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ORIGINAL ARTICLE

Perioperative anesthetic implications of epilepsy surgery: a retrospective analysis

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Abstract

Purpose Drug-resistant epilepsy (DRE) occurs in about 30 % of individuals with epilepsy. For seizure control, a wide range of surgical procedures are performed, depending on the underlying pathology. To address the anesthetic and perioperative concerns in these patients, we analyzed the data of persons with DRE who underwent epilepsy surgery at our institute.

Methods A retrospective analysis of patients who underwent epilepsy surgery from 2005–2010 was performed. For data collection and analysis, patients were divided into three groups: Group I (temporal lobe epilepsy), Group II (extratemporal lobe epilepsy), and Group III (multilobar epilepsy and others).

Results A total of 241 surgical procedures were performed on 235 persons with DRE. The procedures included temporal (149) and extratemporal (47) lobe resection, hemispherotomy (31), corpus callosotomy (5), vagus nerve stimulation (3), and implantation of invasive cerebral electrodes (6). General anesthesia was the more common anesthetic technique; awake craniotomy was performed in only five cases. Intraoperative neuromonitoring was used most frequently in Group II. Patients in Group III had the longest intraoperative course and the greatest blood loss. The overall incidence of postoperative mechanical ventilation was 17.84 %, with 53.84 % of patients in Group III alone. At one-year follow-up, a good outcome was seen in 78 % of temporal lobe resection, 55 % of extratemporal cortical resection, 82 % of hemispherotomy, and 80 % of corpus callosotomy procedures.

Conclusions Careful preoperative selection and meticulous perioperative management are the most significant factors for success of epilepsy surgery. Although temporal and extratemporal lobe surgeries have a fairly stable perioperative course, multilobar epilepsy requiring disconnective surgery poses a greater challenge.

Keywords Anesthesia · Drug-refractory epilepsy · Epilepsy surgery · Perioperative course

Introduction

Epilepsy imposes a major social and economical burden on society. Over 50 million people globally suffer from epilepsy, 80 % of whom live in developing countries, and 30–40 % of patients have drug-resistant epilepsy (DRE). Surgery offers a benefit in about 10–20 % of cases, but is available to only 1 % of these patients [1]. The benefits of surgery include better seizure control and better quality of life [2]. Although the expense of a surgical procedure is discouraging, the past few decades have seen rapid advances in the surgical management of epilepsy, making it a safe and cost-effective choice. Many developing countries, including India, have organized epilepsy programs that make epilepsy surgery available to a large number of patients at reasonable costs [3].

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The surgical management and neurological complications in patients undergoing epilepsy surgery is documented in the literature, but anesthetic course and perioperative complications are less well-described. Anesthesia and the perioperative period of epilepsy surgery poses a variety of challenges, including unique patient profile, associated comorbidities, a wide spectrum of surgical procedures, and the need for intraoperative neurological monitoring. In addition, the general principles of neuroanesthesia, such as maintenance of intracranial hemodynamics, cerebral protection, and rapid neurological recovery, cannot be overemphasized. The present article addresses these issues, as understanding them will result not only in better patient management, but it will also help to counsel patients regarding what to expect in the perioperative period as well as possible benefits and the risks involved.

Materials and methods

After clearance was obtained from the Institutional Ethics Committee, data were analyzed for patients undergoing epilepsy surgery from January 2005 to December 2010. Preoperative screening was performed by a neurologist, and the criterion for DRE was defined as seizures refractory to two or more appropriate antiepileptic drugs (AED) in adequate doses for at least two years. All cases were discussed for possible surgery in a weekly epilepsy surgery case conference, and patients underwent a standard workup, including electroencephalography (EEG), video EEG, magnetic resonance imaging (MRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), and subtraction ictal SPECT co-registered to MRI (SISCOM), depending upon the type and location of lesion.

