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Original Research Article

General anaesthesia with propofol versus etomidate and cognitive dysfunction in the immediate postoperative period: a randomized double-blind study

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ABSTRACT

Background: Propofol and etomidate are commonly used intravenous induction agents for general anaesthesia (GA), but comparative data on postoperative cognitive dysfunction (POCD) alongside haemodynamic and adverse-effect profiles are limited. This study compared propofol and etomidate with respect to POCD, haemodynamic stability, and adverse effects.

Methods: In this prospective, randomized, double-blind, parallel-group trial, 80 ASA I-II patients aged 18-40 years undergoing short elective surgery (dilation and curettage, or fracture reduction/fixation) under GA were randomized 1:1 to propofol 1 mg/kg (Group P, n=40) or etomidate 0.3 mg/kg (Group E, n=40) for induction. Cognitive function was assessed preoperatively and at 30, 60 and 120 minutes postoperatively using the Tirpude GMC-OMC score. Vitals were recorded intraoperatively (0-20 min) and postoperatively (0-60 min), and adverse effects were noted. Data were analysed using SPSS, with between-group differences and 95% confidence intervals reported; $P < 0.05$ was considered significant.

Results: All 80 randomized patients were analysed. Baseline characteristics were comparable between groups. Tirpude GMC-OMC scores did not differ significantly between groups at any time point ($p > 0.05$). Intraoperative vitals were significantly more stable in Group E than Group P at most time points ($p < 0.05$). Hypotension was significantly more frequent in Group P ($p = 0.01$); nausea and vomiting were more frequent, though not significantly, in Group E.

Conclusions: Propofol and etomidate produced comparable, clinically insignificant postoperative cognitive change in young, healthy patients undergoing short elective surgery. Etomidate offered superior intraoperative haemodynamic stability and less hypotension, while propofol was associated with less postoperative nausea and vomiting.

Keywords: Propofol, Etomidate, Postoperative cognitive dysfunction, General anaesthesia, Haemodynamics, Randomized controlled trial

INTRODUCTION

General anaesthesia (GA) may be induced by the inhalational, intravenous, oral or rectal route; intravenous induction is preferred in most elective surgery because of its faster, more predictable onset. Thiopentone, propofol, etomidate and ketamine are the intravenous agents in common use, and propofol and etomidate remain the most widely used induction agents in current practice.¹

Propofol is a GABA-A receptor modulator that potentiates chloride-channel opening, producing hypnosis within 15-30 seconds of injection; its short duration of action (5-10 minutes) reflects rapid redistribution and combined hepatic and extrahepatic clearance.²

Its principal drawback is a dose-dependent fall in systemic vascular resistance and sympathetic tone, which can

produce clinically significant hypotension, particularly at induction.

Etomidate, a carboxylated imidazole introduced into clinical practice in 1972, is likewise a GABA-A receptor modulator, with onset within 30-60 seconds and a short duration of action (3-5 minutes) related to rapid redistribution.¹ Its principal clinical attraction is a comparative lack of effect on the sympathetic nervous system and baroreceptor reflex, which confers greater cardiovascular stability at induction than propofol; this has made it a preferred agent in patients with compromised cardiac reserve. However, its use has been tempered by concerns over pain on injection, myoclonus, postoperative nausea and vomiting, and transient adrenocortical suppression after even a single induction dose, the clinical significance of which remains debated.

POCD was first described by Bedford in 1955, in elderly patients who were “never the same” after surgery under GA.³ POCD is characterised by impaired memory and concentration and reduced social or occupational function in the days to weeks after surgery, and its pathophysiology is thought to involve neuroinflammatory and synaptic mechanisms that remain incompletely understood.^{4,5} Large multicentre studies such as the International Study of Post-Operative Cognitive Dysfunction (ISPOCD1) established POCD as a clinically important and measurable entity, particularly in elderly surgical populations.⁶ The reported incidence of POCD varies widely between studies, reflecting differences in the cognitive test battery used, timing of assessment, and characteristics of the surgical population studied.

