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Original Research Paper

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EVALUATION OF HAEMODYNAMIC STABILITY FOLLOWING INDUCTION OF GENERAL ANAESTHESIA WITH PROPOFOL AND ETOMIDATE IN NORMOTENSIVE AND HYPERTENSIVE PATIENTS: A COMPARATIVE STUDY

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ABSTRACT

Background: Induction of anaesthesia and endotracheal intubation are associated with adverse haemodynamic effects which are detrimental in hypertensive patients. Although etomidate is found to be a cardio stable induction agent, its advantages in hypertensive patients are not yet investigated. Aim of the present study is to compare the haemodynamic parameters following induction of anaesthesia with etomidate and propofol in normotensive and hypertensive patients.

Methods: In a prospective comparative study, 120 patients aged 18 to 60 years, of both sex and ASA status I & II posted for elective surgery under general anaesthesia were divided into 4 groups of 30 each. Anaesthesia was induced with either propofol or etomidate. Heart rate(HR), Systolic Blood Pressure(SBP), Diastolic Blood Pressure(DBP), Mean Arterial Pressure(MAP) and SpO2 were noted down at baseline, pre-induction, after induction, at laryngoscopy and 1, 3 & 5 minutes post intubation.

Results: There was a significant fall in HR after induction with propofol which was more in the hypertensive group. After intubation, a rise in HR was observed in all 4 groups which returned to baseline by 5 minutes. A fall in MAP, SBP and DBP were observed in all the groups following induction, which shooted up after intubation. The fall in MAP with propofol was significantly higher when compared to etomidate which offered stable haemodynamic conditions.

Conclusion: The present study suggests that induction of anaesthesia with etomidate is associated with better stability of MAP in normotensive as well as hypertensive patients when compared with propofol. However, HR is better maintained with propofol. Thus there is no clear evidence supporting induction by etomidate in hypertensive patients.

KEYWORDS : Propofol, Etomidate, Haemodynamics, Hypertensives.

INTRODUCTION

Induction of anaesthesia and endotracheal intubation are associated with potential adverse haemodynamic events such as severe hypotension, accelerated hypertension, dysrhythmias and cardiovascular collapse[1]. Haemodynamic effects of induction agent along with pressor response to laryngoscopy-intubation contribute towards this instability. There is no ideal induction agent described but it is desirable to use a drug with minimal haemodynamic effects.[1]

Propofol, the most commonly used induction agent, is associated with exaggerated hypotension in patients with hypertension and ischemic heart disease.[4] Etomidate has been described as the induction agent of choice in patients with high cardiac risk[4]. But there is no clear evidence in literature suggesting advantages of etomidate over propofol in hypertensive patients.

Hence, the present study was conducted with primary objective to compare the haemodynamic parameters following induction of anaesthesia with etomidate and propofol in normotensive and hypertensive patients. The secondary objective was to evaluate associated side effects.

MATERIALS AND METHODS

The present study was a prospective comparative study. After obtaining approval from the institutional ethical committee and informed consent, 120 patients aged 18 to 60 years, of either sex, ASA physical status I & II (controlled hypertension with 140/90 mmHg as cut off) posted for elective surgical procedures under general anaesthesia (GA) with endotracheal intubation were recruited. Patients with anticipated difficult airway, haemodynamic instability prior to induction, seizure disorder, known allergy to study drugs and primary and secondary steroid deficiency were excluded from the study.

The patients were randomly allocated to four groups of 30 each.

Group P1: Normotensive patients induced with propofol
Group P2: Hypertensive patients induced with propofol
Group E1: Normotensive patients induced with etomidate
Group E2: Hypertensive patients induced with etomidate

A detailed pre-anaesthetic assessment was done and written informed consent was obtained from each subject. The patients were premedicated with alprazolam 0.25 mg night prior and pantoprazole 40 mg on the morning of surgery. Patients were kept nil per orally from 10 pm previous night. Intravenous (IV) access was secured with 18 G IV cannula and a balanced salt intravenous infusion was started on the morning of surgery at 6 am. On arrival to the operation theatre, standard anaesthesia monitors including electrocardiogram (ECG), non-invasive blood pressure (NIBP) and pulse oximeter (SpO_2) were attached and baseline values were recorded. Patients were pre-oxygenated with 100% oxygen via face mask and premedicated with glycopyrrolate 0.2mg, ondansetron 4mg, midazolam 1mg and fentanyl 2mcg/kg. Anaesthesia was induced with either propofol (Groups P1 & P2) or etomidate (Groups E1 & E2). The end points for induction was loss of response to verbal commands for propofol and loss of eye lash reflex for etomidate and the dose of the induction agent required was noted down. Incidence of pain on injection, apnoea or myoclonus if any, was noted. Pain on injection was graded as grade 0 if there was no pain, grade one for verbal complaint of pain, grade two for withdrawal of arm and grade three for both verbal complaint and withdrawal. Whereas, myoclonus was documented as no

