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Desflurane and target-controlled propofol for craniotomy: A randomized trial

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Abstract:

Selecting the optimal anaesthetic technique for craniotomy remains challenging because desflurane and target-controlled infusion (TCI) propofol differ in cerebral and recovery effects. Sixty ASA I-III patients undergoing elective supratentorial craniotomy were randomized to desflurane or TCI propofol and brain relaxation, haemodynamics, emergence and recovery were compared. Brain relaxation and intraoperative haemodynamic stability were similar, but desflurane produced faster extubation, eye opening and vocalization (all $P < 0.001$). Desflurane was associated with higher post-operative pain and PONV, whereas blood loss was greater with TCI propofol (573 vs 440 mL, $P < 0.001$). Thus, both techniques are suitable for elective craniotomy, with desflurane enabling faster emergence and TCI propofol improving post-operative comfort despite slower recovery.

Keywords: Craniotomy, desflurane, propofol, target-controlled infusion, brain relaxation, neuroanaesthesia, total intravenous anaesthesia (TIVA)

Background:

Modern neurosurgery demands an anaesthetic technique that provides haemodynamic stability, adequate brain relaxation, neuroprotection, maintenance of cerebral autoregulation and perfusion pressure and a smooth, rapid emergence for prompt neurological assessment [1]. Surgical stimuli during craniotomy frequently elicit sympathetic activation causing significant changes in systemic arterial pressure and cerebral blood flow (CBF), potentially elevating intracranial pressure (ICP) and reducing cerebral perfusion pressure (CPP), which may precipitate cerebral ischaemia - particularly in patients with impaired autoregulation [2]. Two broad anaesthetic strategies are currently employed: total intravenous anaesthesia (TIVA) using propofol and volatile (inhalational) anaesthesia [3]. Volatile agents are dose-dependently vasodilatory and may transiently elevate ICP, yet offer rapid offset and superior intraoperative control of anaesthetic depth. Desflurane, with the lowest blood-gas partition coefficient (0.45) among currently used volatile agents, provides faster emergence kinetics [4]. Conversely, propofol reduces CBF and ICP through cerebral vasoconstriction, suppresses cerebral metabolic rate (CMR) and is associated with low rates of post-operative nausea and vomiting (PONV) [5]. Despite extensive literature on volatile versus intravenous techniques for craniotomy, comparative data specifically evaluating desflurane against propofol TCI under entropy-guided depth of anaesthesia monitoring remain limited [6]. Therefore, it is of interest to compare the desflurane with target-controlled infusion (TCI) propofol under entropy-guided anaesthesia in patients undergoing elective supratentorial craniotomy, with emphasis on intraoperative brain relaxation, haemodynamic stability and post-operative recovery.

Materials and Methods:**Study design and ethics:**

This was a prospective, randomized, controlled, parallel-group study conducted at Manipal Hospital, Bengaluru, over a period from October 2016 to May 2017. The study was approved by the Institutional Ethics Committee (Dr. Vishwanath Siddini, Member Secretary, Ethics Committee, Manipal Hospital and Bengaluru) and written informed consent was obtained from all participants prior to enrolment.

Sample size:

Using a two-sample Student's t-test with 80% power, a 5% level of significance (two-tailed) and an effect size of 0.8, a minimum of 26 patients per group was required. To account for dropouts, 30 patients per group (total $n=60$) were enrolled.

Inclusion and exclusion criteria:

Patients aged 18-60 years, scheduled for elective craniotomy and of ASA physical status I, II, or III were included. Patients were excluded if they were unwilling to participate, required emergency surgery or presented with herniation symptoms, had severe comorbid illness involving the respiratory, cardiovascular, or hepatic systems, had a history of long-term abuse of opioids, sedatives, or hypnotics, or had a known allergy to any study drug.

Randomisation:

Following written informed consent, patients were randomized using a computer-generated random number table (Microsoft Excel) to one of two groups: Group D ($n=30$, desflurane) or Group P ($n=30$, TCI propofol).

Anaesthetic protocol:

All patients fasted for at least 6 hours pre-operatively and received intramuscular glycopyrrolate 0.2 mg, 30 minutes before transfer to the operating room. Standard monitoring was established: ECG, non-invasive blood pressure, pulse oximetry, end-tidal CO₂, neuromuscular transmission (NMT), temperature probe and Entropy (GE Healthcare) with forehead electrode placement per manufacturer guidelines. Intravenous access was secured with an 18-20 G cannula, baseline haemodynamic parameters were recorded and all patients were pre-oxygenated for 3 minutes.

