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Propofol versus Desflurane in Moyamoya Disease Patients—A Pilot Study

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Abstract

Objectives The choice of inhalational or intravenous anesthetic agents is debatable in neurosurgical patients. Desflurane, a cerebral vasodilator, may be advantageous in ischemic cerebral pathologies. Hence, we planned to compare desflurane and propofol in patients with moyamoya disease (MMD) with the objective of comparing neurological outcomes.

Materials and Methods This prospective pilot trial was initiated after institutional ethics committee approval. Patients with MMD undergoing revascularization surgery were randomized into two groups receiving either desflurane or propofol intraoperatively. Neurological outcomes were assessed using a modified Rankin score (mRS) at discharge and an extended Glasgow outcome score (GOS-E) at 1 month. Intraoperative parameters, including hemodynamic parameters, end-tidal carbon dioxide, entropy, intraoperative brain relaxation scores (BRS), and rescue measures for brain relaxation, were compared.

Statistical Analysis The normality of quantitative data was checked using Kolmogorov–Smirnov tests of normality. Normally distributed data were compared using unpaired *t*-tests, skewed data using Mann–Whitney U tests, and categorical variables using chi-squared tests.

Results A total of 17 patients were randomized, 10 in the desflurane and 7 in the propofol group. mRS (1.3 ± 0.6 and 1.14 ± 0.4, $p = 0.450$) and GOS-E (6.7 ± 0.6 and 6.85 ± 0.5, $p = 0.45$) were comparable between desflurane and propofol groups, respectively. BRS was significantly higher in the desflurane group (3.6 ± 0.5) compared to the propofol group (2.1 ± 0.3, $p = 0.001$), with a significant number of patients requiring rescue measures in the desflurane group (70%, $p < 0.001$). Other outcome parameters were comparable ($p > 0.05$).

Conclusion We conclude that postoperative neurological outcomes were comparable with using either an anesthetic agent, desflurane, or propofol in MMD patients undergoing revascularization surgery. Maintenance of anesthesia with propofol had significantly superior surgical field conditions.

Keywords
- anesthesia
- desflurane
- moyamoya disease
- propofol

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Introduction

Moyamoya disease (MMD) is a chronic cerebrovascular disorder characterized by progressive narrowing or occlusion of intracranial vessels, thus causing ischemic lesions. The occlusion commences from the terminal bifurcation of the internal carotid artery (ICA) and progressively involves the anterior, middle, and posterior cerebral arteries. Due to the stenosis of these arteries, a collateral network of vessels is formed at the base of the brain producing a characteristic "puff of smoke" appearance on angiography.[1] The disease is commonly detected in the Asian population with a bimodal peak age of onset (first peak is seen in the first 10 years, and the second peak at 40–50 years), and male to female ratio is 1:1.65.[2,3]

Medical therapy has minimal influence on the progression of the disease, and surgical revascularization (direct and indirect revascularization procedures) is the definitive treatment of choice.[4] The main goal of surgical revascularization is to prevent cerebral infarctions.[5] Commonly used direct revascularization procedure is the superficial temporal artery to middle cerebral artery (STA-MCA) bypass.[6] The goals of anesthetic management of MMD include maintaining cerebral perfusion, normocapnia, normothermia, normovolemia, and normotension. Total intravenous anesthesia is favored in neurosurgical patients with poorly compliant brains.[7] However, as cerebral vasodilators, inhalational agents may increase blood flow and improve cerebral perfusion in ischemic brain pathologies such as MMD.[8] Recent research on inhalational agents has also documented its promising role in neurosurgical procedures.[9]

As per literature, among all the inhalational agents desflurane has the maximum cerebral vasodilating properties and is known to cause hyperemic response, intraoperatively.[10,11] However, the literature is scarce comparing the effect of intraoperative use of desflurane and propofol on postoperative neurological outcomes in patients with MMD. Thus, we planned to compare propofol and desflurane as anesthesia maintenance agents in patients with MMD undergoing STA-MCA bypass. We hypothesized that due to the inherent vasodilatory properties of desflurane, it may be associated with better neurological outcomes in MMD compared to propofol. The objectives were to compare the neurological outcomes and intraoperative parameters, including hemodynamic parameters, end-tidal carbon dioxide ($EtCO_2$), entropy, intraoperative brain relaxation scores (BRS), and rescue measures to improve the surgical field between the two groups.

Materials and Methods

After obtaining approval from the institutional ethics committee and written informed consent from the parent/guardian of the children (below 18 years), this prospective randomized pilot study was conducted between July 2019 and September 2020. Twenty patients satisfying the inclusion criteria were included and randomized into groups A and B, with 10 patients in each group. American Society of Anesthesiologists (ASA) status I and II patients, of all age groups, undergoing definitive revascularization procedures for MMD were included. The patients whose parent/guardian refused to participate, having severe systemic diseases and severe neurological deficits (monoplegia, hemiparesis, or hemiplegia), were excluded from the study. Group A patients received desflurane for maintenance, while group B received propofol. Randomization was done using a computer-generated random number assignment.

