

Etomidate versus Propofol as induction agent in patients undergoing Endoscopic Retrograde Cholangiopancreatogram (ERCP)

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Abstract

Background: Endoscopic retrograde pancreaticogram (ERCP) requires patient to be sedated and pain free in prone position. Propofol sedation may cause cardiorespiratory depression. Etomidate is a good alternative with stable hemodynamic and respiratory parameters. We have compared these two drugs on their cardiorespiratory, induction time and recovery profiles.

Methods: A total of 100 patients undergoing ERCP were randomly distributed to etomidate or propofol groups. Patients in the etomidate group received etomidate induction and maintenance, while propofol group received propofol anaesthesia. Cardiorespiratory parameters, time for induction and recovery along with adverse effects were noted.

Results: The induction time was longer in the etomidate group than the propofol group ($p < 0.001$). The time for attaining Modified Aldrette score 9 was longer in the etomidate group ($p < 0.001$). The percentage of fall in MAP and HR was higher in propofol group ($p < 0.001$). SpO₂ fall was also significant in propofol group. One patient in etomidate group developed myoclonus. Adverse effects like bradycardia, hypotension, hypoxia were significantly more in the propofol group. Conclusion: Etomidate is a safe and cardiostable induction agent in patients with obstructive jaundice undergoing ERCP.

Keywords: Etomidate, Propofol, ERCP, Modified aldrete score

Introduction

Endoscopic procedures like ERCP are performed with patient under moderate sedation, a technique known as conscious sedation. It aims at reducing patient anxiety, discomfort and pain and enhancing patient co-operation and facilitating the performance of the endoscopist.⁽¹⁾ Various agents are available to provide conscious sedation. These include benzodiazepines⁽²⁾ with an opioid⁽³⁾ with or without propofol,^(4,5) ketamine, dexmedetomidine.⁽⁶⁾ Etomidate for procedural sedation has been used in emergency department since years.⁽⁷⁻⁹⁾

Most patients undergoing ERCP have obstructive jaundice due to malignant or benign disease.

Such patients are prone to hypotension and bradycardia during conscious sedation. Propofol induction results in hypotension, respiratory depression and loss of protective reflexes. Etomidate is a non-barbiturate hypnotic that induces anaesthesia through GABA receptors in CNS⁽¹⁰⁾ and is a safe induction agent for hemodynamically unstable patients because of its low risk of hypotension.⁽¹¹⁾ But it is known to cause adrenocortical suppression with an increased risk of cardiovascular morbidity and prolonged hospital stay.⁽¹²⁾ Etomidate has been used for short procedures for sedation like colonoscopy with stable hemodynamic vitals and shorter recovery and discharge times compared to propofol.⁽¹³⁾

Aims and Objectives

We compared etomidate anaesthesia with propofol during ERCP. The primary outcome was hemodynamic stability and adverse events during the procedure. The

secondary outcome was to note the recovery time after the procedure.

Materials and Methods

After ethical committee approval and written informed consent from patients a randomised controlled trial was carried on 50 patients of ASA1/2, either sex, aged 18-60 years, weighing 45-90 kgs undergoing ERCP for benign disease. We excluded patients with malignancies, known adrenocortical insufficiency, heart failure (EF < 40%) or severe respiratory disease (VC &/or FEV₁ 50%), chronic opioid, sedative or analgesic use, known allergy to used drugs and pregnancy.

Patients who had communication problems were excluded as we had to record Ramsay sedation score and Modified Aldrette score.

A complete preoperative workup including general and systemic examination of the patient was done. Patients were allocated into etomidate group or propofol group using a computer generated programme. On the arrival of the patient in the endoscopy room all vital parameters like heart rate (HR), mean arterial pressure (MAP), and oxygen saturation (SpO₂) were recorded.

A 20 gauge IV cannula was inserted in peripheral vein for 0.9% normal saline infusion and drugs. Patients were premedicated with inj. Glycopyrrolate 0.2 mg, ondansetron 4 mg intravenous. ECG, NIBP and SpO₂ were continuously monitored throughout the procedure. Oxygen was administered at the rate of 5 lit/min by nasal catheter during ERCP. Patient's throat was sprayed with 10% lignocaine spray. Patients were placed in prone position without tracheal intubation. All patients received inj. Fentanyl 1 mcg/kg, inj dexamethasone 8mg

and infusion dexmedetomidine was started at the rate of 0.5mcg/kg/hr.