Short-duration procedures performed under GA in day-care or short-stay settings-such as dilation and curettage or closed fracture reduction-are amongst the most frequently performed surgical procedures worldwide, and the induction agent used in this setting is typically chosen on the basis of institutional availability and anaesthetist preference rather than agent-specific outcome data. Given the very large number of such procedures performed annually, even a modest difference in cognitive or haemodynamic outcome between commonly used induction agents could have meaningful aggregate clinical relevance.

Although the comparative haemodynamic advantage of etomidate over propofol is well established, direct comparative data on postoperative cognitive outcome with these two agents, particularly in younger, healthier patients undergoing short elective procedures of the kind routinely performed in day-care and short-stay surgical settings, are limited; most available comparative literature has focused on elderly or high-risk surgical populations.

Given etomidate's competing profile of haemodynamic stability against adrenocortical suppression and other adverse effects, a concurrent assessment of cognitive, haemodynamic and adverse-effect outcomes is clinically

useful. This study was therefore undertaken to compare propofol and etomidate, used for induction of GA in patients undergoing short elective surgery, with respect to (a) POCD, (b) intraoperative and postoperative haemodynamic variation, and (c) associated adverse effects.

METHODS

This trial is reported in accordance with the CONSORT guidelines for randomized controlled trials (Figure 1).

Trial design and setting

This was a prospective, randomized, double-blind, parallel-group, two-arm superiority trial with a 1:1 allocation ratio, conducted in the Department of Anaesthesiology, GMC Nagpur, between May 2019 and December 2021, after approval from the Institutional Ethics Committee and written informed consent from all participants. There were no changes to the trial design, eligibility criteria, or outcome measures after the study commenced.

Participants

Patients of American Society of Anesthesiologists (ASA) physical status I or II, aged 18-40 years, of either sex, posted for elective dilation and curettage or fracture reduction and splinting under GA, and able to comprehend the cognitive test items, were included.

Patients aged <18 or >40 years; those with moderate-to-severe comorbidity (diabetes, hypertension, ischaemic heart disease, heart block, hepatic or renal disease, or respiratory tract infection/asthma); those with a pre-existing neurocognitive or neuropsychiatric disorder; those on medication known to affect cognition, heart rate or blood pressure (e.g., antipsychotics, antiarrhythmics, digoxin, beta-blockers); and those unwilling to participate were excluded.

Sample size, randomization and allocation concealment

Assuming 95% confidence and 80% power to detect a minimum 10% between-group difference in proportion, a sample size of 80 patients (40 per group) was calculated; no interim analysis or early stopping rule was planned.

The allocation sequence was generated using simple computer-generated randomization in a 1:1 ratio by an investigator who was not involved in patient recruitment or outcome assessment, and was concealed using sequentially numbered, opaque, sealed envelopes (SNOSE) until immediately before induction. Participants were enrolled by the treating anaesthesiologist and assigned to Group P (propofol) or the Group E (etomidate), 40 each, following the sequence contained in the envelopes.

Blinding

Because propofol and etomidate differ in physical appearance, both study drugs were drawn up into identical, coded, opaque syringes by an anaesthesiologist not otherwise involved in the study. The patient, the anaesthesiologist administering the drug and recording intraoperative parameters, and the outcome assessor performing cognitive assessments all remained unaware of group allocation throughout the study.

The primary outcome was the difference in postoperative Tirpude GMC-OMC cognitive score between groups; secondary outcomes were intraoperative and postoperative haemodynamic parameters and the incidence of adverse effects.

Preoperative work-up

All patients underwent preanaesthetic evaluation a day before surgery, including complete blood count, urine examination, random blood sugar, blood urea and serum creatinine, and chest radiograph and electrocardiogram where clinically indicated. Baseline vital parameters were recorded, the study procedure was explained to patients and relatives in their own language, and written informed consent was obtained and documented in the study proforma. Patients were kept nil by mouth for 8 hours before surgery and were premedicated the night before with oral ranitidine 150 mg and diazepam 10 mg to reduce anxiety and provide acid prophylaxis.