On the day of surgery, nil per os status of the patients was confirmed and premedicated with oral midazolam 0.5 mg/kg in the preoperative room under monitoring. Intraoperative monitoring included electrocardiogram, noninvasive blood pressure, pulse oximetry, temperature, urine output, entropy, $EtCO_2$, and arterial blood pressure. Anesthesia was induced with fentanyl 2 µg/kg and propofol 1 to 2 mg/kg, titrated to loss of verbal contact. Vecuronium 0.1 mg/kg was used to facilitate tracheal intubation. Patients were ventilated with 50:50 oxygen and nitrous oxide to maintain $EtCO_2$ of 35 to 40 mm Hg. Normothermia was maintained by forced air warmers and warm fluids.

In group A, anesthesia was maintained with desflurane (1–1.5 minimum alveolar concentration), and in group B, propofol infusion (0.1–0.2 mg/kg/min) was given to achieve an entropy of 40 to 60. In both groups, normal saline was used as intraoperative maintenance fluid to maintain euvolemia (pulse pressure variations $<12\%$). After completion of the surgery, residual neuromuscular block was reversed using neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg and the trachea was extubated.

BRS was assessed by operating surgeon who was blinded to the study drug using 4-point score.[12] In the patients with clinically significant brain bulge, the rescue measures were used to relax the brain. In both the groups after checking the physiological parameters, the following steps were taken in sequence. Raising the head end of the table to 20 to 30 degrees, depth of anesthesia was increased using propofol boluses of 1 mg/kg and switching off nitrous oxide. In desflurane group, if there was severe brain bulge not responding to rescue therapy, maintenance agent was switched to propofol infusion. In such scenarios, the patients were excluded from the study.

Statistical analysis was done using Statistical Package for Social Sciences (version 22). The normality of quantitative data was checked using Kolmogorov–Smirnov tests of normality. For normally distributed data, means were compared using unpaired *t*-tests and presented as mean and standard deviation. The variables with skewed data were analyzed using Mann–Whitney U tests and presented as the median and interquartile range. Categorical variables were analyzed using chi-squared tests and presented as numbers and percentages. A *p*-value of less than 0.05 was considered statistically significant.

Results

Seventeen patients, ten in group A and seven in group B, were analyzed (►**Fig. 1**). Three patients were excluded from the study in group B who were lost to follow-up due to early discharge and incorrect contact details. The demography and

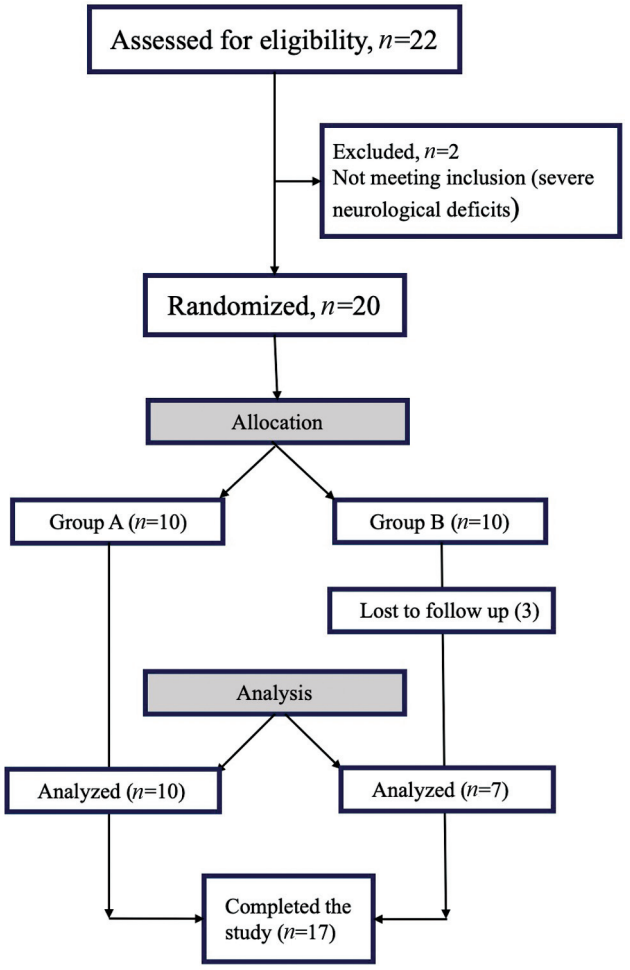

Fig. 1 CONSORT diagram.

