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Research Article

A randomised clinical study to compare the haemodynamic effects of etomidate with propofol during induction of general anaesthesia

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ABSTRACT

Background: Induction agents are frequently associated with changes in heart rate and blood pressure and various adverse effects. Since the introduction of general anaesthesia, no ideal induction agent has yet been discovered in term of providing a stable hemodynamic with fewer adverse effects. This prospective randomized clinical study was conducted to compare propofol and etomidate for their effect on hemodynamic and various adverse effects on patients scheduled for elective surgeries during the induction of general anesthesia.
Methods: 50 patients of ASA I and II of age group 18-60 years scheduled for elective surgeries under general anaesthesia were randomly assigned in two groups (n=25) receiving etomidate (0.3 mg/kg) in group E and propofol (2.5 mg/kg) in group P as an induction agent. Hemodynamic parameters were recorded at various time intervals. Any adverse effect pain on injection and myoclonus was carefully watched. VAS score was recorded for pain on injection. Statistical analysis was done using software (SPSS IBM version 20). P value was considered significant if ($p<0.05$).
Results: Demographic variables were comparable in both the groups. Hemodynamic parameters at baseline were comparable. There were no statistically significant differences among groups E and P in terms of heart rate (HR) ($P>0.05$). Patients in propofol group showed significant fall of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and compared to etomidate ($P<0.05$).) Pain on injection was more in propofol group ($P=0.021$), While incidence of myoclonus activity was higher in etomidate group ($P=0.0027$).
Conclusions: Etomidate is a better induction agent over propofol as it provides more hemodynamic stability and less pain on injection as compared to propofol.

Keywords: Etomidate, Propofol, Induction agent, Hemodynamic changes

INTRODUCTION

Induction agents are frequently associated with changes in heart rate and blood pressure and various adverse effects. Since the introduction of general anaesthesia, no ideal induction agent has yet been discovered in term of providing a stable hemodynamic with fewer adverse effects.

Propofol is an ultra-short-acting sedative-hypnotic agent with its favourable characteristics of smooth induction and rapid recovery are the reasons for using this drug more commonly.[1] Inducing anaesthesia with Propofol (2-2.5 mg/kg) cause hypotension in all the patients regardless of any underlying conditions is due to the reduction of heart's preload and after load.[2, 3]

While other major drawbacks of propofol are pain on injection and dose dependent depression of ventilation.[4] Etomidate, a carboxylated imidazole is characterized by hemodynamic stability, minimal respiratory depression and commonly used for induction and maintenance of anesthesia and induction agent of choice in patients with moderate cardiac dysfunction due to its lack of effect on sympathetic nervous system.[1,5] However some adverse effects of etomidate are myoclonus, pain on injection and

suppression of steroid production by reversible inhibition of 11-beta-hydroxylase enzyme.[6,7]

Present prospective randomized study was done to compare propofol and etomidate for their effect on hemodynamic parameters such as change in blood pressure and heart rate were taken as the primary outcome variables & and pain on injection, myoclonus as a secondary outcome variables during induction of anaesthesia.

METHODS

After obtaining approval from the institutional ethical committee and informed consent obtained from patients, this prospective randomized clinical study was done on total of 50 patients of either sex, aged between 18 - 60 years, with the American Society of Anaesthesiologists (ASA) class I and II, scheduled for elective surgical procedure under general anaesthesia.

Patients with history of adrenal insufficiency, hypertension, valvular disease, patients on steroid since last 6 months, hyper sensitivity to etomidate, propofol and their contents, were excluded from the study.

The patients were randomly assigned by chit and box technique into two groups of 25 each, (group P) received propofol (2.5 mg/kg) and (group E) received etomidate (0.3 mg/kg) as an induction agent of anaesthesia. In the operating room venous access was established with 18G/20G canula and infusion of 5 ml/kg lactated Ringer's solution started. All standard monitors were attached.

Patients were explained preoperatively about pain on injection and VAS scaling. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and heart rate (HR) were recorded as baseline values. The patients SBP, DBP, MAP and HR parameters were measured one minute before premedication and after induction every minute for first five minutes and every five minutes.

Patients were premeditated with inj. glycopyrrolate 0.005 mg/kg and injection fentanyl 2 mcg/kg intravenously ten minutes before induction.

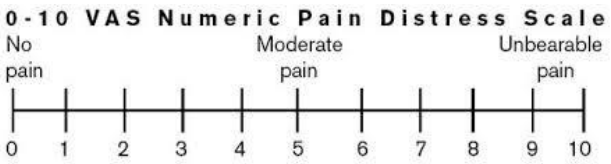

Figure 1: VAS numeric pain distress scale.