Anaesthetic protocol

On the day of surgery, intravenous access was secured in the preoperative holding area with a 20G cannula and a maintenance infusion of 5% dextrose or dextrose-normal saline was started. Patients were then transferred to the operating table, connected to multipara monitors, and baseline heart rate, blood pressure and SpO₂ were recorded. All patients received intravenous pantoprazole 1 mg/kg and ondansetron 0.08 mg/kg 3-5 minutes before induction, were preoxygenated for 3 minutes, and received intravenous diclofenac 75 mg.

Group P received propofol 1 mg/kg and Group E received etomidate 0.3 mg/kg, each administered intravenously over 40-60 seconds by anaesthesia staff not involved in outcome assessment. On loss of the eyelash reflex, patients were maintained on oxygen and nitrous oxide (50:50) via a Bain's circuit on facemask. Heart rate and blood pressure (systolic, diastolic, mean arterial) were recorded intraoperatively at 0, 5, 10 and 20 minutes from induction; the same parameters were recorded postoperatively in the recovery room at 0, 20, 30 and 60 minutes.

Patients were subsequently monitored in the day-care ward for return of consciousness, spontaneous respiration and motor tone before discharge.

Cognitive assessment

Cognitive function was assessed using the Tirpude GMC-OMC score, a composite instrument developed at this institution that incorporates elements of the Short Blessed Test together with a Trail Making Test component adapted for administration in Indian patients.⁷

The tool comprises five items-stating one's name, occupation, and place of residence, counting from 1 to 10 and back, and a timed trail-making task-each scored 1 (unable to recall/complete), 2 (recalled/completed with difficulty) or 3 (recalled/completed immediately), giving a total score of 5-15. A score of 11-15 was defined as no cognitive dysfunction, 6-10 as partial cognitive dysfunction, and 1-5 as severe cognitive dysfunction.

The questionnaire was administered in the patient's preferred regional language (Marathi or Hindi) by a blinded observer, preoperatively (30-60 minutes before surgery) and at 30, 60 and 120 minutes postoperatively; the score obtained was not disclosed to the patient.

Adverse effects

Nausea, vomiting, shivering, headache, skin rash, bradycardia, hypotension and urinary retention were recorded.

Statistical analysis

Data were collected by a blinded observer using a predesigned, pretested proforma and analysed by a statistician blinded to group allocation, using SPSS software.

Quantitative variables are expressed as mean±SD and compared using the unpaired or paired t test, with between-group mean differences and 95% confidence intervals calculated using the pooled-variance method; categorical variables were compared using the chi-square test or Z-test of proportions, with risk differences and 95% confidence intervals calculated using the Wald method; the ordinal Tirpude GMC-OMC scores were compared using the Mann-Whitney U test.

A two-sided $p < 0.05$ was considered statistically significant. Analysis was by intention-to-treat: all 80 randomized participants received their allocated intervention and were included in the final analysis, with no losses to follow-up (Figure 1).

RESULTS

Eighty patients were randomized and completed the study, 40 in each group, with no dropouts, protocol deviations, or losses to follow-up; all randomized participants received their allocated intervention and were included in the intention-to-treat analysis (Figure 1).

