








Comparison of Monitored Anesthesia Care with Propofol Versus Dexmedetomidine for Awake Craniotomy: A Retrospective study

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Abstract

Background Anesthetic agents used for awake craniotomy should be safe, short-acting, titratable, and provide an adequate level of sedation and analgesia, along with facilitating adequate neurological assessment during the functional testing. Our study aims to review the efficacy and safety profile, along with the potential for neurophysiological monitoring, of two commonly used anesthetic regimens, i.e., propofol and dexmedetomidine.

Methods After the Ethics Committee approval, a retrospective analysis of 51 patients who underwent awake craniotomy for brain tumor excision over a period of 7 years was done. Those who received monitored anesthesia care (MAC) were divided into two groups, namely, Group P for that received propofol, and Group D that received dexmedetomidine and their hemodynamic profile, perioperative complications, neuro-monitoring techniques, and postoperative course was noted from the records.

Results A total of 31 patients were administered MAC with propofol and 20 with dexmedetomidine. The baseline demographic data, duration of surgery, intensive care unit (ICU), and hospital stay were comparable between the two. The hemodynamic profile as assessed by the heart rate and blood pressure was also comparable. The incidence of intraoperative seizures was found to be less in Group P, though. Episodes of transient desaturation were observed more in Group P (9.7%) than in Group D (5%), but none of the patients required conversion to general anesthesia. Direct cortical stimulation was satisfactorily elicited in 80% in Group P and 85% in Group D.

Conclusion MAC with propofol and dexmedetomidine are acceptable techniques with comparable hemodynamic profile, intraoperative and postoperative complications, and potential for neurophysiological monitoring.

Keywords

- ▶ awake craniotomy
- ▶ eloquent area
- ▶ propofol
- ▶ dexmedetomidine
- ▶ scalp block
- ▶ seizures

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Introduction

Awake craniotomy (AC) for tumor resections has become the standard of care for lesions located within or close to eloquent areas. It enables the surgeon to maximize tumor resection while the patient is awake with accurate mapping of motor, language areas with continuous neurological monitoring, thus minimizing neurological deficit.

AC offers several advantages over general anesthesia (GA), which includes better hemodynamic stability, lesser use of vasopressors, opioids, and lesser incidences of GA-related side effects such as sore throat and perioperative nausea/vomiting.¹ It is also associated with fewer neurological deficits, maximal tumor resection, and shorter surgical resection time with shorter hospital stays, and reduced cost of care.^{1,2} The patient's acceptance for awake craniotomy under scalp block and sedation has also been found to be better as compared with GA.³

The main intraoperative goal of anesthesia management for AC is to provide an adequate level of sedation without interfering with the functional testing. There is no consensus regarding the choice of intravenous agents for providing sedation and anxiolysis during awake craniotomy. Propofol is a popular choice due to its easy titratability with rapid recovery enabling neuromonitoring in addition to its antiemetic and anticonvulsant properties. Dexmedetomidine, a highly selective α -2 agonist, provides sedation, anxiolysis, and analgesia without respiratory depression and thus does not affect intracranial pressure. However, it can cause hypertension, hypotension, and bradycardia which are dose-dependent. Though there are studies comparing the two drugs, the quest for the most ideal drug for AC continues.

In our center, either the combination of propofol and fentanyl or dexmedetomidine and fentanyl as primary agents for sedation and analgesia in addition to scalp block for AC is used. Our primary objective was to compare the hemodynamic profile and perioperative complications between the two drugs, propofol and dexmedetomidine. The secondary objectives were to compare the feasibility of intraoperative neuromonitoring (IONM) and postoperative recovery.

Materials and Methods

After institutional research and ethics board approval (IRB min no: 10837, dated: 23/08/2017), we retrospectively reviewed all records of patients who underwent AC in our institution from January 2010 to January 2017. Data were retrospectively collected from the anesthesia records, operative notes, postoperative ICU ward records, and inpatient records.