Baseline values of mean arterial BP(MAP), Heart rate (HR), Oxygen Saturation(SpO₂) were measured at the time of patient entry to the endoscopy room and thereafter every five minutes. After dexmedetomidine sedation was started, induction was administered. In the etomidate(E) group, etomidate was administered at the rate of 20 mcg/kg/min until RSS was 4 then continued for 10mcg/kg/mt. In the propofol (P) group, Propofol was given at the rate of 100 mcg/kg/min until RSS reaches 4 and maintained at 25mcg/kg/minute. At RSS 4, endoscope was introduced.

HR, MAP, SpO₂ were monitored every five minutes till the end of procedure and then in the recovery room. T₀ –baseline values, T₁=5 min after entry to endoscopy room when dexmedetomidine infusion was started, T₂ =at RSS 4, T₃= at endoscope intubation, T₄-T₂₅=at 5 minutes interval during procedure. A change in MAP / HR by 20% above or below the baseline were considered significant. When oxygen saturation fell below 90% for more than 10 seconds or when apnoea lasted more than 20 seconds, all infusions were stopped and jaw thrust manoeuvre with mask ventilation was initiated. All procedures lasted for 25 minutes.

Duration of ERCP, induction time and any adverse effects like bradycardia, tachycardia, hypotension, hypertension, desaturation, apnoea, myoclonus and pain during injection was recorded. Post procedure the recovery time i.e. the time for MAS to reach 9 was noted.

Statistical Methods: The statistical analysis was performed by STATA 11.2 (College Station TX USA). Shapiro wilk test has been used to find the normality. Students t-test were used to find the significance difference between the age, heart rate, mean arterial blood pressure, SpO₂, duration of analgesia, time induction, time MAS, height and weight with treatment groups respectively and its expressed as mean and standard deviation. Chi square test has been to measure the association between the gender, ASA grade and

adverse event with treatment groups respectively and it's expressed as frequency and percentage. P<0.05 considered as statistically significance.

Results

The study was completed without any major complications. There were no statistically significant differences in either the demographic data or baseline vitals between the two groups (Table 1). The groups were comparable in respect to the duration of the ERCP too. The induction time was longer in the etomidate group than the propofol group (p<0.001). The time for attaining Modified Aldrette score 9 was longer in the etomidate group(p<0.001)(Table 2). The percentage of fall in MAP and HR was higher in propofol group(p<0.001) (Table 3, Graph 1) and Table 4, Graph 2. The SpO₂ fall was also significant in propofol group (Table 5). One patient in etomidate group developed myoclonus. Adverse effects like bradycardia, hypotension, hypoxia were significantly more in the propofol group (Table 6).

Table 1: Patient characteristics

	Etomidate (n=25)	Propofol (n= 25)	P value
Gender, M/F	12/ 13	12/13	
Age, years	56.24 ± 7.74	56.04 ± 7.32	0.926
Height	159.92 ± 6.44	159.52 ± 7.06	0.838
Weight	57.04 ± 5.82	57.24 ± 5.94	0.905
ASA grade (I/ II)	11/ 14	11/ 14	1.0

Table 2: Procedure characteristics

	Etomidate	Propofol	P- Value
	Mean ± SD	Mean ± SD	
Duration (in Minutes)	19.76 ± 2.54	19.52 ± 1.78	0.701
Induction time	4.77 ± 0.41	3.77 ± 0.47	<0.001
Time MAS=9	22.52 ± 4.51	10.16 ± 3.12	<0.001

Table 3: Mean Arterial blood pressure in mm Hg

	Etomidate		Propofol		P-Value
	Mean ± SD	% of Changes	Mean ± SD	% of Changes	
T0	93.52 ± 6.58		94.92 ± 6.28		0.445
T1	100.08 ± 7.62	7.01%	100.64 ± 6.66	6.03%	0.783
T2	87.32 ± 6.11	-6.63%	75.40 ± 9.35	-20.56%	<0.001
T3	84.0 ± 5.57	-10.18%	73.24 ± 7.45	-22.84%	<0.001
T4	82.24 ± 4.30	-12.06%	71.68 ± 5.73	-24.48%	<0.001
T5	80.64 ± 5.19	-13.77%	69.08 ± 4.11	-27.22%	<0.001
T6	81.0 ± 5.19	-13.39%	70.04 ± 6.72	-26.21%	<0.001
T7	81.24 ± 6.20	-13.13%	72.56 ± 5.70	-23.56%	<0.001
T8	82.88 ± 4.93	-11.38%	74.20 ± 7.66	-21.83%	<0.001