Anatomical grouping: for comparison, the patients were divided into three groups

- Group I (temporal lobe epilepsy: TLE): patients with lesions in the temporal lobe (mesial temporal sclerosis, dysembryoplastic neuroepithelial tumor (DNET), cavernoma, etc.)
- Group II (extratemporal lobe epilepsy: ETLE): patients with a pathology in areas other than the temporal lobe.
- Group III (multilobar epilepsy and others): patients with involvement of multiple sites in ≥2 lobes of the brain (hypothalamic and cerebellar hamartomas).

Detailed data collection pertaining to preanesthetic evaluation, intraoperative course, and postoperative follow-up was completed for each patient. The preoperative data included age, sex, weight, relevant history, including duration of epilepsy, history of neurological insult, and neurological deficits. The intraoperative data included type and duration of surgery, anesthesia, anesthetic technique, use of invasive hemodynamic monitoring, electrocorticography (ECoG), blood loss, and transfusion. Intraoperative complications such as bradycardia (heart rate [HR] ≤20 % of baseline value), tachycardia (HR ≥20 % of baseline value), hypotension (systolic blood pressure [SBP] ≤20 % of baseline value), hypertension (SBP ≥20 % of baseline value), brain bulge, hypothermia (body temperature <35 °C), and hyperthermia (body temperature >38 °C) were also noted. The postoperative data included occurrence of nausea and vomiting, seizures, fever, duration of mechanical ventilation, electrolyte disturbances, intensive care unit (ICU) and hospital stay, and seizure control at discharge and at one-year follow-up. Acute postoperative seizures (APOSs) were defined as seizures occurring in the immediate postoperative period. Postoperative seizure control was classified on the basis of presence or absence of seizure until discharge from the hospital. Seizure control at one year was classified in a range according to the Engel rating scale as free of disabling seizure (Engel class I), rare disabling seizure (Engel II), worthwhile improvement (Engel III), or no worthwhile improvement (Engel class IV) [4].

Statistical analysis

All data were analyzed using the SPSS version 15 software and are presented as mean (SD) or median (range). The categorical data are presented as frequency (percentage). The categorical data were analyzed using the chi-squared or Fisher's exact test, as applicable. The continuous data were analyzed by applying one-way analysis of variance (ANOVA), followed by post hoc comparison using the Bonferroni method. The skewed data were analyzed using the Kruskal–Wallis test. Log transformation was applied to normalize the data. A value of $p < 0.05$ was considered significant.

Results

A total of 241 procedures were performed on 235 consecutive patients of a single neurology unit. Of these, 149 (63.40 %) patients had TLE, 47 (20 %) had ETLE, and 39 (16.59 %) had multilobar involvement. The surgical procedures performed included temporal (149) and extratemporal lobe resection (47), hemispherotomy (31), corpus callosotomy (5), vagus nerve stimulation (3), and implantation of invasive electrodes for chronic electrocorticography (6). The demographic data are presented in Table 1. The age of the patients ranged from 1 to 52 years, the mean age was 19.41 (10.533) years, and mean and median weight

Table 1 Demographic data of patients in the three groups

	Group I (temporal lobe epilepsy) $n = 149$	Group II (extratemporal epilepsy) $n = 47$	Group III (multilobar epilepsy) $n = 39$	p value
Age at onset of seizure (years)	11.1 ± 9.1	6.2 ± 7.1	4.0 ± 5.0	<0.01*
Gender (M:F)	89:60	36:11	22:17	0.08
Weight (kg)	52.2 ± 16.4	47.0 ± 21.3	34.0 ± 21.1	<0.01**

* Between Groups I & II and I & III

** Between Groups I & III and II & III

was 48.14 (19.4) and 50 (1–92) kg, respectively. The history of neurological insult (febrile seizures, perinatal hypoxia, preterm/premature birth, CNS infection, head injury) was present in 28 (18.79 %), 15 (31.91 %), and 18 (46.15 %) patients with TLE, ETLE, and multilobar epilepsy, respectively. Thirty-four (22.81 %) patients with TLE, 18 (38.29 %) patients with ETLE, and 30 (76.92 %) patients in the multilobar epilepsy group had some form of neurological deficit at the time of presentation.

