ORIGINAL ARTICLE

A Comparative Study of Haemodynamic Changes on LMA Insertion with Propofol, Etomidate and Propofol+Etomidate Admixture in Laparoscopic Cholecystectomy

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Abstract

The objective of current study was to compare the efficacy of three different anaesthesia induction approaches i.e. Inj propofol, Inj etomidate and admixture of Inj propofol and Inj etomidate in maintaining hemodynamic stability during induction and following Proseal LMA insertion in laparoscopic cholecystectomy. Patients were randomly divided in to 3 groups with 90 patients each and received 2.5mg/kg of propofol(P), 0.3mg/kg of etomidate(E) and 1mg/kg of propofol+0.2mg/kg of etomidate which was mixed in a 20ml syringe. We also studied side-effects like PONV, myoclonus, pain on Injection, allergic reactions and thrombophlebitis. We found that the use of P-E admixture for induction of Proseal LMA provides hemodynamic stability as it prevents hypotension caused by propofol and also hypertension caused by etomidate when used alone. Admixture was also associated with less incidence of other side effects like PONV, pain on Injection and myoclonus. We concluded that combination of propofol and etomidate for induction of anaesthesia for Proseal LMA is significantly better than either drug used alone.

Key Words

Propofol, Etomidate, Induction of anaesthesia, Hemodynamic stability, Mean arterial pressure

Introduction

Propofol and Etomidate are two widely used induction agents with their own advantages (1,2). Propofol is the commonest drug used for induction of general anaesthesia due to satisfactory recovery, short half-life, rapid elimination from blood circulation, causing fewer sedative effects and vomiting. Its unwanted complaints are hemodynamic instability such as hypotension and bradycardia in some patients (3). It also causes pain at the site of Injection. Etomidate is a short acting drug which provides best cardiovascular stability with no release of histamine, (4,5) but can cause nausea and vomiting, myoclonus, pain on Injection and adverse effects on endocrine system. It leads to suppression of corticosteroid synthesis by reversibly inhibiting 11-beta hydroxylase , an enzyme important in adrenal steroid production leading to adrenal suppression which was main cause of high morbidity and mortality in ICU patients due to which its use was discontinued .Rediscovery of beneficial effect of etomidate and lack of new reports of adrenocortical suppression leads to renewed interest in etomidate (6). The drug was reformulated using lipid emulsion and reintroduced in 2007 in India. So, it theoretically seems that propofol and etomidate combination may balance the opposing hemodynamic effects. The technique of co-induction is applied to produce more appropriate desired outcomes with fewer side effects compared to single drug use.

Material and Methods

After obtaining informed written consent and approval

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from the Hospital Medical Ethical Committee, randomized controlled study was conducted in the Department of Anaesthesiology and Intensive Care Unit, Government Medical College and Associated Hospitals, Jammu. 90 patients of either sex, ranging in age from 18-60 yrs. belonging to ASA Grade I & II undergoing elective laparoscopic cholecystectomy surgeries under general anaesthesia (GA) with Proseal LMA insertion were taken up for the study. Patients were randomly allocated to one of three groups of 30 patients each. Group P- received propofol 2.5 mg/Kg, Group E- received Etomidate 0.3mg/Kg, Group P+ E – received 1mg/kg (1%) Propofol + 0.2 mg/kg etomidate which was mixed in a 20ml syringe. The drug was Injected in 10sec.

Exclusion criteria include: patient refusal to participate in the study, hypersensitivity to the study drugs, hemodynamically unstable patients, patient with sepsis, history of seizure disorder, presence of known primary or secondary adrenal insufficiency or on steroid medication, pathology in the larynx or pharynx, mouth opening <2.5cms, Mallampati score of 3-4, habituation to analgesics, sedatives and antianxiety drugs and more than 3 attempts during LMA Proseal insertion. All Patients received Tab. Alprazolam 0.25mg orally and Tab Ranitidine 150mg night before surgery and kept fasting overnight. In the pre-operative room, i/v line with 20G cannula was established, Inj Ringer lactate started at 6ml/kg. Inj Glycopyrrolate 0.2mg i/m and Inj Ondansetron 4mg i/v was given.