Institutional Monitored Anesthesia Care Protocol

Either propofol at 75–100 μ g/kg/min or dexmedetomidine 1 μ g/kg over 20 minutes followed by 0.3–0.8 μ g/kg/min infusion is initiated. Fentanyl 0.5–1 μ g/kg is administered to make the patient calm and comfortable. The dose of the intravenous agent is titrated to achieve modified Observer's Assessment of Alertness/Sedation Scale (OAASS) between 5 (responds readily to words spoken in normal tone) during the awake neuro-

monitoring period and 2 (responds only after mild prodding or shaking) during the asleep phase. In the initial stages of anesthesia management, the depth of anesthesia monitors was not used in our institute but of late, we are using the Bispectral Index System (BIS) for all our patients and titrating it to a value between 60 and 80. A nasal cannula with 2 L of oxygen with end-tidal CO₂ measurement is placed for continuous respiratory rate monitoring for all patients undergoing AC. After ensuring adequate sedation, regional scalp block is administered for all patients initially with inj. lignocaine 2% 7 mg/kg with inj. adrenaline 5 μ g/mL and inj. ropivacaine 0.5% 2.5 mg/kg with inj. adrenaline 5 μ g/mL. The sedation is titrated after the bone flap removal and discontinued after dura opening. After the tumor resection, the sedation is again restarted to make the patient comfortable and additional analgesia is administered when required. Postoperatively, the patient is sent to the ICU for observation and monitoring.

Institutional Intraoperative Neuromonitoring Protocol

For brain mapping and functional IONM, a bipolar stimulator with the tips 5 mm apart is used for the cortical stimulation (Nicolet Biomedical Inc., Madison, WI, USA). A strip of electrodes is placed over the cortex near the stimulation zone to detect after-discharges during stimulation and if detected, the stimulating current is reduced to avoid generating an intraoperative seizure. The current of 1 mamp for 1 millisecond duration increasing by increments of 1 mamp to a maximum of 6 mamps is used until responses are obtained. Contralateral motor movements occur on stimulating motor areas and patients report paresthesia when the primary sensory area is stimulated. Language assessment is done by a neuropsychologist who administers the tests in the patient's native language. Naming, reading and serial counting, calculation and color naming tests are used for assessment. Sudden speech arrests can occur on stimulating the language areas. The cortical stimulation and brain mapping are done till the tumor resection is over, after which only clinical neurological monitoring to check for the patient's gross motor power and language function is done till the surgery is over.

Details of Intraoperative Data collection

Hemodynamics

The heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded.

Intraoperative Complications

Intraoperative complications such as hypotension (defined as fall in MAP by >20% from baseline), hypertension (defined as an increase in MAP by >20% from the baseline), bradycardia (decrease in HR < 60 bpm), tachycardia (sustained increase in heart rate requiring treatment), number of desaturation episodes (SpO₂ < 92%), pain requiring additional analgesics ([numeric rating scale (NRS) > 4]), agitation and deep sedation-induced loss of airway, requiring conversion to GA, the occurrence of intraoperative seizures, motor

deficit, aphasia, brain swelling requiring hyperosmolar therapy, were noted. Once the bone and dura are opened, the status of brain relaxation is evaluated with the 4-point scale grading by the surgeon, which includes 1: completely relaxed, 2: satisfactorily relaxed, 3: firm brain, and 4: brain bulge. Any incidence of brain bulge was also noted. Intraoperative blood loss was estimated and recorded by the anesthetist managing the case. It is usually determined by the visual inspection of the operative field, from the surgical suction bottles and the volume of blood in surgical drapes. Any significant blood loss requiring intraoperative blood transfusion was also noted.

IONM

The ability to record cortical stimulation using direct cortical stimulation with bipolar electrodes was noted as satisfactory/not satisfactory.

Postoperative Data

The number of episodes of postoperative nausea and vomiting (PONV), shivering and pain (NRS > 4). Neurological complications such as seizures, worsening of motor deficit (defined as a drop in motor score by one point), or a new-onset motor/sensory deficit or aphasia were extracted. The number of episodes of desaturation ($SpO_2 < 92\%$) or respiratory obstruction requiring rescue maneuvers during the ICU stay was recorded.