Syringes were covered with masking tape to conceal any details of induction agent. Induction of anaesthesia was either with injection propofol 2.5 mg/kg (group P) or inj. etomidate 0.3 mg /kg (group E). Loss of verbal response was considered to be the end point of induction.

VAS score was recorded for pain on injection as:

Presence of myoclonus was observed and graded as:-

- ***Mild*** –Short movement of body segment (a finger or shoulder).
- ***Moderate*** -Slight movement of two different muscles or muscle groups of the body.
- ***Severe*** - Intense clonic movements in two or more muscle groups of the body (fast abduction of a limb).

This was followed by injection vecuronium 0.1mg/kg, ventilation using intermittent positive pressure ventilation and intubation was done by same anaesthesiologist. After intubation is confirmed, the patient was connected to breathing circuit and intermittent positive pressure ventilation. Halothane was started after recording of all desire parameter.

The patient was supplement with 66% N2O in O2 with halothane and injection vecuronium as needed continued till the completion of surgery. Patient was reversed from neuromuscular blockade by injection neostigmine 0.05 mg/kg and injection glycopyrrolate 10mcg/kg and extubated. Patients were observed for twenty four hours in post-operative room.

Statistical analysis

Statistical analysis was done using software SPSS IBM version 20. Data were presented as mean±SD for continuous variables and as number and percentage for nominal variable. The categorical variables were compared using Chi square test and continuous variables using unpaired t test. P value <0.05 was considered significant.

RESULTS

Demographic Profile of both groups was comparable in age, sex, and weight with no statistically significant differences (p>0.05) (Table 1).

Table 1: Demographic profile.

Demographic profile		Group E (n=25)	Group P (n=25)	P value
Mean age (years)		36.64±10.85	32.12±13.89	0.21
Mean weight (kg)		50.72±6.81	54.44±11.33	0.16
Sex	Male	5	8	0.33
	Female	20	17	

Pre-operative baseline vitals HR, SBP, DBP, MAP were comparable between two groups (p>0.05).Changes in HR were statistically comparable between two groups

(***P***>0.05) at all-time intervals. In group E, baseline means SBP (128.04±11.94 mm Hg) decreased up to 121.88±19.91mm Hg at 3 min of induction.

While in group P baseline Mean SBP (134.52±15.50 mm of Hg) decreased up to 101.68±11.54 mm Hg at 4 min of induction. The difference of SBP between two groups was statically significant (P<0.05) at all-time intervals except baseline value which was comparable DBP showed a fall in both the groups at 1, 2, 3 min (81.16±9.28, 79.28±10.18, 78.2±15.93 in group E v/s 73.64±13.41, 69.6±17.49, 66.72±15.05 in group P, respectively) after induction but the fall was more in propofol group and was statistically significant (P<0.05. Etomidate group showed a slight fall in MAP from baseline (100.08±10.21 to 96.24±17.09mm Hg) at 3 min but in group P baseline MAP (103.64±12.42 mmHg) decreased up to (81.84±15.79 mmHg) at 3 min.

Table 2: Comparison of hemodynamic parameters.

Time and group	HR			SBP			DBP			MAP		
	Etomi-date	Propo-fol	P	Etomi-date	Propofol	P	Etomi-date	Propofol	P	Etomidate	Propofol	P
Base line	95.08± 16.21	91.28± 16.15	0.35	128.04± 11.94	134.52± 15.50	0.104	81.48± 7.92	81.04± 10.66	0.87	100.08± 10.21	103.64± 12.42	0.27
1 min	94.74± 12.91	95.24± 16.28	0.67	126.64± 12.88	110.68± 7.61	0.001	81.16± 9.28	73.64± 13.41	0.03	97.64± 10.01	90.28± 14.15	0.047
2 min	98.72± 18.98	92.08± 13.70	0.84	125.76± 14.43	106.4± 8.68	0.002	79.28± 10.18	69.6± 17.49	0.04	97.21± 10.83	86.84± 17.96	0.011
3 min	96.36± 16.37	93.48± 15.65	0.91	121.88± 19.91	101.76± 11.42	<0.001	78.2± 15.93	66.72± 15.05	0.01	96.24± 17.09	81.84± 15.79	0.002
4 min	100.6± 19.74	97.08± 17.34	0.58	123.88± 19.64	101.68± 11.54	<0.001	79.96± 16.07	70.16± 24.26	0.09	97.76± 18.00	82.44± 25.28	0.0017
5 min	99.92± 13.47	97.84± 16.06	0.22	126.44± 15.54	108.44± 12.62	<0.001	80.52± 12.87	76.88± 15.63	0.37	99.36± 13.29	91.92± 16.09	0.019
10 min	99.64± 14.57	97.44± 18.92	0.38	126± 16.60	122.± 17.28	0.466	81.28± 11.77	78.04± 14.66	0.39	100.28± 13.84	96.36± 14.32	0.33

The difference between two groups was statistically significant at all time periods (P<0.05) except baseline values (Table 2).