myoclonus as degree zero, degree one as mild with movement of a single muscle, degree two as moderate with movement of two different muscles and degree three as severe with movement of two groups of muscles. Trachea was intubated with appropriately sized endotracheal tube three minutes following the intubating dose of atracurium (0.5mg/kg) IV. Heart rate (HR), Systolic Blood Pressure(SBP), Diastolic Blood Pressure(DBP), Mean Arterial Pressure(MAP) and SpO2 were noted down at baseline, pre-induction, after induction, at laryngoscopy and one, three, five minutes post intubation which were noted as T0, T1, T2, T3, T4, T5 and T6 respectively. No surgical stimulus was given till five min post intubation, when the study concluded. Anaesthesia was maintained with oxygen 40%, nitrous oxide 60%, isoflurane and intermittent bolus doses of atracurium. Ephedrine 6mg bolus was given as a rescue drug if MAP dropped by >20% of the baseline value. At the end of surgery, the residual neuromuscular blockade was antagonized with neostigmine (0.05mg/kg) and glycopyrrolate (0.01mg/kg) IV and patients were extubated awake.

RESULTS

Statistical Analysis

Data was analysed using SPSS 22 version software (IBM SPSS Statistics, Somers NY, USA). Categorical data was represented in the form of frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. ANOVA (Analysis of Variance) was the test of significance to identify the mean difference between more than two groups for quantitative data. p value of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Distribution Of Demographic Data.

In the study there was significant difference in mean age between four groups. Groups P1 and E1 which constituted normotensive patients were comparable with regards to mean age. Similarly, groups P2 and E2 which constituted hypertensive patients were comparable with regards to mean age. All the groups were comparable with regards to gender distribution and weight. Though we found a significant difference in ASA grade between four groups, all the patients in normotensive groups P1 and E1 belonged to ASA grade I and those in hypertensive groups P2 and E2, belonged to ASA Grade II and were comparable.

Table 1: Distribution Of Demographic Data.

Category	P1	P2	E1	E2	P value
Age (yrs)	39.3± 6.9	47.8 ±5.9	39.4 ±6.5	48.4 ± 5.0	<0.001
Sex (male/female)	14/16	14/16	16/14	15/15	0.947
Weight (kg)	59.7±5.9	58.1±5.8	59.4±5.7	59.4±6.3	0.642
ASA grade (1/2)	30/0	0/30	30/0	0/30	<0.001

Heart Rate

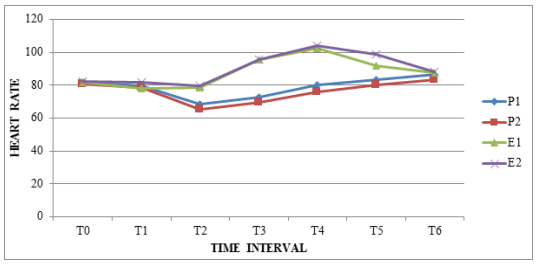
In the present study, the mean HR at baseline and after premedication was comparable among all four groups. A drop in HR was observed following premedication in all the groups. There was a significant fall in heart rate after induction with propofol but no such change was noted with etomidate. A statistically significant difference was observed between groups P1 and E1 and groups P2 and E2 with a greater reduction seen in the hypertensive groups. After intubation, a rise in HR was observed in all 4 groups. In groups E1 and E2, heart rate shooted above the baseline value and returned to baseline by 5 minutes. The highest HR was observed at T4, 24.39% rise above baseline in group E1 and 26.69% in group E2. In groups P1 and P2, heart rate increased slowly to reach the baseline value by 5 minutes.

Table 2: Heart Rate Comparison Between Four Groups At Different Time Intervals.