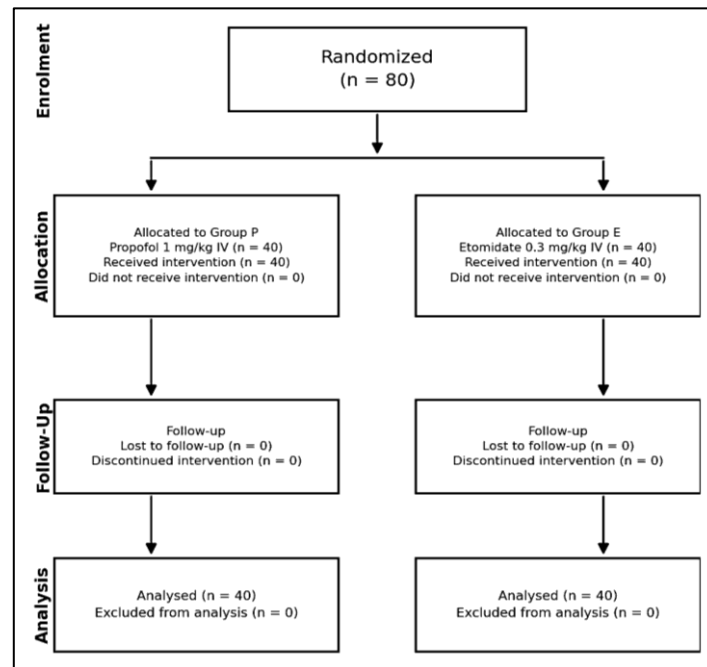


Figure 1: CONSORT participant flow diagram.

Baseline demographic characteristics (age, sex, ASA grade, weight, height, BMI), type of surgery, and preoperative haemodynamic parameters were comparable between the two groups (Table 1). There was no significant difference in heart rate, blood pressure or oxygen saturation before and after intravenous cannulation in either group ($p > 0.05$), with the exception of a small but statistically significant rise in SpO_2 in Group E ($97.68 \pm 1.02\%$ to $98.08 \pm 1.29\%$, $p = 0.04$).

Intraoperative haemodynamic

Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were significantly better preserved in Group E than Group P at most intraoperative time points, with between-group mean differences and 95% confidence intervals summarized in Table 2. The deviation from baseline was consistently greater in Group P than Group E across all four haemodynamic parameters at every time point studied, most markedly for heart rate and mean arterial pressure at 10 and 20 minutes. Oxygen saturation did not differ significantly between groups at any intraoperative time point.

Postoperative haemodynamic

Heart rate, blood pressure and oxygen saturation increased gradually in both groups over the 60-minute recovery period, consistent with resolving effects of the induction agent and emergence from anaesthesia. Heart rate was significantly lower in Group P than Group E at 20 and 30 minutes; systolic, diastolic and mean arterial pressures and SpO_2 did not differ significantly between groups at any postoperative time point (Table 3).

Cognitive function

Median Tirpude GMC-OMC scores were 15 (no cognitive dysfunction) in both groups preoperatively. A slight, statistically non-significant decline was observed in both groups at 30 and 60 minutes postoperatively, with scores returning to the preoperative median of 15 by 120 minutes; there was no significant between-group difference at any time point, indicating a similar, clinically insignificant and fully reversible pattern of transient cognitive change with both agents (Table 4).

Adverse effects

Hypotension was significantly more frequent in Group P than Group E (22.5% vs 2.5%; risk difference 20.0%, 95% CI 6.2-33.8; $p = 0.01$); no patient in either group required pharmacological treatment for hypotension. Nausea (25.0% vs 12.5%) and vomiting (15.0% vs 7.5%) were more frequent in Group E than Group P, though the difference did not reach statistical significance. Shivering, headache and bradycardia occurred infrequently in both groups without significant between-group difference. No patient in either group developed myoclonus, injection-site pain, skin rash/itching or urinary retention; the absence of myoclonus and injection pain in the etomidate group is attributable to the use of a lipid-emulsion (Etomidate Lipuro) formulation (Table 5). Overall, the pattern of results indicates that etomidate conferred a consistent haemodynamic advantage over propofol throughout the intraoperative period without a corresponding cognitive advantage, while propofol was associated with a lower incidence of postoperative nausea and vomiting but a higher incidence of hypotension.