Statistical Analysis

Summary data are presented as mean (standard deviation) for normally distributed data and as median (interquartile range) if data were skewed. The parameters between the two groups were compared using *t*-test and Mann-Whitney *U* test for the continuous data and Chi-square/Fisher's exact test for the categorical data as appropriate. Statistical

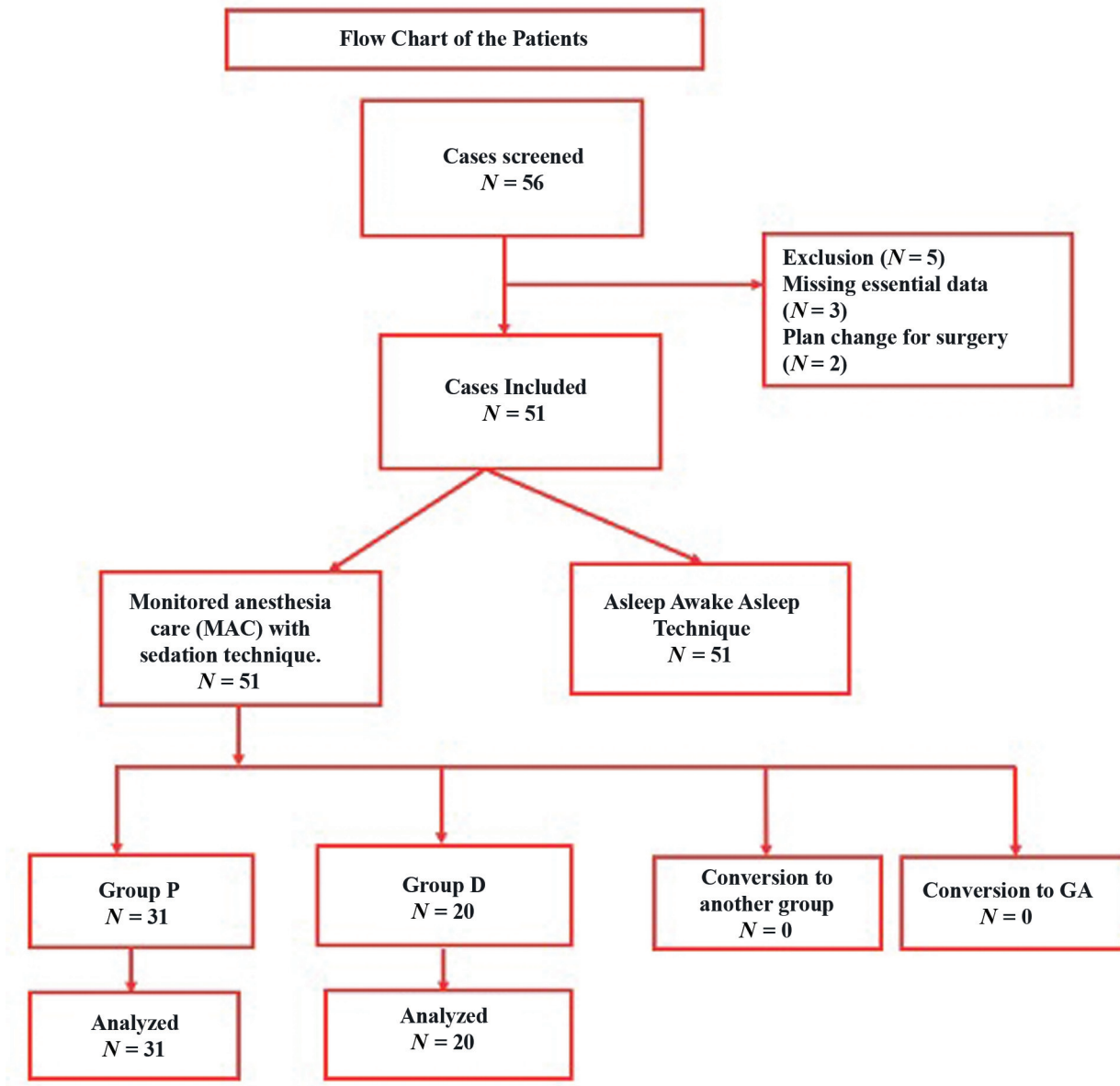


Fig. 1 Study flow chart.

significance was defined as $p < 0.05$. All statistical analyses were performed using the SPSS software version 25.0 (Chicago, SPSS inc.)

Results

A total of 56 patients' charts were screened, of which 51 were included for analysis (►Fig. 1). Nineteen patients had a frontal intracranial space-occupying lesion, 23 had parietal, and 7 had a temporal lesion. Their histological diagnosis included DNET (3.9%), pilocytic astrocytoma (1.9%), astrocytoma (19.6%), oligoastrocytoma (29.4%), oligodendroglioma (11.7%), anaplastic astrocytoma (19.6%), and glioblastoma multiforme (11.7%). The patient and surgical-related variables are depicted in ►Table 1. The youngest patient to undergo AC was a 14-year-old child who received dexmedetomidine. Only one patient, belonging to Group D required an ICU stay of > 1 day due to multiple episodes of seizures, in the postoperative period.