HR	Group								P value
	P1		P2		E1		E2		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
T0	81.8	4.4	80.7	5.8	82.0	7.6	82.4	5.1	0.716
T1	79.6	5.7	78.5	5.9	78.2	5.0	81.6	6.2	0.102
T2	68.5	3.6	65.3	5.3	78.8	6.0	79.7	5.8	<0.001*
T3	72.9	3.4	69.6	6.0	95.7	6.6	95.5	5.8	<0.001*
T4	80.4	4.0	76.1	6.0	102.7	7.6	104.1	6.5	<0.001*
T5	83.5	4.2	80.1	5.7	92.0	13.6	98.7	8.1	<0.001*
T6	86.6	3.9	83.2	5.4	87.8	5.5	88.3	4.3	<0.001*

Table 3: Heart Rate Comparison Between Groups At Different Time Intervals.

	P1 vs P2	E1 vs E2	P1 vs E1	P2 vs E2
T0	1.000	1.000	1.000	1.000
T1	1.000	0.150	1.000	0.244
T2	0.105	1.000	<0.001*	<0.001*
T3	0.139	1.000	<0.001*	<0.001*
T4	0.044*	1.000	<0.001*	<0.001*
T5	0.786	0.02*	0.001*	<0.001*
T6	0.046*	1.000	1.000	0.001*



Graph 1: Line Diagram Showing Heart Rate Comparison Between Four Groups At Different Time Intervals.

MAP, SBP & DBP

In our study, although a statistically significant difference existed at baseline in MAP, SBP and DBP between the four groups, it was comparable between the two normotensive (P1, E1) and the two hypertensive (P2, E2) groups. Following premedication MAP, SBP and DBP were found to be comparable among all the 4 groups. A fall in MAP, SBP and DBP was observed in all the groups following induction.

MAP, SBP and DBP increased in all the study groups after intubation. In group P1, all the parameters slowly reached the baseline by 5 minutes whereas in group P2 they remained below the baseline at all the time intervals. In the patients induced using etomidate, MAP, SBP and DBP remained stable in both normotensive and hypertensive groups. A statistically significant difference existed between the groups E1-E2 which could be explained as the reflection of statistically significant difference in the baseline values. Following induction, the fall in MAP with propofol was significantly higher when compared to etomidate which offered stable haemodynamic conditions. The difference in MAP was statistically significant in hypertensives all the time whereas only at 1 min post intubation in normotensive patients. The changes in SBP as well as DBP followed the same trend and paralleled the changes in MAP. MAP was found to be lowest at T2, the fall being 23.97% from baseline in group P1, 33.33% in P2, 10.22%

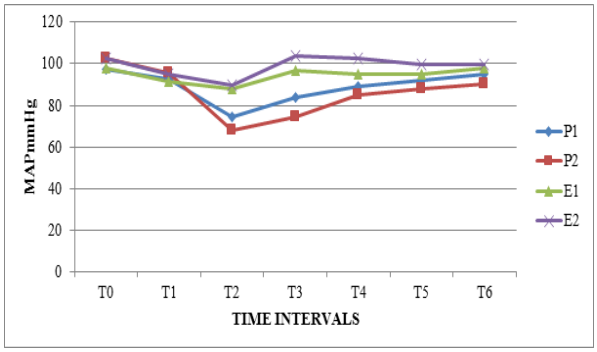
in E1and 12.21% in E2.

Table 4: MAP Comparison Between Four Groups At Different Time Intervals.

MAP	Group								P Value
	P1		P2		E1		E2		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
T0	97.6	4.5	102.3	5.3	97.8	4.2	102.4	2.7	<0.001*
T1	92.5	4.9	95.3	6.0	91.6	4.4	95.1	5.8	0.015*
T2	74.2	6.4	68.2	7.8	87.8	6.1	89.9	5.8	<0.001*
T3	83.8	7.1	74.2	4.7	96.9	8.0	103.9	7.1	<0.001*
T4	88.9	6.4	84.8	6.4	95.1	11.3	102.6	9.9	<0.001*
T5	92.2	5.6	87.9	5.6	95.0	7.0	99.4	5.9	<0.001*
T6	95.1	3.8	90.1	4.4	97.7	3.6	99.5	3.7	<0.001*

Table 5: MAP Comparison Between Four Groups At Different Time Intervals.

