mg/kg) in group A and propofol (2-2.5 mg/kg) in group B and at 1, 3, 5, 10 min after the induction. They concluded that patients receiving Etomidate have more stable hemodynamic condition, if there would be no contraindications; it could be preferred over propofol for general anesthesia. Our study got similar results of better hemodynamic conditions with etomidate as compared to propofol.

In a study by Mölleret al.¹³ which used propofol and etomidate in general anesthesia induction accompanied by BIS monitoring, the MAP, cardiac index (CI) and systemic vascular resistance index (SVRI) values of 48 patients were compared. The hemodynamic data were found to be higher in the etomidate group up to 7 minutes after intubation. A significantly high level of hypotension incidence was found in the propofol group and a significantly high level of hypertension incidence in the etomidate group. Compared with etomidate, the use of propofol was determined to have caused less hypertension and tachycardia after intubation. In the current study, the MAP values after induction in the propofol group were significantly lower than those of the etomidate group. Following intubation, the MAP and HR values of the etomidate group were statistically significantly higher than those of the propofol group.

Conclusion

Etomidate provides a more stable hemodynamics during general anesthesia as compared to propofol.

Complications

No significant complications were found except 6 cases in Group A (Etomidate) and 2 cases in Group B (Propofol) had incidence of myoclonus during induction. 3 cases hypertension occurred after induction in Group A (etomidate) which persisted for few minutes and

hypotension occurred in 2 cases in Group B (Propofol) after intubation which lasted for sometime.

Result of the study also indicated that there was no difference related with extubation period, eye opening time, coughing, keeping breath, uneasiness.

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