Graph 1

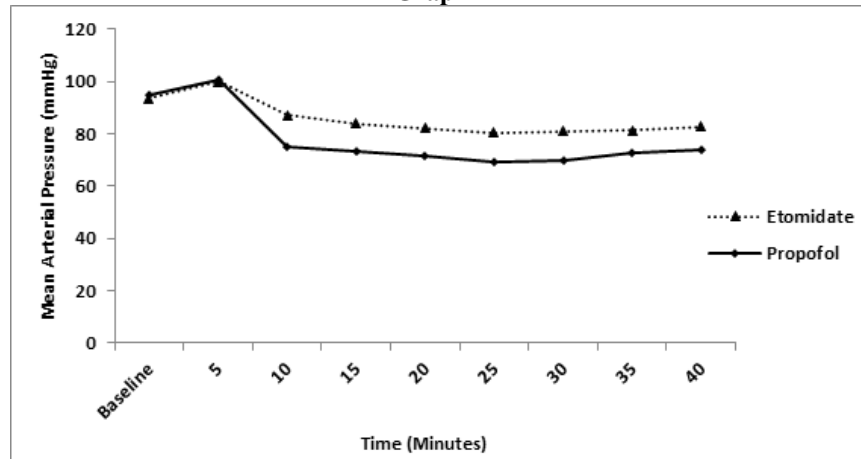


Table 4: Heart rate in beats/minute

	Etomidate		Propofol		P-Value
	Mean ± SD	% of Changes	Mean ± SD	% of Changes	
T0	87.60 ± 11.29		90.64 ± 12.69		0.394
T1	95.0 ± 13.37	8%	97.28 ± 14.72	7.33%	0.569
T2	78.92 ± 8.38	-10%	68.84 ± 6.85	-24.05%	<0.001
T3	75.08 ± 7.99	-14%	67.24 ± 6.25	-25.82%	<0.001
T4	72.88 ± 7.39	-17%	65.92 ± 6.37	-27.27%	<0.001
T5	71.04 ± 7.03	-19%	65.65 ± 5.32	-27.57%	0.003
T6	71.40 ± 6.59	-18%	64.92 ± 5.08	-28.38%	<0.001
T7	71.64 ± 6.49	-18%	65.80 ± 5.41	-27.41%	0.001
T8	71.36 ± 5.94	-19%	67.0 ± 6.39	-26.08%	0.016

Graph 2

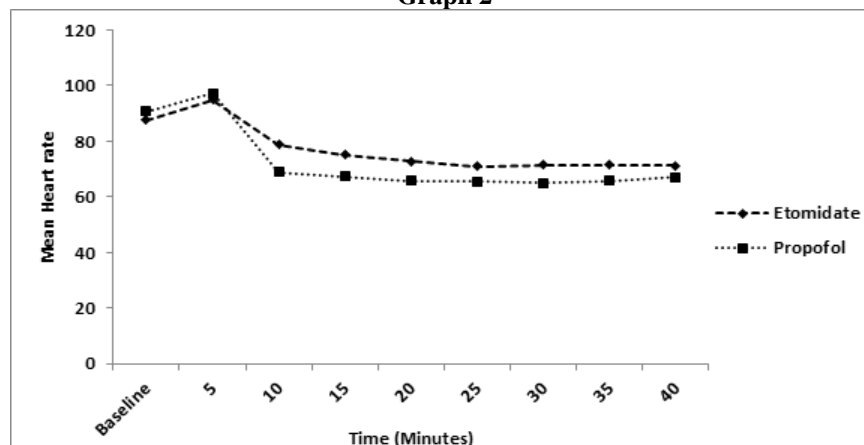


Table 5: SpO2 in percentage

	Etomidate		Propofol		P-Value
	Mean ± SD	% of Changes	Mean ± SD	% of Changes	
T0	98.72 ± 1.14		97.60 ± 1.63		0.007
T1	98.60 ± 1.15	-0.12%	98.08 ± 1.58	0.49%	0.190
T2	94.32 ± 2.88	-4.46%	96.84 ± 2.37	-0.78%	0.002
T3	95.20 ± 3.27	-3.57%	93.12 ± 4.07	-4.59%	0.052
T4	95.60 ± 3.77	-3.16%	90.64 ± 4.29	-7.13%	<0.001
T5	95.44 ± 3.98	-3.32%	89.24 ± 5.35	-8.57%	<0.001

T6	96.24 ± 4.00	-2.51%	87.72 ± 6.01	-10.12%	<0.001
T7	97.52 ± 2.84	-1.22%	91.96 ± 4.18	-5.78%	<0.001
T8	98.72 ± 1.31	0.00%	95.28 ± 2.94	-2.38%	<0.001