	P1 vs P2	E1 vs E2	P1 vs E1	P2 vs E2
T0	<0.001*	<0.001*	1.000	1.000
T1	0.279	0.069	1.000	1.000
T2	0.003*	1.000	<0.001*	<0.001*
T3	<0.001*	0.001*	<0.001*	<0.001*
T4	0.437	0.007*	0.043*	<0.001*
T5	0.045*	0.033*	0.427	<0.001*
T6	<0.001*	0.429	0.073	<0.001*



Graph 2: Line Diagram Showing MAP Comparison Between Four Groups At Different Time Intervals.

Dosage Of Induction Agent.

The difference in mean dose of induction agent between four groups was statistically significant. The mean dose of propofol required for induction was significantly less in hypertensives when compared to normotensives. The requirement of etomidate for induction was found to be comparable in both normotensive and hypertensive groups. But in all the four groups the required dose was less than what has been suggested in literature.

TABLE 6: Mean Dosage of induction agent distribution of subjects in four groups.

GROUP	Dose of induction agent mg/kg	
	Mean	SD
P1	1.9	0.3
P2	1.1	0.4
E1	0.2	0.1
E2	0.2	0.1
P value	<0.001*	

Pain On Injection Grade Comparison Between Four Groups.

Propofol was found to be associated with higher incidence of pain where 50% of subjects in group P1 and 54% in group P2 experienced higher degrees of pain. In contrast, etomidate groups showed a favourable outcome with only 7% in group E1 and 26% in group E2 having pain. The overall incidence of pain with propofol was 51% and with etomidate was 15%.

Table 7: Pain On Injection Grade Comparison Between Four Groups

Pain on injection grade	GROUP											
	P1	P2	P1+P2	E1	E2	E1+E2						
	Count	%	Count	%	Count	%	Count	%	Count	%	Count	%
0	15	50.0%	14	46.7%	29	48.3%	28	93.3%	23	76.7%	51	85%
1	13	43.3%	12	40.0%	25	41.6%	2	6.7%	5	16.7%	7	11.6%
2	2	6.7%	3	10.0%	5	8.3%	0	0.0%	1	3.3%	1	1.6%
3	0	0.0%	1	3.3%	1	1.6%	0	0.0%	1	3.3%	1	1.6%

$\chi 2 = 22.78$, df = 9, p = 0.007*

Myoclonus Degree Comparison Between Four Groups.

None of the patients induced with propofol experienced myoclonus, whereas in etomidate groups various degrees of myoclonus were seen. The overall incidence of myoclonus was observed to be 46.6% with 44% in group E1 and 50% in group E2.

Table 8: Myoclonus Degree Comparison Between Four Groups.

Degree Of myoclonus	GROUP											
	P1	P2	P1+P2	E1	E2	E1+E2						
	Count	%	Count	%	Count	%	Count	%	Count	%	count	%
0	30	100%	30	100%	60	100%	17	56.7%	15	50.0%	32	53.3%
1	0	0.0%	0	0.0%	0	0.0%	6	20.0%	10	33.3%	16	26.6%
2	0	0.0%	0	0.0%	0	0.0%	4	13.3%	3	10.0%	7	11.6%
3	0	0.0%	0	0.0%	0	0.0%	3	10.0%	2	6.7%	5	8.3%

$\chi 2 = 39.29$, df = 9, p <0.001*

Apnoea Comparison Between Four Groups.

In the present study, there was no significant difference in the incidence of apnoea between four groups. Highest incidence of apnoea was seen with propofol as evident by 40% in group P1 and 33% in group P2 when compared to13% of subjects in group E1 and 23% in group E2. The overall incidence of apnoea was more with propofol (36.6%) when compared to etomidate (18.3%), although the difference was not statistically significant.

Table 9: Apnoea Comparison Between Four Groups.

Apnoea	GROUP											
	P1	P2	P1+P2	E1	E2	E1+E2						
	Count	%	Count	%	Count	%	Count	%	Count	%	Count	%
No	18	60.0%	20	66.7%	38	63.3%	26	86.7%	23	76.7%	49	81.6%
Yes	12	40.0%	10	33.3%	22	36.6%	4	13.3%	7	23.3%	11	

$\chi 2 = 6.144$, df = 3, p = 0.105

DISCUSSION

Induction of anaesthesia is a dynamic stage associated with haemodynamic variations of varying degree depending on several factors. HR and MAP are used as the hemodynamic targets for perioperative management as instability of these parameters is associated with increased incidence of morbidity[2]. Sudden hypotension and tachycardia have deleterious effects on maintaining perfusion to vital organs, especially in patients with coronary artery disease, valvular stenosis, uncontrolled hypertension and shock[1]. The magnitude of hypotension is directly proportional to the plasma concentration of the induction agent which in turn depends on many factors such as age, gender, body weight, dose, infusion rate and cardiac output[4].