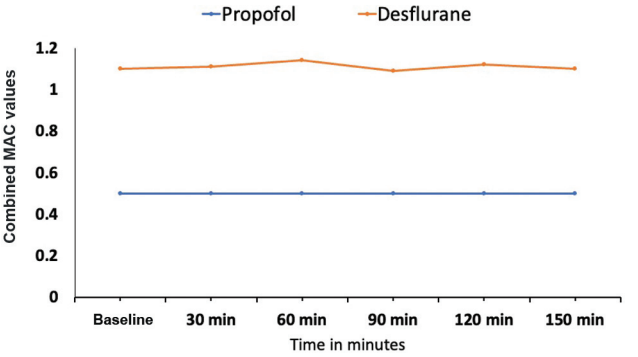

Fig. 2 Line diagram showing the combined minimum alveolar concentration (MAC) values at various time points in both the groups.

baseline parameters were comparable between the groups (►**Table 1**). The mean age was 19 ± 16.9 in group A and 24 ± 13.1 in group B. Two patients in group A were ASA II, had type-II diabetes and hypertension, and one patient had epilepsy. None of our patient required a combined minimum alveolar concentration value of more than 1.1 to achieve the target depth of anesthesia (►**Fig. 2**). None of the patients required to switch the anesthetic agents. The postoperative neurological outcomes (modified Rankin score at discharge and extended Glasgow outcome score at 1 month) were similar between the groups (►**Table 2**). Intraoperative BRS and use of rescue drugs were significantly higher in group A than in group B (►**Table 2**). Other outcome parameters were similar, such as heart rate, mean arterial pressure, $EtCO_2$, and entropy (►**Fig. 3**).

Discussion

In the current study, we compared desflurane and propofol as intraoperative anesthetic agents and observed that the neurological outcomes were comparable between the groups. A few animal studies reported that desflurane offers greater neuroprotection against focal cerebral ischemia and reduces infarct size and reperfusion injury in rat models.[13,14] Another study on pigs found that desflurane improves neurological and histological outcomes.[15] A study conducted in

Table 1 Demography and baseline characteristics

	Group A	Group B	*p*-Value
Age (years), mean ± SD	19 ± 16.9	24 ± 13.1	**0.520**
Gender, *n* (%)			
Male	7 (70%)	4 (57.14%)	**0.580**
Female	3 (30%)	3 (42.85%)	
ASA, *n* (%)			**0.760**
I	8 (80%)	6 (85.71%)	
II	2 (20%)	1 (14.28%)	
Comorbidities, *n* (%)	2 (20%)	0	**0.450**
Neurological deficit, *n* (%)	1 (10%)	0	
Power (right), mean ± SD	4.9 ± 0.42	5	**0.787**
Power (left), mean ± SD	5	5	

Abbreviations: ASA, American Society of Anesthesiologists; SD, standard deviation.
Data are presented as *n* (%) and mean ± SD.
p-Value <0.05 was considered statistically significant.

Table 2 Intraoperative and neurological outcome parameters

Parameters	Group A	Group B	*p*-Value
BRS, mean ± SD	3.6 ± 0.5	2.1 ± 0.3	0.001[a]
Required rescue measures, *n* (%)	7 (70%)	0	<0.001[a]
mRS at discharge, mean ± SD	1.3 ± 0.64	1.14 ± 0.4	0.450
GOS-E at 1 month, mean ± SD	6.7 ± 0.64	6.85 ± 0.5	0.450

Abbreviations: BRS, brain relaxation score; GOS-E, extended Glasgow outcome scale; mRS, modified Rankin score; SD, standard deviation.
Data are presented as *n* (%) and mean ± SD.
[a]*p*-Value <0.05 was considered statistically significant.

patients with MMD undergoing revascularization procedures found that cerebral oxygen supply and demand were better maintained in desflurane-based anesthesia than in propofol.[16] However, clinical studies failed to demonstrate the neuroprotective effects of desflurane, but they did observe the hyperemic response.[17,18] These studies were conducted in supratentorial tumors and good-grade aneurysms with minimal disturbance in cerebral physiology. A retrospective study conducted in MMD also failed to find the difference in outcome using desflurane or propofol.[19] Hence, the type of anesthetic agent has minimal effect on the final neurological outcome.

We found that the patients in the desflurane group had higher BRS, and rescue measures for brain bulge were required in a more significant number of patients. Similarly, a prospective study on traumatic brain injury patients found that intravenous anesthesia with propofol provides better intraoperative BRS.[20] In contrast, a Cochrane review and other clinical studies conducted in various disease pathologies found that BRS was comparable between inhalational and intravenous agents.[9,19,21,22] Such findings may be due to the differences in the drug dosage, varied population, and variable pathophysiology in different diseases.