Hemodynamics

Only one patient in Group D had an episode of bradycardia after 15 minutes of starting the infusion, with a heart rate of 48 bpm from a baseline of 90 bpm persisting for a period of > 5 minutes despite stopping the infusion and needed intravenous atropine 0.6 mg. The surgery had not been initiated until then. The dexmedetomidine infusion was continued after the HR returned to normal. The change in SBP, DBP, and MAP between the two groups was comparable (►Table 2). One patient in Group D had intraoperative hypertension, which did not respond to fentanyl, propofol, and labetalol bolus and needed nitroglycerine infusion at 5

µg/min. which was titrated and stopped after the MAP returned within 20% baseline value.

Intraoperative Complications

Episodes of focal motor seizures were observed in three patients (5.8%) in Group D during cortical stimulation (►Table 3). Cold saline irrigation, a subanesthetic dose of propofol and midazolam were given to control the seizures. One patient developed focal motor seizures in the contralateral foot, whereas the other patient had behavioral confusion, and the third patient had two episodes of focal motor seizures involving the contralateral elbow and hand. All three had a preoperative history of seizure disorder and were given the regular morning dose of the antiepileptic agent.

Episodes of transient desaturation (fall in SpO₂ < 92%) was observed in three patients in Group P (9.7%) and one patient in Group D (5%). Simple airway maneuvers such as chin lift and jaw thrust and dose reduction of sedative agents were needed to treat the hypoxia and none required conversion to GA.

Intraoperative brain bulge was present in one patient in Group D, which was treated with further elevating the head by 15 degrees, mannitol administration (0.5 g/kg), and by asking the patient to hyperventilate by himself. One patient experienced pain, and discomfort which was treated with an additional bolus of fentanyl and by the local infiltration with lignocaine by the surgeon.

The neurological deficits were observed in nine patients (29%) belonging to Group P and three patients (15%) in Group D. Aphasia in the form of sudden speech arrest was observed in two patients (6.4%) in Group P and one (5%) belonging to Group D. Only one patient persisted to have aphasia and

Table 1 Demographic details between two sedative agents propofol and dexmedetomidine

Parameters (Mean ± SD)	Group P (N = 31)	Group D (N = 20)	p-Value
Age (y)	39.42 ± 11.40	35.75 ± 11.40	0.26
Weight (kg)	63.97 ± 15.83	66.08 ± 11.33	0.60
Height (cm)	163.19 ± 10.54	162.85 ± 7.18	0.89
BMI	24.54 ± 4.64	24.83 ± 3.74	0.81
Sex (male:female) Number (%)	23:8 (74.1%: 25.8%)	14:6 (70%: 30%)	0.743
ASA Status I:II:III Number (%)	9:21:1 (29%: 67%:3%)	12:8:0 (60%:40%:0)	0.077
Side of the lesion Right:left Number (%)	13:18 (41.9%:58%)	13:7 (65%:35%)	0.10
Duration of surgery (h) Median (IQR)	2 (2–3)	2.5(2–3)	0.42
ICU stay (days) Mean ± SD	1.03 ± 0.18	1 ± 0.0	0.42
Hospital stay (days) Median (IQR)	4(3–5)	3(3–6)	0.79

Significant $p < 0.05$.

Table 2 A comparison of the hemodynamic variables such as heart rate, systolic blood pressure, mean arterial pressure, and diastolic blood pressure between propofol and dexmedetomidine