Direct laryngoscopy and endotracheal intubation are noxious stimuli that can provoke adverse responses in the cardiovascular, respiratory and other physiological systems[2]. Tracheal intubation under light plane of anaesthesia leads to significant pressor response with resultant hypertension and tachycardia. The degree of the response is proportional to force and duration of laryngoscopy. The elevation in the arterial pressure typically starts within 5 secs of direct laryngoscopy, peaks in 1 to 2 mins and return to baseline levels by 5 mins. Change in haemodynamic parameters start within seconds of direct laryngoscopy and there is a further increase in HR and BP with passage of endotracheal tube[2].

Heart Rate Changes:

This hemodynamic parameter is an important determinant of myocardial oxygen consumption-supply balance by influencing myocardial oxygen demand and coronary perfusion by virtue of the effect on diastolic duration[2]. Heart rate was better preserved in patients induced with propofol as compared to etomidate. The fall in HR observed with propofol induction may be attributed to its centrally mediated sympatholytic or vagotonic action. As it also attenuates the baroreceptor response, compensatory tachycardia does not accompany the fall in BP[4]. This was also explained by Maruyama K et al, who investigated the effects of intravenous atropine to prevent bradycardia and hypotension during total intravenous anaesthesia with propofol and remifentanil[17]. In contrast, compensatory tachycardia in response to fall in systemic vascular resistance has been observed with etomidate due to an active baroreceptor reflex. The significant difference in HR observed between P1-E1 and P2-E2 can be explained by the differential action on baroreceptor reflex by the two drugs.

Meena et al, in their study, found a significant difference in HR following induction and intubation in all the three groups induced with propofol, etomidate and propofol etomidate combination[5]. The HR returned to baseline by 5 minutes in the propofol group while tachycardia was persistent in the etomidate group. In our study, the results were similar with propofol induction but with etomidate, we observed stable heart rate throughout except the occurrence of tachycardia at intubation, which was < 20% of baseline.

Yukari Sawano et al, in their study observed that a high dose of fentanyl (4μg/kg) was effective in preventing tachycardia in response to intubation when compared to a standard dose of fentanyl 2μ/kg in hypertensive patients[13]. However, the escalated dose of fentanyl did not offer any added advantage in normotensive patients. In our study, fixed dose of fentanyl (2μg/kg) administered to all the study groups could have been inadequate to blunt the intubation response in hypertensive patients.

In the study conducted by Das et al, HR remained stable from preinduction period till 10 min following intubation in etomidate group[9]. Whereas a significant fall in HR was observed after induction followed by significant tachycardia with propofol induction. This was in contrast to the results of our study.

Changes In MAP, SBP & DBP

The significance of maintaining MAP within 20% of baseline value necessary for adequate tissue perfusion has been well appreciated and is the goal of anaesthetic management. This mandates careful induction including choice of induction agent, technique, judicious use of vasopressors and fluid management[3]. We found that MAP was maintained within the allowable range with etomidate when compared with propofol[4]. Pharmacodynamics of propofol and etomidate can explain the results of our present study. Hypotension induced by propofol is mediated by inhibition of sympathetic nervous system and impairment of baroreflex regulatory mechanisms[3]. Conversely, etomidate causes minimal fluctuations in blood pressure by virtue of preservation of both sympathetic out flow and autonomic reflexes[3].

In the study conducted by Meena et al in normotensive patients, MAP decreased after induction and the fall was more in patients induced with propofol than those induced with etomidate or combination of both[5]. In the propofol group, MAP was observed to increase slowly to reach the baseline value following intubation. Etomidate and etomidate-propofol combination were associated with stable haemodynamics and a statistically significant difference was found between propofol and the other two groups. These findings were corroborated by our study in normotensive as well as hypertensive patients.

Schmidt et al inferred that hypotension caused by propofol is a result of reduction in preload and afterload, not synchronized with compensatory increase in cardiac output and HR[20]. This could explain the hypotension associated with propofol induction in the groups P1 and P2 in our study.

Mehrdad et al, explored the cardiovascular response to induction of anaesthesia with etomidate and propofol[15]. They suggested that etomidate could be preferred over propofol for general anaesthesia as it offers greater haemodynamic stability.