Table 1: Baseline demographic, clinical and preoperative haemodynamic profile

Characteristics	Group P, (n=40)	Group E, (n=40)	P value
Demographics			
Age (in years), mean±SD	32.03±7.70	30.43±6.71	0.33
Sex			
Male	18 (45.0)	15 (37.5)	0.50
Female	22 (55.0)	25 (62.5)	-
ASA grade			
I	28 (70.0)	25 (62.5)	0.48
II	12 (30.0)	15 (37.5)	-
Weight (kg), mean±SD	62.48±9.67	64.85±11.43	0.32
Height (cm), mean±SD	161.45±7.76	161.40±8.41	0.98
BMI (kg/m ²), mean±SD	24.00±3.58	25.18±5.66	0.27
Surgery type			
D and C	21 (52.5)	24 (60.0)	>0.05
Fracture reduction/fixation	19 (47.5)	16 (40.0)	-
Preoperative (baseline) haemodynamic parameters, mean±SD			
Heart rate (bpm)	81.58±6.83	80.60±7.27	0.54
Systolic BP (mmHg)	128.35±11.54	128.20±11.74	0.95
Diastolic BP (mmHg)	78.75±5.86	78.85±5.43	0.94
Mean arterial pressure (mmHg)	95.28±6.71	95.30±6.43	0.99
SpO ₂ (%)	97.50±1.87	97.05±1.69	0.26

*D and C: dilation and curettage; BP: blood pressure; SpO₂: oxygen saturation. Chi-square test / unpaired t-test as applicable; p<0.05 considered statistically significant.

Table 2: Intraoperative haemodynamic parameters at different time intervals.

Time interval	Group P, mean±SD	Group E, mean±SD	Mean difference (95% CI) ^a	P value
Heart rate (bpm)				
0 minute	78.23±4.90	81.70±6.37	-3.47 (-6.00, -0.94)	0.008*
5 minutes	70.30±7.22	75.63±6.95	-5.33 (-8.48, -2.18)	0.001*
10 minutes	68.63±4.45	75.15±7.73	-6.52 (-9.33, -3.71)	<0.001*
20 minutes	64.70±4.22	72.93±7.00	-8.23 (-10.80, -5.66)	<0.001*
Systolic blood pressure (mmHg)				
0 minute	124.80±12.54	125.40±10.39	-0.60 (-5.73, 4.53)	0.82
5 minutes	115.50±16.71	124.50±13.07	-9.00 (-15.68, -2.32)	0.009*
10 minutes	113.40±10.67	118.40±11.29	-5.00 (-9.89, -0.11)	0.045*
20 minutes	116.40±10.67	119.80±11.47	-3.40 (-8.33, 1.53)	0.17
Diastolic blood pressure (mmHg)				
0 minute	78.20±7.54	78.45±5.29	-0.25 (-3.15, 2.65)	0.86
5 minutes	70.80±14.16	76.80±7.86	-6.00 (-11.10, -0.90)	0.022*
10 minutes	70.55±6.88	73.60±7.02	-3.05 (-6.14, 0.04)	0.05
20 minutes	70.95±6.96	72.80±4.94	-1.85 (-4.54, 0.84)	0.17
Mean arterial pressure (mmHg)				
0 minute	93.73±6.87	94.10±4.82	-0.37 (-3.01, 2.27)	0.78
5 minutes	85.70±13.79	92.70±8.62	-7.00 (-12.12, -1.88)	0.008*
10 minutes	84.83±5.25	88.53±6.97	-3.70 (-6.45, -0.95)	0.009*
20 minutes	86.10±5.48	88.47±4.64	-2.37 (-4.63, -0.11)	0.04*
SpO₂ (%)				
0 minute	97.43±1.95	97.38±1.86	0.05 (-0.80, 0.90)	0.91
5 minutes	97.80±1.64	97.88±1.60	-0.08 (-0.80, 0.64)	0.84
10 minutes	97.48±1.71	97.93±1.65	-0.45 (-1.20, 0.30)	0.24
20 minutes	98.20±1.62	98.03±0.70	0.17 (-0.39, 0.73)	0.53

*Unpaired t-test (pooled-variance method for mean difference and 95% CI). ^aGroup P minus Group E. *p value<0.05, statistically significant.

Table 3: Postoperative haemodynamic parameters at different time intervals.