Table 3: Incidence of myoclonus and pain on injection.

	Etomidate (n=25)	Propofol (n=25)	P
Myoclonus	40% (10)	4% (01)	0.0027
Pain on injection	24% (06)	56% (14)	0.0021

In etomidate group there was an incidence of myoclonus in forty percent of the patients was statistically significant as compared to propofol group (P<0.05).

Incidence of pain on injection with propofol observed in fifty six percent of the patients was statistically significant as compared to etomidate group (P<0.05) (Table 3).

DISCUSSION

Anaesthesia-induced hemodynamic fluctuations are a matter of concern for anesthesiologists. The main aim of this randomized clinical study was to confirm the hemodynamic profile of propofol and etomidate and their adverse effects such as pain on injection, myoclonus at time of induction in patients undergoing general anaesthesia.

Induction of anaesthesia is associated with hemodynamic instability of various degrees depending upon many factors like age, gender, body weight, dose and cardiac output.

The change in mean HR between the group E and group P were comparable & not statistically significant (P >0.05). None of the patient in both the group developed tachycardia or bradycardia. similar result were observed by Masoudifar M, Beheshtian E et al. who did Comparison of cardiovascular response to laryngoscopy and tracheal intubation after induction of anaesthesia by propofol and etomidate and found that there was no significant difference among groups in terms of heart rate (P>0.05). [8]

The changes in SBP, DBP in our study shows that propofol group had significantly decreased blood pressure as compared to etomidate group. Similar results were observed in other study done by Song JC, Lu ZJ, et al who compared etomidate with propofol anaesthesia during ERCP and concluded that average percent change to baseline in MBP was 8.4±7.8 and -14.4±9.4 (P =

0.002) decreased significantly in propofol group compared to etomidate group (P<0.05).[9]

In a study by Möller et al who used propofol and etomidate in anaesthesia induction accompanied by BIS monitoring, the MAP, cardiac index (CI) and systemic vascular resistance index (SVRI) values were compared and found that propofol significantly reduced the MAP and delayed and inhibit the sympatho-excitation.[10]

Aono H et al compared sympathetic nerve activity and baroreflex sensitivity in thiopental, propofol and etomidate groups.

They observed patient who received propofol have more hypotension due to reduce sympathetic activity which caused vasodilatation of vascular smooth muscles whereas hemo-dynamic stability seen with etomidate is due to its lack of effect on the sympathetic nervous system and on baroreceptor functions.[11]

Ray DC, et al. observed hemodynamic stability of etomidate group not only limited to normotensive patients and also had less cardiovascular depression and minimize use of vasopressor agents than other induction agent in critically ill patients.[12]

Doenicke AW, Roizen MF et al has been reported incidence of myoclonus in 50 to 80 percent patients who did not receive any premedication with etomidate.[13]

Ebru Kelsaka et al observed myoclonus in 2 vs. 30 patients with propofol and etomidate group and concluded that incidence of myoclonus can be reduced to about 8 to 40 percent by using opoids like fentanyl, remifentanil as pre-medication with etomidate.[14]

In present study incidence of Myoclonus was forty percent in patients of etomidate group who received fentanyl as premedication. Pain on Injection is a bad experience for patient and significant clinical problem with propofol and etomidate use. M. Mayer et al compared propofol and etomidate lipuro as induction agent and found that pain on injection was significantly more with propofol.[15]

CONCLUSION

They concluded pain on injection can be reduced by pre-treatment with lidocaine and new (medium chain triglyceride and soya bean) emulsion formulation. Anaesthesia induced hemodynamic fluctuations are a matter of concern for anaesthesiologists.

Propofol and etomidate are most frequently used intravenous induction agents with similar onset and duration of action and to some extent different adverse effects. This assumption has been confirmed by results of our study which showed that etomidate is a safe, effective induction agent, could be preferred over propofol in terms of superior hemodynamic stability and less pain on injection for patients undergoing general anaesthesia.

Limitation

Limitation of study is small in sample size (total of 50 patients) scheduled for elective surgeries. As the study was conducted in a government institute we had to use the drugs provided in free supply, which was another limitation to use non lipuro formulation of propofol.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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