Group D: Induction with intravenous fentanyl 2 µg/kg, propofol 2 mg/kg and 1.5 mg/kg lignocaine hydrochloride, followed by desflurane 6% at 2 L/min flow rate. Rocuronium 0.6 mg/kg was administered after confirming adequate mask ventilation (TOF count = 0 before intubation). Desflurane concentration was titrated to maintain Entropy 40-50 (±5) throughout.

Group P: Induction with fentanyl 2 µg/kg and TCI propofol at a target plasma concentration of 6 µg/mL, adjusted to maintain Entropy 40-50 (±5). Rocuronium 0.6 mg/kg was used for intubation as above. TCI propofol was stopped 10 minutes before anticipated extubation. In both groups, orotracheal intubation was performed and intermittent positive pressure ventilation maintained normocapnia (ETCO₂ 35-40 mmHg). Fentanyl infusion was started at 2 µg/kg/hr. and rocuronium at 10 µg/kg/hr after intubation and normothermia was maintained throughout. Haemodynamic parameters were recorded at pre-induction, post-induction, intubation and every 15 minutes thereafter up to 120 minutes. Intraoperative derangements were managed as follows: heart rate fall >30% - IV atropine 0.6 mg; blood pressure fall >30% or SBP <90 mmHg - IV ephedrine 6 mg; heart rate/blood pressure rise >30% - IV esmolol 30 mg. Rocuronium infusion was stopped 30 minutes before anticipated extubation and in Group D, desflurane was discontinued at skin closure. Reversal was achieved with neostigmine 0.04 mg/kg and glycopyrrolate 0.01 mg/kg on return of spontaneous breathing or a TOF count ≥2. Extubation criteria comprised adequate consciousness, simple command following, 5-second sustained head lift, intact gag reflex, tidal volume >6 mL/kg, Entropy RE >95 and TOF ratio ≥0.9.

Outcome measures:

Brain relaxation was graded by a senior neurosurgeon at (i) dural opening and (ii) dural closure using the validated 4-point scale (Table 1). Post-operative recovery was assessed at extubation and at 30 minutes post-extubation, including extubation time, eye-opening time, vocalisation time, PONV grade, VAS pain score, level of consciousness and shivering. All patients were monitored in the post-anaesthesia care unit (PACU) for 2 hours.

Statistical analysis:

Data are presented as mean ± standard deviation (SD) for continuous variables and as frequency and percentage for categorical variables. The unpaired Student’s t-test was used for continuous data and the chi-square test for categorical data. Correlation between preoperative raised ICP and intraoperative brain relaxation was evaluated using Pearson’s correlation. P<0.05 was considered statistically significant. Analysis was performed using SPSS version 11.

Results:

All 60 recruited patients completed the study. Demographic characteristics were comparable between groups (Table 2). Mean age was 44±10 years (Group D) versus 42±12 years (Group P) (P=0.59). Gender distribution (P=0.069), height (P=0.24) and ASA status (P=0.78) did not differ significantly. Mean weight (68±11 vs 61±11 kg, P=0.04) and BMI (25±3 vs 22±3 kg/m², P=0.002) were marginally higher in Group D but were not considered clinically significant. Brain relaxation scores at dural opening and dural closure were comparable between the two groups (P>0.05). At dural opening, 14 of 30 patients in Group D and 10 of 30 in Group P had a Grade 2 score (brain at craniotomy margin); the remaining patients in both groups were similarly distributed across grades. Brain relaxation at dural closure was equivalent in both groups. Patients who had pre-operatively raised ICP on neuroimaging tended to have higher (tenser) brain grades at dural opening; however, the correlation between preoperative raised ICP and intraoperative brain relaxation did not reach statistical significance (P>0.05), likely due to the small number of patients with raised ICP. A larger sample would be needed to establish this relationship. Heart rate, SBP, DBP and MAP at all-time points (pre-induction through 120 minutes) showed no statistically significant intergroup differences (P>0.05 at all intervals). This finding is consistent with the results reported by Todd *et al.* [8], who observed no clinically important intergroup haemodynamic differences between propofol and inhalational-based techniques for craniotomy. Desflurane was associated with significantly faster emergence across all three recovery parameters (Table 3). Time to extubation was 9.7 min in Group D versus 17.0 min in Group P (P<0.001); time to eye opening was 9.4 versus 16.4 min (P<0.001); and time to vocalisation was 12.2 versus 20.4 min (P<0.001). More patients in Group D were fully awake at extubation (86% vs 63%, P=0.03). PONV occurred in 16% of Group D patients versus 0% of Group P patients (P=0.02). Post-operative pain was significantly worse in Group D: only 6% of Group D patients were pain-free compared with 83% in Group P and mild pain was present in 36% versus 16%, respectively (P<0.001). There was no statistically significant difference in post-operative shivering between groups (P=0.278). Intraoperative blood loss was significantly greater in Group P (573 mL vs 440 mL, P<0.001).