Leslie J Weiss-Bloom et al, studied the haemodynamic response to anaesthetic induction and tracheal intubation following induction with etomidate 0.3mg/kg and the lowest dose of fentanyl that would blunt the intubation response[21]. They concluded that though etomidate has been shown to be devoid of adverse cardiovascular effects in patients with pre-existing cardiovascular disease, it does not blunt the haemodynamic response to laryngoscopy and tracheal intubation reliably. Therefore, it is not ideal as a sole agent for anaesthetic induction in patients with cardiovascular disease. Brief episodes of hypertension and tachycardia may not contribute to adverse outcomes but prolongation of these

episodes most probably would. The authors recommended administration of 5-10μg/kg fentanyl administered 60 sec prior to induction with etomidate, 0.3 mg/kg to blunt the intubation response. However haemodynamic parameters remained stable in our study despite using a standard dose of fentanyl 2μg/kg.

Moller Peterson et al, suggested that etomidate has potential to cause hypotension along with compensatory tachycardia despite using bispectoral index (BIS) to titrate the infusion to adequate anaesthesia depth[14]. They observed that etomidate did not provide more stable haemodynamic conditions compared to propofol, especially because of its inability to prevent an increase in HR and blood pressure at and after intubation. We observed stable HR with propofol but MAP was maintained better with etomidate. This was in contrast to our results, which suggest stable haemodynamics following etomidate induction.

Kaur et al conducted a study in cardiac patients induced with propofol and etomidate[12]. They observed a fall in both SBP & DBP for 15 minutes after induction with propofol whereas with etomidate it remained stable. Etomidate increases coronary perfusion in patients with moderate cardiac dysfunction, making it an induction agent of choice in cardiac patients.

Paris A et al, conducted in-vivo and in-vitro studies to investigate the structural similarity of etomidate to dexm edetomidine which is an alpha2-adrenoceptor agonist[19]. The agonistic action of etomidate at alpha2B-adrenoceptors appeared to mediate the increase in blood pressure, contributing to the cardiovascular stability following induction of anaesthesia with etomidate.

Maruyama K et al, studied the effect of pre-treatment with intravenous atropine during total intravenous anaesthesia with propofol and remifentanil[17]. They observed that intravenous atropine could prevent bradycardia, but not hypotension. They explained that bradycardia was mainly caused by centrally mediated sympatholytic and vagotonic actions of propofol and remifentanil, whereas a fall in BP was mainly the result of their direct vasodilating actions.

Correlation Between Dose Of Induction Agent And Weight.

The induction dose of propofol was titrated based on loss of response to verbal commands and that of etomidate, taking loss of eyelash reflex as the end points[3]**.** Mean dose of propofol required for induction was significantly less in hypertensives (1.1mg/kg) when compared to normotensives which was 1.9mg/kg. In hypertensive patients, the changes in intravas cular volume and volume of distribution of drugs may have contributed to the decrease in mean dose requirement[24]. The requirement of etomidate for induction was found to be comparable in both normotensive and hypertensive groups which is 0.2mg/kg. Hypertensive patients in the etomidate groups could have been optimally treated along with normalization of pharmacokinetic profile. However, this was not further investigated in our study. In all the four groups, the dose requirement was less than what has been suggested in literature.

Shagun Bhatia Shah et al, concluded that the dose required for induction is reduced when entropy guidance is used[10]. Induction dose needed to achieve adequate depth of anaesthesia was found to be 0.15 mg/kg for etomidate and 0.98 mg/kg for propofol respectively, which was less when compared to our results. Various studies have reported induction doses ranging from 0.2 to 0.45 mg/kg. Titration of dose has been advised to prevent haemodynamic instability.
Akasapu Karunakara Rao et al, concluded that the induction dose of propofol guided by electroencephalogram entropy was significantly higher than the induction dose based on loss of verbal response[11]. They also observed similar haemodyna mic profiles using either technique. It was concluded that conventional method is adequate to access the level of hypnosis and titrate the dose of induction agent. There have been contradictory results regarding the use of BIS or entropy for titration of dose to achieve haemodynamic stability. This was the basis for choosing clinical endpoints for titrating the dose of induction agent in our study.

Incidence Of Pain On Injection.