In the preoperative period, AEDs were continued until morning and on the day after surgery in all patients. Four patients with multilobar epilepsy had status epilepticus and were on midazolam infusion. Three of these patients were operated for hemispherotomy, and one underwent chronic ECoG recording. Standard ASA monitoring was performed intraoperatively in all cases. Invasive arterial monitoring was performed in 83 % and central venous access obtained in 21 % of cases. Propofol was used for induction in 121 (50 %), thiopentone in 72 (29.75 %), and sevoflurane in 49 (20.24 %) procedures. Isoflurane was used for maintenance of anesthesia in 197 (81.40 %) procedures, followed by propofol in 30 (12.39 %) and sevoflurane in 15 (6.19 %).

ECoG-guided resection was performed in 65 patients, during which 38 (58.46 %) patients received inhalational anesthetics (inspired concentration of isoflurane 0.25–1.25 %), five patients underwent awake craniotomy, and the remainder received propofol-based intravenous anesthesia. Intracranial electrodes for chronic invasive monitoring were placed in six patients in Group II under general anesthesia. The duration of postoperative monitoring ranged from one to five days. One patient in this group developed meningitis, aspiration pneumonia, and prolonged ventilation, followed by death.

Surgery duration, anesthesia, and blood loss and other complications are tabulated in Table 2. Group III patients had the longest duration of anesthesia and suffered the most blood loss. The most frequent complications in this group were intraoperative hypotension and hypothermia. There was a significant association between hypothermia and surgery in all three groups ($\chi^2 = 6.98$, $p < 0.05$). The percentage of patients suffering from hypothermia was different among the three groups. To identify the significant pair of groups, partitioned chi-squared analysis was applied for Groups I and II, II and III, and I and III. The results suggest that the difference in percentage of hypothermia between Groups I and III (i.e., TLE and multilobar epilepsy) was statistically significant ($\chi^2_{\mathrm{I\ \&\ III}} = 7.01$, $p < 0.05$). However, the differences between Groups I and II, (i.e., TLE and extratemporal epilepsy ($\chi^2_{\mathrm{I\ \&\ II}} = 0.59$, $p > 0.05$) and II and III (i.e., extratemporal epilepsy and multilobar epilepsy) ($\chi^2_{\mathrm{II\ \&\ III}} = 2.35$, $p > 0.05$) were not statistically significant. Long duration of surgery, high exposed body surface area, and major fluid shifts in pediatric patients were responsible for hypothermia. Even mild intraoperative hypothermia could result in increased surgical bleeding as well as prolongation of drug metabolism, leading to delayed awakening. Therefore, prevention of hypothermia was an important concern in this group.

Delayed extubation and elective ventilation was a significant problem in Group III, and was seen in 19 of the 31 patients who underwent hemispherotomy. The cause of delayed extubation was long duration of surgery, with major fluid shifts (8), drowsiness (8), and perioperative seizure (3). Excessive postoperative drowsiness in patients with hemispherotomy was correlated with the use of clobazam. Of 31 patients, 28 were on clobazam, along with other AEDs. Clobazam dosage was reduced over the following 4–5 days in order to increase alertness. Overall, 17.84 % of patients required mechanical ventilation in the postoperative period, and 53.84 % of these belonged to Group III (19 hemispherotomy, 3 corpus callosotomy). The duration of ventilator stay ranged from five hours to five days (median, 12 hours). The postoperative course and length of intensive care and hospital stay are depicted in tabular form in Tables 3 and 4.

