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SCIENTIFIC ARTICLE

A comparative study between propofol and etomidate in patients under general anesthesia



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KEYWORDS

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Hemodynamic
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Mean arterial
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Abstract

Background and objectives: Induction of anesthesia is a critical part of anesthesia practice. Sudden hypotension, arrhythmias, and cardiovascular collapse are threatening complications following injection of induction agent in hemodynamically unstable patients. It is desirable to use a safe agent with fewer adverse effects for this purpose. Present prospective randomized study is designed to compare propofol and etomidate for their effect on hemodynamics and various adverse effects on patients in general anesthesia.

Methods: Hundred ASA I and II patients of age group 18–60 years scheduled for elective surgical procedure under general anesthesia were randomly divided into two groups of 50 each receiving propofol (2 mg/kg) and etomidate (0.3 mg/kg) as an induction agent. Vital parameters at induction, laryngoscopy and thereafter recorded for comparison. Adverse effect viz. pain on injection, apnea and myoclonus were carefully watched.

Results: Demographic variables were comparable in both the groups. Patients in etomidate group showed little change in mean arterial pressure (MAP) and heart rate (HR) compared to propofol ($p > 0.05$) from baseline value. Pain on injection was more in propofol group while myoclonus activity was higher in etomidate group.

Conclusions: This study concludes that etomidate is a better agent for induction than propofol in view of hemodynamic stability and less pain on injection.

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PALAVRAS-CHAVE

Propofol;
Indução da anestesia;
Mioclonia;

Estudo comparativo entre propofol e etomidato em pacientes sob anestesia geral

Resumo

Justificativa e objetivos: A indução da anestesia é uma parte crítica da prática de anestesia. Hipotensão súbita, arritmias e colapso cardiovascular são complicações ameaçadoras após a

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Estabilidade hemodinâmica; Pressão arterial média

injeção de agente de indução em pacientes hemodinamicamente instáveis. É aconselhável o uso de um agente seguro com menos efeitos adversos para esse propósito. O presente estudo prospectivo, randômico teve como objetivo comparar propofol e etomidato quanto a seus efeitos sobre a hemodinâmica e aos vários efeitos adversos em pacientes sob anestesia geral. *Métodos:* Cem pacientes ASA I e II, idades entre 18-60 anos, programados para procedimento cirúrgico eletivo sob anestesia geral foram divididos aleatoriamente em dois grupos de 50 cada para receber propofol (2 mg/kg) e etomidato (0,3 mg/kg) como um agente de indução. Os parâmetros vitais na indução, laringoscopia e posteriormente foram registrados para comparação. Efeitos adversos como dor à injeção, apneia e mioclonia foram cuidadosamente monitorados.

Resultados: As variáveis demográficas foram comparáveis em ambos os grupos. Os pacientes do grupo etomidato apresentaram pouca alteração da pressão arterial média (PAM) e da frequência cardíaca (FC) em comparação com o grupo propofol ($p < 0,05$) a partir do valor basal. Houve mais dor à injeção no grupo propofol, enquanto houve mais atividade mioclônica no grupo etomidato.

Conclusões: Este estudo conclui que etomidato é um agente melhor para a indução que propofol em relação à estabilidade hemodinâmica e menos dor à injeção.

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Introduction

Induction agents are drugs that, when given intravenously in an appropriate dose, cause a rapid loss of consciousness. Induction agents are used to induce anesthesia prior to other drugs being given to maintain anesthesia, as the sole drug for short procedures, to maintain anesthesia for longer procedures by intravenous infusion, to provide conscious sedation during procedures undergoing in local anesthesia and intensive care unit.

Propofol, 2,6-diisopropylphenol is most popular induction agent with its favourable characteristics of rapid and smooth induction and recovery, decrease incidence of nausea and vomiting, etc.^{1,2} While on other side decrease blood pressure, dose dependent depression of ventilation, pain on injection are the major drawbacks.³⁻⁵

Etomidate, carboxylated imidazole is characterized by hemodynamic stability, minimal respiratory depression and cerebral protective effects. Its lack of effect on sympathetic nervous system, baroreceptor reflex regulatory system and its effect of increased coronary perfusion even on patients with moderate cardiac dysfunction makes it an induction agent of choice in cardiac disease patients.⁶⁻⁹ However, the adverse effects such as pain on injection, thrombophlebitis and myoclonus are some undesirable adverse effects.^{10,11}

This study is an attempt to evaluate the effects of propofol and etomidate by comparing certain parameters such as change in blood pressure and heart rate during induction and intubation as a primary outcome and pain on injection, myoclonic movements, Post-operative nausea and vomiting as a secondary outcome; so that we can choose a safer induction agent.

Methods

This prospective randomized double blind study is conducted on 100 patients of American Society of Anaesthesiologist

(ASA) grade I and II between 18 and 60 years of age of either sex, scheduled for elective surgical procedure under general anesthesia with endotracheal intubation.