In the operation theatre, Routine monitors like NIBP, ECG, SPO2, Etco2 were attached and baseline vital parameters like HR, SBP, DBP, MAP & Spo2 were recorded. Inj Midazolam 0.025 mg/kg I/V, Inj Lidocaine 1 mg /Kg I/V was given. After preoxygenation with 100% O2 for 3 min, patients were induced with one of the study drugs and asked for pain on Injection until the loss of verbal contact followed by low dose Inj Suxamethonium 1 mg/kg I/V. Patient were ventilated for 45sec. Proseal LMA size calculated according to the body weight of the patient and lubricated with lignocaine jelly was inserted. Proper placement of Proseal LMA was confirmed by observing bilateral chest movements, auscultation for breath sounds during controlled ventilation and capnographic tracing. Following LMA insertion, anaesthesia was maintained with isoflurane 1-1.5% and mixture of O2 – N2O (40:60). Muscle relaxation was maintained by loading dose of non-depolarizing muscle relaxant Inj Atracurium 0.5mg/kg and top up doses of Inj Atracurium 0.1 mg/kg Rating Scale (VRS) i.e., No nausea = 0, mild nausea = 1, moderate nausea =2, and no vomiting =0, less than 4 episodes = 1, more than 4 episodes = 2. Patients with any episode of vomiting in the postoperative period was given Inj I/V. Patient were mechanically ventilated. Paracetamol infusion 100ml i.v was also given intraoperatively. At the end of surgery residual muscular paralysis was reversed by administering Inj Neostigmine (0.05 mg/kg) and Inj Glycopyrrolate (0.01mg/kg I/V) and LMA was taken out when respiration was adequate and patient was able to obey verbal command. Heart rate, Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Mean arterial pressure (MAP) were continuously monitored and recorded before induction (Tb), before LMA insertion((T0), 1min(T1), 3min(T3), 5min(T5) and 10min(T10) after LMA insertion. For 2hrs in the postoperative recovery room, patient was monitored hemodynamically and any episode of nausea and vomiting was noted. PONV were rated as per Visual Metoclopramide 10mg i/v as a rescue antiemetic. The patients were also observed for any other untoward effects of the drugs like myoclonus, pain on Injection, allergic reactions and thrombophlebitis etc.

Results

All the three groups were comparable in age, sex and weight with no statistically significant difference ($p>0.05$). *(Table 1)* Observation and results of the study are shown from *Table 2 to Table 7.*

Discussion

On comparing age, sex and weight of the patients we found no statistical difference in three groups. The main finding of the study was that combination of etomidate and propofol provided more stable hemodynamics compared to etomidate and propofol used alone. Yagen *et al.* found that etomidate-propofol combination may be valuable alternative when extremes of hypotension and hypertension responses due to propofol and etomidate are best to be avoided (7).

In our study there was increase in heart rate from baseline value in etomidate and etomidate + propofol group but fall in propofol group at induction. Hosseinzadeh *et al.* observed that H.R was significantly lower in propofol group than etomidate group and propofol-etomidate admixture (8). Significant bradycardia after induction with propofol has been observed by other authors as well (7,9). Karki *et al.* noted that etomidate provides greater stability of hemodynamics than propofol

Table 1: Demographic Profile

Parameters	Group P	Group E	Group P+E	p-value
Age(yrs.)	40.6±12.81	40.6±11.60	38.5±12.69	0.770
Weight (kgs)	59.0±10.21	61.5±8.08	60.79±9.46	0.579
Gender(M/F)	9/21	15/15	16/14	0.144