APOSs were seen in 15 % of patients: 60 % ETLE, 22 % TLE, and the remainder in the multilobar group. Three patients had intraoperative seizure during awake craniotomy that responded to cold saline irrigation. Seizure control at discharge was 87.24 %, 63.82 %, and 76.92 % in Groups I, II, and III, respectively. At one-year follow-up, a good outcome (Engel I and II) was seen in 78 % and 55 % of temporal and extratemporal lobe resection, respectively,

Table 2 Intraoperative variables of the three groups [number (percentage)]

	Group I (temporal lobe epilepsy) $n = 149$	Group II (extratemporal epilepsy) $n = 53^{a}$	Group III (multilobar epilepsy) $n = 39$	p value
Hypertension	29 (19.46)	06 (11.32)	04 (10.25)	0.3
Hypotension	20 (13.42)	05 (9.43)	10 (25.64)	0.1
Bradycardia	14 (9.39)	04 (7.54)	02 (5.12)	0.6
Hypothermia	24 (16.10)	11 (20.75)	14 (35.89)	0.03**
Brain bulge	02 (1.34)	01 (1.88)	–	0.7
Duration of anesthesia (min)	307 ± 66	310 ± 78	450 ± 128	<0.01***
Duration of surgery (min)	243 ± 67	250 ± 68	410 ± 83	<0.01***
Blood loss (ml)	275 ± 167	252 ± 186	380 ± 258	<0.01****

A value of $p < 0.05$ was considered significant

** Clinically between Groups III & I and III & II ($p = 0.03$), statistically significant with Group I ($p = 0.008$) only

*** Between Groups I & III and II & III

**** Between Groups II & III

[a] In Group II, 6 patients underwent diagnostic subdural grid placement for invasive video EEG recordings, followed by definitive surgery, bringing the total number of procedures to 53

Table 3 Postoperative complications in the three groups [number (percentage)]

	Group I (temporal lobe epilepsy) $n = 149$	Group II (extratemporal epilepsy) $n = 53^{a}$	Group III (multilobar epilepsy) $n = 39$	p value
Postoperative ventilation	11 (7.38)	11 (20.75)	21 (53.84)	<0.001**
Postoperative nausea vomiting	06 (4.02)	03 (5.66)	–	0.3
Hypernatremia	–	02 (3.77)	–	0.3
Hyponatremia	03 (2.01)	01 (1.88)	–	0.7
Fever	19 (12.75)	09 (16.98)	11 (27.50)	0.08
Respiratory complications	–	01 (1.88)	02 (5.12)	0.03

** Significant with all pairs

[a] In Group II, 6 patients underwent diagnostic subdural grid placement for invasive video EEG recordings, followed by definitive surgery, bringing the total number of procedures to 53

Table 4 Outcome of patients following surgery [median (range)], [number (percentage)]

	Group I (temporal lobe epilepsy) $n = 149$	Group II (extratemporal epilepsy) $n = 47$	Group III (multilobar epilepsy) $n = 39$	p value
ICU stay (days)	02 (1–10)	02 (1–8)	03 (1–10)	<0.01*
Hospital stay (days)	07 (3–28)	07 (1–20)	12 (2–37)	<0.01*

* Between Groups I & III and Groups II & III

82 % in hemispherotomy, and 80 % in corpus callosotomy procedures. One patient with cerebellar hamartoma and three patients with frontal cortical dysplasia required a second surgery.

Discussion

In developing countries, there is a wide surgical treatment gap, as few centers are involved in the surgical management of DRE [5]. Little is known with regard to the anesthetic concerns and intensive care involved. The present article addresses perioperative concerns and complications in patients who underwent epilepsy surgery at a tertiary care center in India.

Both awake and general anesthetic techniques are used for epilepsy surgery. The choice of technique depends on the use of intraoperative functional neurological testing to define the extent of corticectomy. Although awake craniotomy is better for such testing, general anesthesia offers the advantage of comfort, for both patient and surgeon, in cases with well-demarcated seizure focus on preoperative structural and functional mapping [6]. With advances in specialized neuroimaging facilities, more cases are considered for general anesthesia. In our series, ‘awake craniotomy’ for epilepsy was performed in five patients with lesions near the eloquent cortex. Bispectral index (BIS)-titrated propofol was used for the ‘asleep–awake–asleep’ technique in these cases. This has been shown to be safe in a large series of patients [7].