Time	Group	HR (mean ± SD)	p-Value	SBP (mean ± SD)	p-Value	MAP (mean ± SD)	p-Value	DBP (mean ± SD)	p-Value
Baseline	P	97.87 ± 15.31	0.67	131.42 ± 13.95	0.36	96.4 ± 10.09	0.89	79.03 ± 9.6	0.67
	D	96.25 ± 9.13		135.20 ± 14.97		96.9 ± 12.14		77.75 ± 12.20	
15 min	P	94.35 ± 16.87	0.26	129.84 ± 14.16	0.86	95.1 ± 9.94	0.25	77.74 ± 9.21	0.80
	D	89.00 ± 15.91		130.55 ± 14.97		94.8 ± 11.64		77.00 ± 11.93	
30 min	P	95.45 ± 15.95	0.07	125.65 ± 14.74	0.52	89.6 ± 9.9	0.45	71.65 ± 9.25	0.52
	D	87.30 ± 15.21		128.45 ± 16.66		91.7 ± 9.14		73.35 ± 9.23	
1 h	P	94.68 ± 15.81	0.022*	126.23 ± 16.56	0.57	87.9 ± 11.91	0.44	68.77 ± 10.98	0.41
	D	85.10 ± 11.07		128.95 ± 16.64		90.4 ± 10.03		71.15 ± 8.54	
2 h	P	88.52 ± 21.82	0.27	121.81 ± 18.06	0.94	87.0 ± 13.3	0.68	69.71 ± 11.83	0.45
	D	82.95 ± 8.84		122.15 ± 11.58		85.7 ± 4.9		67.60 ± 4.38	
3 h	P	90.12 ± 12.68	0.042*	120.76 ± 9.97	0.74	86.2 ± 9.6	0.72	69.60 ± 10.67	0.81
	D	81.00 ± 7.00		122.10 ± 10.60		87.5 ± 6.6		70.00 ± 6.55	
4 h	P	81.00 ± 1.41	0.20	117.50 ± 10.60	0.91	82.5 ± 8.2	0.73	65.00 ± 7.07	0.58
	D	70.00 ± 9.16		119.33 ± 20.03		86.2 ± 12.2		69.67 ± 8.96	

*Significant $p < 0.05$, D, Group D; DBP, diastolic blood pressure; HR, heart rate; P, Group P; MAP, mean arterial pressure; SBP, systolic blood pressure.

Table 3 Intraoperative complications between two sedative agents propofol and dexmedetomidine

Intraoperative complications	Group P	Group D
	Total Number = 31	Total Number = 20
Bradycardia	0	1 (5%)
Hypertension	0	1 (5%)
Desaturation	3 (9.6%)	1 (5%)
Brain bulging	0	1 (5%)
Bleeding	1 (3.2%)	0
Pain	1 (3.2%)	0
Seizures	0	3 (15%)
Motor deficit	9 (29%)	3 (15%)
Aphasia	2 (6.4%)	1 (5%)
Total	10 (32.2%)	6 (30%)

manifested as the Gerstmann syndrome in the postoperative period. A transient neurological deficit was observed in one patient with left frontal glioma who belonged to Group P. This patient had right upper limb weakness, which was observed after the tumor resection and during the dural closure when the propofol was restarted, which improved 20 minutes after stopping the propofol infusion.

IONM

The feasibility of IONM was found in 24 patients (80%) in group P and 17 patients (85%) in group D ($p = 0.65$).

Postoperative Data

The incidence of postoperative complications was compared between the groups and it is depicted in ► **Table 4**.

Discussion

It has been shown that propofol has been widely used to provide sedation for awake craniotomy with the advantage of easy titration, antiemetic properties, and lower incidence of seizures.⁴ In our study, the number of patients who received propofol was higher compared with dexmedetomidine, and the incidence of seizure was seen to be lower with propofol.

Our study revealed that the BP was comparable between the two groups, and HR was lower in Group D, similar to other study results.^{5,6} Only one patient in Group D who had relatively resistant hypertension had a baseline BP of 150/102 mm Hg. This patient was not a known hypertensive and the hypertension can probably be attributed to anxiety. Dexmedetomidine is also known to evoke a biphasic response resulting in an initial hypertensive response due to its action on the α -2B adrenergic receptor (AR) receptors, which could have further exacerbated the high initial BP.