Table 2: Showing Mean HR (beats/min) Among Various Groups

Time Interval	Group P		Group E		Group P+E		p-value
	Mean	SD	Mean	SD	Mean	SD	
Tb	78.57	5.606	76.93	6.158	77.53	6.004	0.560
T0	69.93	5.071	88.50	7.210	82.10	6.205	<0.001*
T1	76.83	5.331	99.93	7.817	93.07	7.046	<0.001*
T3	83.30	5.826	94.67	7.480	89.97	6.815	<0.001*
T5	85.63	6.189	92.00	7.168	89.57	6.867	<0.001*
T10	87.57	5.649	91.60	6.252	91.97	6.677	0.018*

**Statistically significant difference (p-value<0.05).*

Above table shows that the baseline (Tb) HR values are comparable among all the three groups [P, E and P+E] with no statistically significant difference ($p > 0.05$). At T0, T1, T3, T5 and T10 there was significant difference among all the three groups ($p < 0.05$).

Table 3: Showing Mean SBP (mmHg) Among Various Groups

Time Interval	Group P		Group E		Group P+E		p-value
	Mean	SD	Mean	SD	Mean	SD	
Tb	129.37	6.031	127.87	6.146	127.80	5.359	0.506
T0	99.63	5.169	116.37	5.568	117.90	4.901	<0.001*
T1	111.30	5.325	134.23	6.521	130.33	5.967	<0.001*
T3	121.63	5.436	125.30	6.243	125.27	5.570	0.021*
T5	126.87	6.202	122.73	5.982	122.63	5.183	0.007*
T10	130.53	6.146	119.57	5.946	118.63	5.196	<0.001*

**Statistically significant difference (p-value<0.05).*

Base line values were comparable among all the three groups (P, E and P+E) with no statistically significant difference ($p > 0.05$). But SBP at T0 and T1, T3, T5, T10 after Proseal insertion showed statistically significant difference (p-value<0.05)

Table 4: Showing Mean DBP (mmHg) Among Various Groups

Time Interval	Group P		Group E		Group P+E		p-value
	Mean	SD	Mean	SD	Mean	SD	
Tb	76.67	5.358	75.93	6.147	76.50	4.562	0.859
T0	60.57	4.224	68.40	5.462	69.33	4.318	<0.001*
T1	66.70	4.757	78.17	6.438	74.30	4.435	<0.001*
T3	69.13	4.769	73.70	6.012	72.70	4.481	0.002*
T5	73.90	4.339	71.63	5.696	71.20	4.156	0.043*
T10	75.90	5.261	70.30	5.658	70.13	4.554	<0.001*

**Statistically significant difference (p-value<0.05).*

Baseline values of DBP were comparable among all the groups with no statistically significant difference ($p > 0.05$). But at T0 and T1, T3, T5, T10 after Proseal LMA insertion DBP were statistically significant ($p< 0.05$)

Table 5: Showing MAP (mmHg) Among Various Groups

Time Interval	Group P		Group E		Group P+E		p-value
	Mean	SD	Mean	SD	Mean	SD	
Tb	94.23	5.122	93.24	6.003	93.60	4.698	0.764
T0	73.60	4.081	84.34	5.389	85.55	4.304	<0.001*
T1	81.56	4.540	96.90	6.349	92.92	4.710	<0.001*
T3	86.57	4.607	90.88	5.967	90.20	4.637	0.003*
T5	91.47	5.060	88.61	5.700	88.33	4.361	0.033*
T10	94.03	5.000	86.66	5.652	86.32	4.619	<0.001*

Statistically significant difference (p-value<0.05).

Baseline values (Tb) were comparable among all the three groups with no statistically significant difference (p >0.05). At T0 and T1, T3, T5, T10 after Proseal LMA insertion MAP values were statistically significant.