Time interval	Group P, mean±SD	Group E, mean±SD	Mean difference (95% CI) ^a	P value
Heart rate (bpm)				
0 minute	65.08±3.88	67.28±6.98	-2.20 (-4.71, 0.31)	0.09
20 minutes	69.75±5.03	73.10±5.71	-3.35 (-5.75, -0.95)	0.01*
30 minutes	75.60±5.70	79.35±3.68	-3.75 (-5.89, -1.61)	<0.001*
60 minutes	82.05±2.80	81.20±4.25	0.85 (-0.75, 2.45)	0.29
Systolic blood pressure (mmHg)				
0 minute	118.30±7.44	121.35±7.84	-3.05 (-6.45, 0.35)	0.08
20 minutes	123.40±8.17	122.55±7.72	0.85 (-2.69, 4.39)	0.63
30 minutes	124.75±11.38	122.88±7.70	1.87 (-2.46, 6.20)	0.39
60 minutes	123.35±9.92	123.45±10.57	-0.10 (-4.66, 4.46)	0.97
Diastolic blood pressure (mmHg)				
0 minute	70.70±6.09	68.35±4.96	2.35 (-0.12, 4.82)	0.06
20 minutes	72.40±5.99	70.80±3.24	1.60 (-0.54, 3.74)	0.14
30 minutes	77.80±5.43	76.70±2.21	1.10 (-0.75, 2.95)	0.24
60 minutes	77.65±5.14	78.35±3.94	-0.70 (-2.74, 1.34)	0.50
Mean arterial pressure (mmHg)				
0 minute	86.57±5.60	86.02±4.13	0.55 (-1.64, 2.74)	0.62
20 minutes	89.40±5.33	88.05±3.33	1.35 (-0.63, 3.33)	0.18
30 minutes	93.45±5.48	92.09±2.63	1.36 (-0.55, 3.27)	0.16
60 minutes	92.88±5.32	93.38±4.63	-0.50 (-2.72, 1.72)	0.66
SpO₂ (%)				
0 minute	97.93±1.64	97.77±0.84	0.16 (-0.42, 0.74)	0.60
20 minutes	98.03±1.40	97.70±1.59	0.33 (-0.34, 1.00)	0.34
30 minutes	97.43±1.74	97.25±1.56	0.18 (-0.56, 0.92)	0.64
60 minutes	98.65±1.05	98.90±1.22	-0.25 (-0.76, 0.26)	0.33

*Unpaired t-test (pooled-variance method for mean difference and 95% CI). ^aGroup P minus Group E. *P<0.05, statistically significant.

Table 4: Preoperative and postoperative Tirpude GMC-OMC cognitive score.

Time point	Group P, median	Group E, median	P value
Preoperative	15	15	0.32
Postoperative, 30 minutes	15	15	0.79
Postoperative, 60 minutes	15	15	0.58
Postoperative, 120 minutes	15	15	1.00

*Mann-Whitney U test. Score range 1-15 (higher score indicates better cognitive function); 11-15: no cognitive dysfunction, 6-10: partial cognitive dysfunction, 1-5: severe cognitive dysfunction. No significant between-group difference at any time point.

Table 5: Adverse effects in the two groups.

Adverse effect	Group P, N (%)	Group E, N (%)	Risk difference, % (95% CI) ^a	P value
Nausea	5 (12.5)	10 (25.0)	-12.5 (-29.4, 4.4)	0.15
Vomiting	3 (7.5)	6 (15.0)	-7.5 (-21.3, 6.3)	0.29
Shivering	2 (5.0)	3 (7.5)	-2.5 (-13.1, 8.1)	0.65
Headache	2 (5.0)	1 (2.5)	2.5 (-5.8, 10.8)	0.56
Skin rash/itching	0 (0)	0 (0)	-	-
Bradycardia	3 (7.5)	1 (2.5)	5.0 (-4.5, 14.5)	0.30
Hypotension	9 (22.5)	1 (2.5)	20.0 (6.2, 33.8)	0.01*
Urinary retention	0 (0)	0 (0)	-	-

*Z-test of proportions (Wald method for risk difference and 95% CI). ^aGroup P minus Group E. *P<0.05, statistically significant.