The use of propofol has been associated with a higher incidence of respiratory depression during AC.^{5,7} Our study also proved the same finding. The incidence of intraoperative seizures was observed only in Group D during cortical stimulation. Though this was not found to be statically significant presumably because of less sample size, it can be considered as a clinically relevant finding as intraoperative seizures in neurosurgical patients with skull fixation can be associated with significant morbidity. The lesser incidence of intraoperative seizure in the Group P might be

Table 4 Postoperative complications between two sedative agents propofol and dexmedetomidine

Postoperative complications	Group P	Group D
	Total Number = 31	Total Number = 20
Bradycardia	0	0
Tachycardia	1 (3.2%)	0
Hypertension	1 (3.2%)	0
Hypotension	0	0
Pain	0	0
Shivering	0	0
PONV	1 (3.2%)	0
Seizures	2 (6.4%)	1 (5%)
Motor deficit	10 (32.2%)	7 (35%)
Aphasia	2 (6.4%)	1 (5%)
Total	17 (54.8%)	9 (45%)

due to its anti-epileptic properties. Ghazaway et al also reported the protective effect of propofol against seizures during awake craniotomy.⁷ Also, there is emerging evidence that dexmedetomidine use has been independently associated with the occurrence of intraoperative seizures leaving scope for further research to understand the association.⁸

Özlü has reported a high incidence of pain (30%) despite adequate scalp block.⁹ In our study, the incidence of moderate pain during surgery was extremely low (one patient, 5%) compared with the incidence quoted in the literature, which could be due to the performance of scalp block by the experienced neuroanesthesiologist.

Sokhal et al in their retrospective study, had one patient with severe brain bulge for which conversion to GA was needed.¹⁰ Hypoventilation, airway obstruction, and hypercarbia are some of the anesthetic factors which can lead to brain swelling, and perilesional edema, venous air embolism leading to coughing in an awake patient, seizures, and hematoma are the surgical factors.⁹ In our study, a brain bulge was observed in Group D, which causes less respiratory depression and airway complications as compared with propofol and so the cause was attributed to neurological or surgical-related factors. There was no increase in EtCO₂ value as measured by the nasal cannula and hence hypercarbia was ruled out. His preoperative MRI brain with contrast showed a diffuse, 5 × 4.5 × 2 cm lesion in the right supplementary motor area with perilesional edema. This patient had intraoperative seizures twice in the form of focal motor seizures of contralateral upper limbs. Intraoperative brain bulge can be attributed to this. In our institute, if the brain scan reveals perilesional edema or mass effect, the requirement of osmotherapy during the surgery is discussed with the surgeons in the preoperative period. These patients are catheterized on the night before the procedure.

Mild exacerbation or unmasking of focal neurological deficit in the form of limb weakness and ataxia has been reported with midazolam and propofol compared with fentanyl and dexme-

detomidine, especially in patients with high-grade glioma.¹¹ In our study, one patient had delayed motor deficit when the propofol was restarted during the surgical closure, which resolved 20 minutes after stopping the propofol. This patient had presented with a left frontal opercular tumor, and Broca's area was located with cortical stimulation. During the tumor resection, there were no motor deficits or speech arrest, but he developed a right upper limb weakness when the propofol infusion was initiated during closure. It has been found that brain remodeling occurring as a result of tumor development can alter synaptic and intracortical connectivity, which is presumably compensated. It has been speculated that this compensation may get suppressed during a sedative administration.¹¹ Moreover, propofol through its GABAergic mechanism can alter the dopamine and serotonergic activity, which are the two important neurotransmitters associated with brain reorganization and post-injury plasticity that may occur as a consequence of the tumor.^{11,12} Dexmedetomidine has been observed to produce the least effect on the focal brain function, which can be because of its highly selective action on locus coeruleus.¹¹ Because propofol can exacerbate the focal neurological deficit, the extent of tumor resection can vary between the groups.

IONM is an essential component of the procedure to ensure the maximum resection with minimum postoperative deficits. In this study, the ability to perform intraoperative brain mapping was comparable using propofol and dexmedetomidine, which is similar to the findings by Goettel et al.⁵

There are some limitations to our study. This is a retrospective study with small sample size. Episodes of hemodynamic fluctuations and respiratory depression could be underreported. It is difficult to quote the incidence of anesthetic-induced complications based on the retrospective data. The patient satisfaction and surgical satisfaction scores of the overall procedures were not noted. We did not compare the extent of tumor resection between the groups.

Conclusion

MAC with conscious sedation combined with scalp block was the primary anesthetic technique utilized for AC. Both propofol and dexmedetomidine provided better quality sedation while ensuring the maximum comfort and safety of the patient. The incidence of seizure is lower with propofol compared with dexmedetomidine. Cortical stimulation and brain mapping were successfully possible with both agents. Careful patient selection, titrated sedation with anesthetics, and vigilant monitoring provide successful outcomes.

Conflict of Interest

None declared.

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