Although co-registration of imaging modalities is increasingly used to delineate seizure focus, ECoG remains an important tool for defining the epileptogenic zone and guiding its complete resection [8]. However, anesthetic agents may interfere with ECoG due to their inherent anticonvulsant and proconvulsant properties [9]. Isoflurane, with or without nitrous oxide, remains a commonly used anesthetic agent during ECoG recordings [10–12]. We used a low concentration of isoflurane (0.25–1.25 %) during ECoG. We have previously reported optimal recordings with the BIS-titrated dose of either isoflurane or propofol without nitrous oxide [12]. Use of sevoflurane has been associated with generation of widespread irritative response and thus is not favored [13]. While some centers elicit intraoperative seizure activity with drugs, we do not practice it [14]. Chronic invasive cerebral monitoring is performed in patients who have had inconclusive noninvasive investigations, dual pathology, or discordant noninvasive data. Placement of intracranial electrodes carries the risk of meningitis, subdural or intracranial hematoma, and herniation [15, 16].

A number of procedures are performed under the ambit of epilepsy surgery, and temporal lobe remains, by far, the most common culprit [17]. In addition, in our study, patients with TLE formed the largest group of surgical candidates. This group had a fairly stable perioperative course. Few patients required short-term ventilator support, and their overall ICU and hospital stay was the shortest among the three groups. There is also good evidence in support of surgery for ETLE. This group of patients required more intraoperative neurophysiological monitoring to demarcate the areas of resection. Cases with an epileptogenic zone near the eloquent cortex were taken up for awake craniotomy, the remainder were operated under general anesthesia, and ECoG was used for intraoperative localization of the epileptogenic zone.

Patients in Group III underwent disconnective procedures such as hemispherectomy/hemispherotomy and corpus callosotomy. These procedures are based on the interruption of the epileptic network rather than removal of the epileptogenic zone. These patients required more vigilance. Functional hemispherotomy techniques have gradually replaced cerebral hemispherectomy, as the latter is associated with greater morbidity and mortality due to massive blood loss, electrolyte and metabolic disturbances, coagulopathy, cerebral hemorrhage, and seizure [18–21]. In our series, 36 disconnective surgeries were performed, which included hemispherotomy (31) and corpus callosotomy (5). This group of patients had the longest duration of anesthesia and the greatest blood loss. Many authors suggest delayed extubation in these patients due to the need for large-volume resuscitation and the high potential for postoperative complications [22]. In our series, long operative time, major blood loss, and hypothermia also hampered early recovery in these patients.

Implantation of a vagus nerve stimulation device is used to control intractability [23]. In light of the modest seizure control achieved, the cost involved, and palliative nature of the procedure, it is not widely used in developing countries. At our center, three patients underwent left vagus nerve stimulation under general anesthesia. The perioperative course was uneventful. Although rare, intraoperative severe bradycardia, cardiac arrest, and vocal cord and laryngeal muscle dysfunction have been reported with vagus nerve stimulation [24, 25].

Varying levels of success in seizure control have been reported after surgical treatment of epilepsy, depending upon the underlying pathology and type of procedure. Tellez-Zenteno et al. reported long-term seizure control of 66 %, 46 %, and 27 % with temporal, occipitoparietal, and frontal lobe resections, respectively. Only 35 % of patients with DRE were free of disabling seizure after corpus callosotomy [26]. Our results at one-year follow-up are comparable to those described in the literature.

To conclude, although the data analyzed in this study are retrospective in nature and with limited follow-up, our primary aim was to identify the perioperative turbulence in managing these patients. When surgery is performed in a center with adequate resources and expertise for team management of perioperative care, operative complications are negligible, and surgery for epilepsy can be safely offered.

Conflict of interest None.

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