Pain is a bad experience for patients while it is an embarrassing situation for the anaesthesiologist. In the present study we found a significant difference in the grade of pain on injection between the four groups with a favourable outcome offered by etomidate. Our findings were well supported by multiple studies carried out by Wu et al[16], Y Nyman et al[18], Kaur et al[12] and S Aggarwal et al[1].

Pain occurs with propofol injection as its structure has long chain fatty acids and the incidence increases with higher concentration of the drug and solvent like 2.25% glycerol[4]. Mixing of propofol with lidocaine decreases the incidence of pain but it is not recommended because it will cause coalescence of oil droplets, posing a risk of pulmonary embolism.[3] For this reason we had avoided mixing lidocaine with propofol in our study.

Commercial preparation of etomidate has 35% propylene glycol converting it into a lipid emulsion which is associated with pain on injection. Pain on injection, venous irritation and haemolysis has been abolished by new-fat emulsion of etomidate (medium chain triglycerides and soyabean named etomidate-lipuro) but the incidence of myoclonus is not reduced with the new preparation.[4]

Y Nyman et al, in their study concluded that etomidate-lipuro is associated with significantly lower injection pain(5%) compared with propofol with added lidocaine(47.5%)[18]. But a higher incidence of myoclonic activity of 85% was seen in the etomidate- lipuro group compared with the propofol–lid ocaine group of 15%.

In our study we took measures to reduce pain on injection by giving a titrated dose of the drugs with a running drip and also premedicated the patients with opioids and midazolam. Despite these measures, propofol showed a higher incidence of pain on injection. We did not use etomidate lipuro due to its unavailability.

Incidence Of Myoclonus.

The lower incidence as well as lesser degree of myoclonus in our study than that suggested in literature may be explained by a lower dose of etomidate used. R Carlos et al, concluded that premedication with fentanyl (10 μkg/kg) and diazepam (150 μg/kg) can effectively prevent myoclonus, when administered 10 min prior to induction with etomidate[23]. The standard dose of fentanyl 2μg/kg in our study would not have been sufficient to suppress myoclonus. This may explain the difference in incidence of myoclonus compared to our study. Abbas Sedighinejad et al, found that pre-treatment with low dose etomidate can reduce myoclonus when compared to low-dose midazolam, magnesium sulphate, remifentanil[6]. Wu J et al suggested that a lower dose of etomidate, supplemented with fentanyl and midazolam, is associated with lesser adverse effects like myoclonus and postoperative nausea and vomiting, similar to our study[16].

Incidence Of Apnoea

Propofol produces dose-dependent depression of ventilation, with apnoea occurring in 25% to 35% of patients after induction of anaesthesia. The depressant effects of etomidate on ventilation seem to be less although apnoea may

occasionally accompany a rapid IV injection of the drug.[4]

Giese JL et al, observed a lesser incidence of apnoea with etomidate when compared with thiopental[22]. This was attributed to fentanyl pre-treatment which significantly decreased the incidence of pain on injection and myoclonus, but increased the incidence of apnoea. Kaur et al observed apnoea in 90% patients with propofol and 66.7% patients with etomidate[12]. Higher incidence of apnoea could be due to premedication with fentanyl and midazolam along with higher doses of etomidate and propofol. In our study, titration of dose of drugs could have resulted in lower incidence of apnoea.

LIMITATIONS.

- In the present study, we did not use BIS or entropy guidance to titrate the dose of induction agent to adequate depth, which could have further decreased the dose requirement, contributing to haemodynamic stability.
- Among the hypertensive groups, the duration of hypertension and the details of treatment with respect to number and class of antihypertensive drugs may impact the haemodynamic response to induction and intubation.
- We did not evaluate incidence of adrenal suppression by following plasma cortisol and adrenocorticotropic hormone levels.

Future Recommendations- Information obtained by monitori ng myocardial oxygen consumption and cardiac stress reflected by RPP may provide more clarity about haemodyna mic stability offered in hypertensive patients. Monitoring this index in future studies may provide valuable inputs.

CONCLUSION

- The present study suggests that induction of anaesthesia with etomidate is associated with better stability of MAP in normotensive as well as hypertensive patients when compared with propofol. However, HR is better maintained with propofol. Thus there is no clear evidence supporting induction by etomidate in hypertensive patients.
- The dose requirement of propofol as well as etomidate for induction, guided by clinical end points is lesser than the standard dose calculation suggested by literature based on body weight.
- Propofol is associated with higher incidence of apnoea and pain on injection, whereas myoclonus occurs only with etomidate.

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