DISCUSSION

POCD

In this randomized double-blind study of young, ASA I-II patients undergoing short elective surgery, propofol and

etomidate produced comparable, clinically insignificant, transient change in the Tirpude GMC-OMC cognitive score, with no significant between-group difference at any postoperative time point. This finding differs from reports in elderly or high-risk surgical populations, where agent-related differences in postoperative cognitive outcome

have been described. Ghavipeykar et al studying patients over 60 years undergoing orthopaedic surgery, found a lower Mini-Mental State Examination score in the propofol group than the etomidate group on the first postoperative day, a difference that reversed by the third postoperative day, whereas delirium on the first postoperative day was significantly less frequent with propofol than with etomidate.⁸ Micha et al and Goswami et al similarly reported greater early postoperative cognitive impairment with propofol than with sevoflurane, the former in an elderly surgical population and the latter in adult patients undergoing laparoscopic cholecystectomy, while Zhang et al reported comparatively better preserved early cognitive function with propofol relative to sevoflurane in older adults undergoing general surgery.⁹⁻¹¹ At a mechanistic level, Martin et al demonstrated in an animal model that etomidate can impair synaptic plasticity and memory performance through increased $\alpha 5$ -GABA-A receptor activity, an effect reversible with a selective antagonist; Jiang et al similarly found differential effects of etomidate and propofol on memory in immature rats.^{12,13} Taken together, the comparative cognitive literature on intravenous and volatile anaesthetic agents more broadly is heterogeneous and at times contradictory, which likely reflects differences in patient age, comorbidity, surgical stimulus, anaesthetic depth, and the cognitive instrument used; the propofol-etomidate comparisons discussed above share this same heterogeneity.^{14,15} The absence of a significant between-group cognitive difference in the present study, despite these mixed reports, is most plausibly explained by the younger, healthier study population (ASA I-II, 18-40 years) and the short surgical duration, both recognised protective factors against POCD.

The Tirpude GMC-OMC score used in this study is a composite instrument combining elements of the Short Blessed Test with a Trail Making Test component, and has practical advantages for perioperative use given its brevity and applicability across literacy levels when administered in the patient's own language. However, unlike more extensively validated instruments such as the Mini-Mental State Examination or a full neuropsychological test battery, it has not been as widely cross-validated in the Indian surgical population, which is a relevant consideration when comparing findings across studies that use different cognitive instruments; this heterogeneity of testing tools is itself a recognised contributor to the wide variation in reported POCD incidence across the literature.

Haemodynamic stability

Etomidate produced more stable intraoperative haemodynamics than propofol in this study, consistent with a substantial and consistent body of comparative literature.¹⁶⁻²⁸ Zheng et al similarly found more stable heart rate and mean arterial pressure with etomidate during induction using a bispectral-index-guided protocol.¹⁶ The hypotension observed with propofol is thought to reflect

reduced sympathetic activity causing vasodilatation, a direct effect on intracellular calcium mobilization, and inhibition of endothelial prostaglandin synthesis, whereas the relative haemodynamic stability of etomidate reflects its comparative lack of effect on the sympathetic nervous system and baroreceptor reflex, together with its ability to stimulate peripheral $\alpha 2B$ -adrenergic receptors and produce mild vasoconstriction.¹ Aggarwal et al in a direct clinical comparison, similarly found little change in heart rate and mean arterial pressure with etomidate relative to propofol, with more injection pain in the propofol group and more myoclonus in the etomidate group.¹⁸ This mechanistic distinction likely explains the significantly higher incidence of hypotension with propofol observed in the present study (22.5% vs 2.5%), a finding consistent with several previous comparative trials in both cardiac and non-cardiac surgical populations.^{17,19-23} Etomidate's relative preservation of haemodynamic stability compared with propofol has also been demonstrated directly in a study of catecholamine and haemodynamic responses to induction with the two agents and confirmed in a bispectral-index-guided randomised trial.^{29,30} Reich et al in a large retrospective analysis of predictors of post-induction hypotension, similarly identified induction agent as one of several independent risk factors, alongside older age, lower baseline blood pressure and higher ASA physical status, while Goodchild and Serrao, in an editorial commentary, argued that propofol, at clinically used concentrations, does not produce a direct negative inotropic effect or arterial relaxation, proposing that reduced venous return and sympathetic withdrawal, rather than direct myocardial depression, are the dominant mechanisms underlying propofol-associated hypotension.^{31,32} Propofol has additionally been shown to blunt baroreflex sensitivity, further contributing to its haemodynamic lability relative to etomidate, which largely preserves baroreflex-mediated compensatory responses during induction. Notably, the haemodynamic advantage of etomidate over propofol has been demonstrated consistently across diverse surgical contexts in the cited literature, ranging from cardiopulmonary bypass surgery to general and orthopaedic procedures, suggesting a robust, generalisable pharmacological effect rather than a population-specific finding.