After approval from institutional ethical committee, written informed consent was obtained from all the patients. The total 100 patients were randomly assigned into 2 groups of 50 patients each according to a computer generated table of random numbers.

- Group I ($n = 50$): received Inj. Propofol 1% (2 mg/kg of body weight)
- Group II ($n = 50$): received Inj. Etomidate (0.3 mg/kg of body weight)

Patients with history of allergy to study drugs, history of seizure disorder, presence of primary and secondary steroid deficiency/on steroid medication and hypotensive patients were excluded from study.

All patients were pre-medicated with tablets alprazolam 0.25 mg and ranitidine 150 mg, the night before the surgery and instructed for fasting for 8 h. On arrival at operation theatre, patients were attached with standard anesthesia monitoring including Electrocardiogram (ECG), Non-invasive blood pressure (NIBP), Pulse oximeter and baseline vital parameters were recorded. An 18G intravenous (I.V.) cannula was secured in left hand and ringer lactate 10 mL/kg/h was started.

Glycopyrrolate 0.2 mg, midazolam 0.02 mg/kg and fentanyl 3 mg/kg I.V. were injected followed by an induction dose of either propofol (Propofol spiva 1%, Claris Lifesciences Limited) or etomidate (Etomidate Lipuro, B. Braun, India). Pain on injection and myoclonic movements were recorded, if any at induction. Trachea was intubated with appropriate size of endotracheal tube after 3 min of intubating dose of vecuronium (0.1 mg/kg) I.V. Endotracheal tube was secured after confirming correct position and positive pressure ventilation was initiated. Anesthesia

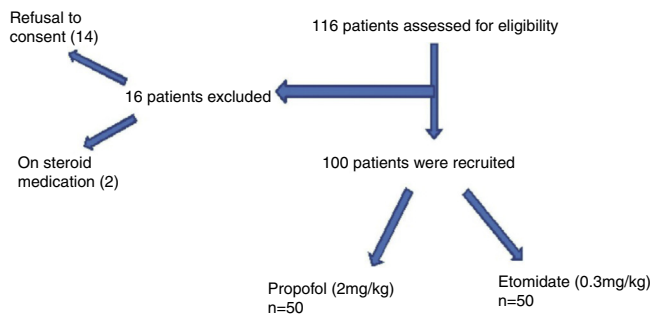


Figure 1 Study design.

was maintained with oxygen and nitrous oxide (70:30) in isoflurane along with intermittent boluses of vecuronium, as required throughout the surgery. At the end of surgery, the residual neuromuscular block was antagonized with neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg) I.V. and extubation was performed when respiration was adequate and patient was able to obey verbal commands.

Systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate were continuously monitored and recorded before induction, at induction and laryngoscopy followed by 1, 3, 5 and 10 minutes after intubation. Pain on injection was measured using 4 graded scale; 0 – no pain, 1 – verbal complaint of pain, 2 – withdrawal of arm, 3 – both verbal complaint and withdrawal of arm. The incidence and degree of myoclonic movements also recorded as follows: 0 = no myoclonic movements, 1 = minor myoclonic movements, 2 = moderate myoclonic movements, 3 = major myoclonic movements. Episode of apnea, if occurred was recorded.

Statistical analysis

Data are presented as mean ± SD. Patient characteristic data were analysed with one way ANOVA for continuous variables and chi-square test for categorical variables. Statistical analysis was done using SPSS 20 (IBM SPSS Statistics). *p*-Value <0.05 was considered significant.

Results

A total of 116 patients were assessed for eligibility from December 2013 to May 2014, out of which 16 patients were excluded from study on account of refusal to consent (fourteen patients) and on steroid medications (two patients). 100 patients were completed the study after randomization in two groups (Fig. 1).

Both groups were comparable in age, sex, weight and ASA physical status, with no statistically significant differences (*p* > 0.05) (Table 1). Pre-operative vitals (HR, SBP, DBP and MAP) were comparable in both groups with no statistically significant differences (*p* > 0.05). Decrease in MAP and increase in heart rate was more from baseline in propofol group than etomidate group at induction (*p* > 0.05) (Figs. 2 and 3). Fifty percent of patients received propofol complained pain while only four percent patient in etomidate group (*p* > 0.05). Also, the severity of pain was more with propofol (Table 2). Incidence of apnea was similar

Table 1 Demographic characteristic of patients (*p* > 0.05).