Table 6: Incidence of Nausea and Vomiting Among Various Groups

	Group P (%)	Group E (%)	Group P+E (%)	P-value
Nausea	20%	56.7%	23.3%	0.004
Vomiting	0	23.3%	3.3%	0.003

Statistically significant difference (p-value<0.05)

Table 7: Showing Side Effects Among Various Groups

Time Interval	Group P		Group E		Group P+E		p-value
	Mean	SD	Mean	SD	Mean	SD	
Tb	94.23	5.122	93.24	6.003	93.60	4.698	0.764
T0	73.60	4.081	84.34	5.389	85.55	4.304	<0.001*
T1	81.56	4.540	96.90	6.349	92.92	4.710	<0.001*
T3	86.57	4.607	90.88	5.967	90.20	4.637	0.003*
T5	91.47	5.060	88.61	5.700	88.33	4.361	0.033*
T10	94.03	5.000	86.66	5.652	86.32	4.619	<0.001*

Statistically significant difference (p-value<0.05)

and therefore can be used as agent of choice for induction of patients with cardiac disease (10).

On comparing the effect of these drugs on SBP, DBP and mean arterial pressure we found that values at induction (T0) and at 1,3,5 and 10 min after induction were statistically significant. On intergroup comparison it was found that SBP, DBP and MAP was lower in propofol group but stable in other two groups. Propofol induced hypotension is mediated by inhibition of the sympathetic nervous system and the impairment of the baroreceptor reflex regulatory mechanism. Propofol may lead to a reduction in the systemic vascular resistance and cardiac output. On other side brief episode of increase in Blood pressure was found in etomidate group at T1 which may however not contribute to adverse outcome. Hemodynamic stability observed with etomidate may be due to its unique lack of effect on the sympathetic nervous system and on baroreceptor functions. The results of our study have shown that the individual properties of etomidate and propofol can be seen with the admixture of the drugs and can provide a more stable systolic, diastolic and mean LMA insertion, after LMA insertion and arterial pressure before intraoperatively than etomidate and propofol when used alone.

Our results were in accordance with Hosseinzadeh *et al.* and Saricaoglu *et al.* (8,11). They observed that the admixture is associated with hemodynamic stability as compared to other drugs separately.

In our study on comparing the results of group P and group E it was seen that the induction dose of propofol

leads to a significant decrease ($p<0.05$) in systolic, diastolic and mean blood pressure while the etomidate leads to increase in these parameters.

Our results are also supported by Yagan *et al.* who studied hemodynamic variations with propofol, etomidate and admixture and concluded that etomidate - propofol combination may be a valuable alternative when extremes of hypotension and hypertensive response due to propofol and etomidate are best to be avoided (7).

Hypotension caused by propofol is due to the reduction of heart's preload and afterload which are not synchronised with the heart's compensatory response such as increase in cardiac output and heart rate (12). In our study we got similar results in propofol group as after induction, there was hypotension and bradycardia because compensatory response was blunted.

The incidence of Post-Operative nausea and vomiting was maximum in E group followed by P+E and P group in our study. The reduced incidence of PONV in P+E group may be due to reduced dose of etomidate and antiemetic effect of propofol.

The other negative characteristic noted with etomidate is high incidence of myoclonic jerks. Our study showed insignificant results between the groups which may be due to the fact that we used iv midazolam (0.025mg/kg) and lignocaine(1mg/kg) prior to induction. Huter *et al.* has reported that iv midazolam before induction of anaesthesia with etomidate is effective in reducing myoclonic movements (13).

Pain during Injection of anaesthetic agent is a bad experience for patient while it is embarrassing situation for an anaesthesiologist. Etomidate showed a favourable outcome when compared to propofol and is very well supported by Saricaiglou *et al.* (11). No patient in admixture group reported pain at injection which may be attributed to decrease concentration of propofol and presence of LCT/MCT in etomidate-lipuro. Similar results were shown by Nyman *et al.* (14). No patient in our study had allergic reactions and none had thrombophlebitis.

Conclusion

The admixture of etomidate and propofol for induction of anaesthesia provides better hemodynamic stability than etomidate or propofol alone. Admixture is also associated with less incidence of PONV, pain on injection and myoclonus.

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