Adverse effects

Nausea and vomiting, although not statistically significant in this study, were numerically more frequent with etomidate, consistent with its recognised adverse-effect profile. Etomidate is also associated with pain on injection and myoclonus in some reports; neither was observed in this study, most likely because of the lipid-emulsion (Etomidate Lipuro) formulation used, which is known to reduce injection-related discomfort compared with the older propylene-glycol formulation. A further consideration in etomidate use, not directly assessed in this study, is transient suppression of adrenocortical steroidogenesis following even a single induction dose; while the clinical significance of this effect after a single

bolus in otherwise healthy patients undergoing short surgery remains debated, it is a relevant consideration when selecting an induction agent, particularly in critically ill or septic patients, and merits caution when extrapolating the present results to such populations.

Clinical implications and limitations

To our knowledge, this is among a limited number of studies to concurrently evaluate cognitive, haemodynamic and adverse-effect outcomes using a validated composite cognitive instrument in a specifically young, ASA I-II day-care surgical population, a group that has been comparatively underrepresented in the existing propofol-etomidate literature, which has focused predominantly on elderly or cardiac surgical cohorts. These findings suggest that, in young, healthy patients undergoing short elective surgery, the choice between propofol and etomidate for induction is unlikely to influence postoperative cognitive outcome, and may instead be guided by the relative importance of haemodynamic stability versus postoperative nausea and vomiting in the individual patient. Etomidate may be particularly advantageous in patients with limited haemodynamic reserve or a labile cardiovascular status, while propofol may be preferable where postoperative nausea and vomiting, or the cumulative risk of adrenocortical suppression with repeated or prolonged etomidate exposure, is a greater concern.

This study has several methodological strengths: it was designed, conducted and is reported in accordance with the CONSORT guidelines; patients and outcome assessors were blinded to group allocation, allocation was concealed using sequentially numbered, opaque, sealed envelopes, cognitive assessment was performed at multiple standardized postoperative time points using a consistent instrument, and follow-up was complete with no dropouts. These features reduce the likelihood of assessment and selection bias and strengthen confidence in the internal validity of the comparative findings. The study nonetheless has certain limitations.

CONCLUSION

It was conducted at a single centre with a modest sample size, and was restricted to ASA I-II patients aged 18-40 years undergoing short procedures; the findings may not extend to elderly, high-risk or haemodynamically compromised patients, to patients with pre-existing cognitive impairment, or to longer or more extensive surgery, in whom the neuroprotective and haemodynamic advantages of etomidate, and the clinical relevance of adrenocortical suppression, may be more pronounced. Adrenocortical function was not directly assessed in this study. Larger, multicentric studies across a broader age and risk spectrum, incorporating both cognitive and endocrine outcomes, are needed to further define the comparative safety profile of these two agents.

In conclusion, propofol and etomidate produced comparable postoperative cognitive outcomes in young, healthy patients undergoing short elective surgery under GA. Etomidate offered superior intraoperative haemodynamic stability and a lower incidence of hypotension, while propofol was associated with less postoperative nausea and vomiting.

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