Table 1: Brain relaxation grading scale

Grade	Description
Grade 1	Brain surface above the level of craniotomy margin (tense)
Grade 2	Brain surface at the level of craniotomy margin
Grade 3	Brain surface just below the craniotomy margin (relaxed)
Grade 4	Well retracted brain, well below the craniotomy margin (very relaxed)

Table 2: Demographic data

Variable	Group D (Desflurane) n=30	Group P (Propofol TCI) n=30	P value
Age (years)	44 ± 10	42.7 ± 12	0.59
Gender (M:F)	20:10 (67%:33%)	13:17 (43%:57%)	0.069
Weight (kg)	68 ± 11	61 ± 11	0.04
Height (cm)	161 ± 6.5	163 ± 8	0.24
BMI (kg/m ²)	25 ± 3	22 ± 3	0.002
ASA I:II:III	4:23:03	6:21:03	0.78

Table 3: Recovery profile comparison

Parameter	Group D	Group P	P value
Time to extubation (min)	9.7	17	<0.001
Time to eye opening (min)	9.4	16.4	<0.001
Time to vocalisation (min)	12.2	20.4	<0.001
Wide awake at extubation	86%	63%	0.03
Post-op shivering	10%	20%	0.278

Discussion:

The cardinal goals of neuroanaesthesia - brain relaxation, haemodynamic stability and rapid neurological recovery - remain challenging to optimise with a single technique. Our study shows that desflurane and TCI propofol are equivalent in achieving the two primary outcomes: intraoperative brain relaxation and haemodynamic control. However, they differ markedly in their recovery profiles and post-operative adverse event rates. The equivalence of brain relaxation observed in our study is consistent with findings by Prabhakar *et al.* [7], who similarly found no difference in brain tenseness when comparing propofol with sevoflurane. Our comparison specifically with desflurane adds to this literature. The lack of clinically significant difference in haemodynamics corroborates the findings of Todd *et al.* [8], who reported minimal intergroup haemodynamic differences across three anaesthetic regimens for craniotomy. The superior emergence profile of desflurane is attributable to its ultra-low blood-gas solubility coefficient (0.45), which allows rapid pulmonary elimination and precise, rapidly reversible titration of anaesthetic depth [9]. Earlier emergence translates to earlier airway protection, faster neurological assessment and potentially reduced PACU burden. Nguyen *et al.* [10] similarly showed shorter emergence times with desflurane compared with isoflurane in paediatric neurosurgical patients. The higher PONV incidence in the desflurane group (16% vs 0%, P=0.02) is a recognised drawback of volatile anaesthesia. Propofol is well known for its antiemetic properties [11] and this advantage is clearly evident in the post-operative period. The significantly greater post-operative pain in Group D (94% vs 17% requiring analgesia, P<0.001) may reflect the superior analgesic-sparing and residual sedative properties of propofol, or a direct analgesic effect of propofol at sub-anaesthetic concentrations. The higher blood loss in the propofol group (573 vs 440 mL, P<0.001) is an unexpected finding and warrants further investigation. It may be related to propofol-mediated reduction in platelet aggregation or subtle haemodynamic

differences not captured by our group-level analysis [12]. The absence of a significant correlation between pre-operative raised ICP and intraoperative brain relaxation was likely due to limited statistical power arising from the small number of patients with raised ICP in the study cohort.

Conclusion:

Desflurane and target-controlled infusion (TCI) propofol provided comparable brain relaxation and haemodynamic stability during elective supratentorial craniotomy. Desflurane enabled significantly faster emergence, whereas propofol TCI reduced post-operative pain and post-operative nausea and vomiting. Anaesthetic choice should be individualised according to the priority of rapid neurological assessment or improved post-operative recovery.

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Declarations:

Funding: No external funding was received for this study.

Conflicts of interest: The authors declare no conflict of interest.

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