The mean arterial pressure and heart rate were comparable in both groups, except for mean arterial pressure at 150 minutes, where the values were statistically significant but clinically nonsignificant. Our results were in line with the previous studies comparing inhalational and intravenous agents.[23] The current study has certain limitations of this study. The sample size is very small, and the results should be cautiously extrapolated. The outcome parameters are mainly clinical. The biomarkers for cerebral ischemia could have given some more insight. Cerebral hemodynamic monitors such as near-infrared spectroscopy, jugular venous oximetry, and micro-Doppler would have provided additional information.

Conclusion

We conclude that the choice of anesthetic agents, such as propofol and desflurane, has minimal effect on postoperative neurological outcomes and other hemodynamic parameters in MMD patients undergoing revascularization surgery. The use of desflurane in these patients was associated with significant brain bulge requiring treatment. This unfavorable surgical condition may preclude recruiting patients with this protocol in future trials.

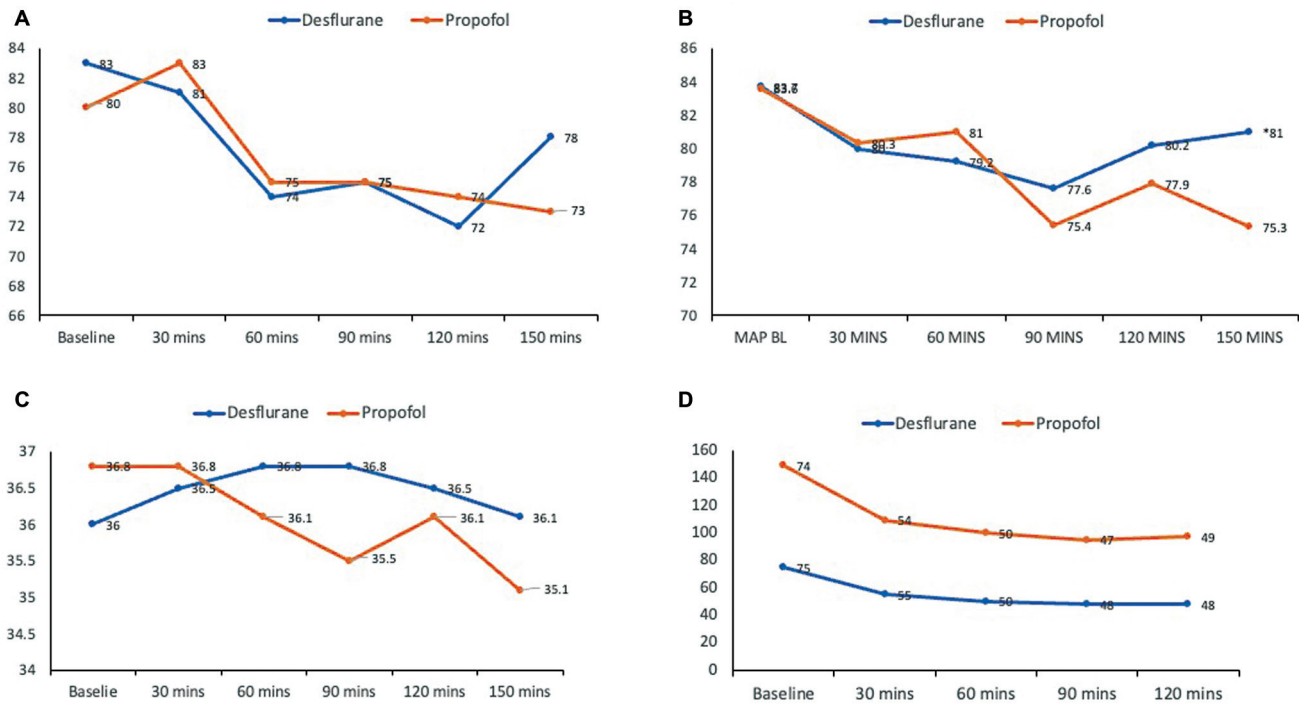

Fig. 3 Intraoperative parameters in group A and B for (**A**) heart rate, (**B**) mean arterial pressures (MAP), (**C**) end-tidal carbon dioxide and (**D**) entropy.

Ethical Approval Statement

The original work has been done after approval from Institutional Ethics Committee (No: NK/5730/MD/456) and Helsinki guidelines were followed.

Authors' Contributions

R.R.A., K.J., N.B.P., and H.B. conceptualized and designed the study. K.J., K.K., and A.A. were involved in acquisition, analysis, and interpretation of data. K.J., K.K., A.B., and R.R.A. helped in manuscript preparation. K.J., K.K., A.A., A.B., N.B.P., and H.B. helped in critical revision of the manuscript for important intellectual content. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of Interest

None declared.

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