Variable	Group I	Group II
Sex (female:male)	30:20	27:23
Age (years) mean ± SD	29.16 ± 11.38	27.86 ± 10.09
Weight (kg) mean ± SD	56.02 ± 11.03	57.4 ± 11.16
ASA grade I/II	26/24	23/27

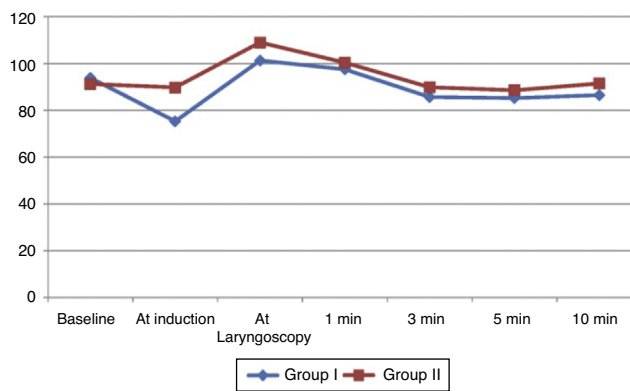


Figure 2 Showing MAP at different time intervals. A significant decrease in MAP from baseline at induction with propofol in compare to etomidate is observed (*p* > 0.05), there after MAP became comparable to etomidate (*p* > 0.05).

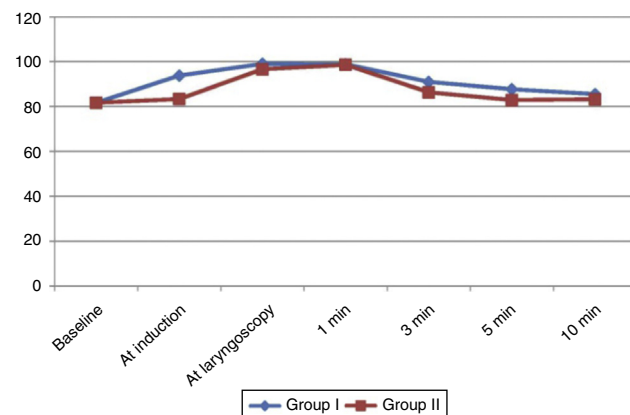


Figure 3 Showing HR at different time intervals. Increase in heart rate from baseline at induction is significantly high in propofol group (*p* > 0.05), then became comparable to etomidate (*p* > 0.05).

in both groups (*p* > 0.05) (Table 3). Myoclonic movements were only seen in etomidate group (*p* > 0.05). Severity of myoclonus was noted as grade 1 (20%), grade 2 (14%) and grade 3 (2%) (Table 4).

Table 2 Incidence and grading of pain on injection.

Group	Pain on injection			<i>p</i> -Value
	Grade 0	Grade 1	Grade 2	
Group I	25 (50%)	16 (32%)	9 (18%)	0.002
Group II	48 (96%)	2 (4%)	0 (0%)	

Table 3 Incidence of apnea on induction in both groups.

Group	Apnea on induction		p-Value
	Yes	No	
Group I	38 (76%)	12 (24%)	0.271
Group II	33 (66%)	17 (34%)	

Table 4 Incidence of myoclonic movements in both groups.

Myoclonic movements	Group I	Group II	p-Value
Grade 0	50 (100%)	32 (64%)	0
Grade 1	0 (0%)	10 (20%)	
Grade 2	0 (0%)	7 (14%)	
Grade 3	0 (0%)	1 (2%)	

Discussion

Induction of anesthesia is associated with hemodynamic variation of mild to moderate degree depending upon many factors. In our study, we observed that propofol caused significant hypotension and tachycardia at induction in comparison to etomidate. Hypotension occurs with propofol is mainly due to reduction of sympathetic activity causing vasodilation or its direct effect on vascular smooth muscles.^{12,13} Sudden hypotension and tachycardia has deleterious effects on maintaining the circulation to vital organs in patients of coronary artery disease, valvular stenosis, uncontrolled hypertension and shock. On another side hemodynamic stability observed with etomidate may be due to its unique lack of effect on the sympathetic nervous system and on baroreceptor functions.^{14,15} Mayer et al.¹⁶ and Wu et al.¹⁷ also concluded that etomidate preserve hemodynamic stability during anesthesia.

Etomidate does not have its limitation to normotensive patients for its hemodynamic peculiarity. In various studies, etomidate shown less cardiovascular depression and minimize use of vasopressor agents than other induction agent in sepsis and critically ill patients. 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.¹⁸⁻²¹

Pain during injection of anesthetic agent is a bad experience for patient while it quite embarrassing situation for anesthesiologist. Etomidate shown a favourable outcome and it was very well supported by Saricaoglu et al.²² and Wu et al.¹⁷ in their studies. Both agents had shown similarity in their respiratory depressant effect. The episodes of apnea were transient and not associated with any fall in oxygen saturation. Boysen et al.²³ in their study concluded that there was no significant difference between two groups (propofol and etomidate) as regard to apnea following induction. The only negative characteristic noted with etomidate was high incidence of myoclonic jerks. Miner et al.²⁴ was also concluded high incidence of myoclonus (20% vs. 1.8%) in etomidate and propofol group respectively.

Conclusion

In conclusion, etomidate is better for its hemodynamic stability over propofol along with less incidence of pain on injection. Only drawback was high incidence of myoclonus. We therefore suggest that etomidate is a better option in patients particularly prone to hemodynamic fluctuation at induction like uncontrolled hypertension, septic, critically ill and patients with coronary artery disease.

Conflicts of interest

The authors declare no conflicts of interest.

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