Graph 3

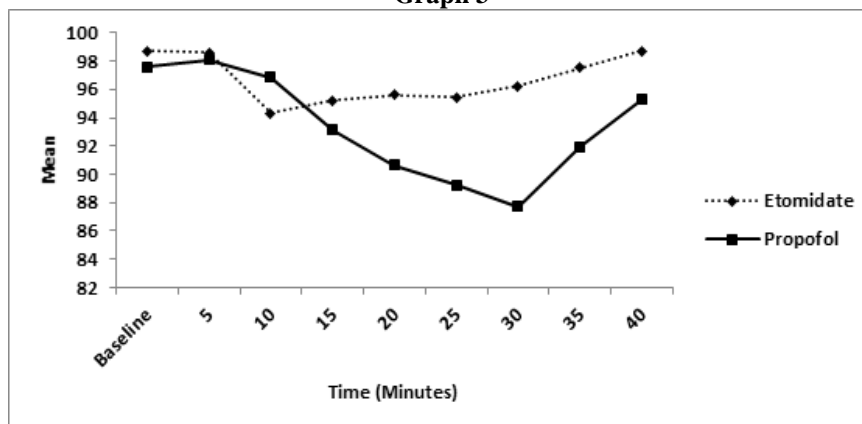


Table 6: Adverse event in detail

	Etomidate	Propofol	Total
Nil	23	4 (16%)	27
Bradycardia		7 (28%)	7
Bradycardia, Hypotension		1 (4%)	1
Bradycardia, hypoxia		1 (4%)	1
Hypotension		2 (8%)	2
Hypotension, hypoxia		1 (4%)	1
Myoclonus	2 (8%)	0	2
Hypoxia		9 (36%)	9
Total	25	25	50

Discussion

Our study has shown that although etomidate anaesthesia during ERCP involved more stable cardiorespiratory vitals than propofol, the latter is a faster inducing agent and also has a rapid recovery profile.

The ERCP procedure required the patient to be sedated, immobile and pain free. The major challenge was that the patient had to be positioned prone without tracheal intubation. Oxygen was delivered via nasal prongs @4-6 l/minute. Glycopyrrolate was administered intravenously to reduce secretions leading to laryngospasm. A mouth gag was placed in situ for the passage of the endoscope prior to sedation. This helped in maintaining upper airway patency. An assistant at the head end held the upper jaw to prevent tongue fall. Injection fentanyl provided analgesia. Dexmedetomidine infusion without a bolus dose was preferred for sedation over midazolam due to its analgesic and sparing of respiratory depressing properties.

In our study, the cardiorespiratory parameters were stable in the etomidate group. Hypotension, bradycardia

and decline in oxygen saturation were encountered in the propofol group. Etomidate has been used for conscious sedation.^(15,16) It has a safe cardiovascular risk profile causing no significant drop in blood pressure than other induction agents.⁽¹⁷⁾ It has limited suppression of ventilation, lack of histamine liberation and offers protection from myocardial and cerebral ischemia.⁽¹⁸⁾ Etomidate's haemodynamic stability may be due to its unique lack of effect in the sympathetic nervous system and on baroreceptor function.⁽¹⁹⁾ Our patients undergoing ERCP, had obstructive jaundice. These patients have decreased sensitivity to both sympathetic and vagal components of baroreflex.⁽²⁰⁾ Reich et al suggested that alternative to propofol (e.g. etomidate) should be considered in patients older than 50 yrs of age with ASA>111.⁽²¹⁾ In a similar study, Jin-Chao Song et al concluded that etomidate anaesthesia during ERCP, caused more stable haemodynamic responses than propofol.⁽²²⁾

We encountered a longer induction time with etomidate than propofol. Propofol is a good hypnotic with a rapid onset, rapid recovery in endoscopic procedures.⁽²³⁻²⁵⁾ But, it was reported in a guideline of sedation and anaesthesia in Gastrointestinal endoscopy that transient hypotension occurs in 4-7% cases using propofol sedation and transient hypoxia in 3-7% cases.⁽²⁶⁾

Toku et al⁽²⁷⁾ found that average recovery time was shorter with etomidate than propofol when used as sedation in colonoscopy. But we encountered the time to reach modified aldrete score, nine was significantly longer in the etomidate group. This may be due to more synergistic action of dexmedetomidine with etomidate than with propofol causing more sedation.

Myoclonus is a known adverse effect of etomidate⁽²⁸⁾ but only 2 patients in the etomidate group developed self-limited myoclonus. This is due to the concomitant dexmedetomidine sedation.⁽²⁹⁾

A limitation of our study was that as we included only the benign cases of obstructive jaundice, our patients were discharged the very next day, we could not study the plasma cortisol and adrenocorticotrophic hormone levels, nor we could comment on the survival analysis or morbidity pattern between the two drugs. Adrenocortical suppression is an important adverse effect of etomidate.⁽³⁰⁾

Thus we conclude that etomidate is a good anaesthetic agent in ASA I and II patients undergoing ERCP, however recovery time is lesser when propofol is used for the same.

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