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Postoperative Neurological Complications after a Cranial Surgery: A Multicentre Prospective Observational Study

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Abstract

Background Cranial surgery is associated with multiple postoperative complications varying from simple nausea and vomiting to devastating complications such as stroke and death. This multicentre collaborative effort was envisioned to collect observational data regarding postoperative complications in cranial surgeries among the Indian population. The aim of this study was to describe the postoperative neurological complications occurring within the first 24 hours after surgery and to identify the predictive factors.

Methods Data was collected from three participating tertiary care academic institutions. The study was prospective, observational, multicentre design with data collected over a period of two months or 100 cases, whichever is earlier, from each participating institute. A predesigned Microsoft excel sheet was distributed among all three centers to maintain uniformity. All patients aged 18 years and above of both sexes undergoing elective or emergency craniotomies were included in the study. The postoperative neurological complications (within 24 hours) assessed were: (1) Neurological deficit (ND) defined as new focal neurological motor deficit relative to preoperative status. (2) Sensorium deterioration (SD) defined as reduction in Glasgow coma score (GCS) by 2 or more points compared with preoperative GCS. (4) Postoperative seizures (SZs) defined as any seizure activity. All possible variables associated with the above neurological complications were tested using Chi-square/Fisher exact test or Mann–Whitney U test. The predictors, which were statistically significant at $p < 0.2$, were entered into a multiple logistic regression model. Alpha error of 5% was taken as significant.

Results Data from three institutions was collected with a total of 279 cases. In total, there were 53 (19%) neurological complications. There were 28 patients with new postoperative NDs (10.04%), 24 patients had SD (8.6%), and 17 patients had seizures (6.1%). Neurological deficits were significantly less in institution 2. Diagnosis

Keywords
- postoperative complications
- neurosurgery
- neurological deficit

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of traumatic brain injury (TBI) was associated with very low risk of ND, and vascular pathology was associated with higher chance of a ND. The duration of anesthesia was found to be significantly predictive of SD (OR/CI = 1.01 / 1–1.02). None of the factors were predictive of PS.

Conclusion The incidences of postoperative ND, SD and postoperative seizures were 10%, 8.6%, and 6.1%, respectively. Studies with a much larger sample size are required for a better and detailed analysis of these complications.

Introduction

Neurosurgery is associated with high-rates of mortality and morbidity, due to the complexity of brain structures. The complications can range from mild postoperative nausea and vomiting to devastating neurological deterioration. Many times the complications are analyzed in a specific group of patients. A large number of studies have been dedicated to reporting specific complications in specific subgroups of surgeries.[1-7] However, it is important to have an overview of all the complications occurring in a neurosurgical setup, which will help in planning and execution of measures required for effective management of neurosurgical patients. Such data are currently lacking in India. This multicenter collaborative effort was envisioned to collect observational data regarding postoperative complications within 24 hours in cranial surgeries among the Indian population and also, to identify the predictive factors for those complications.

Methods

Three institutes participated in the study. They are National Institute of Mental Health and Neuro Sciences, Bangalore; All India Institute of Medical Sciences, New Delhi; and Postgraduate Institute of Medical Education and Research, Chandigarh. Data was collected after obtaining the ethics committee approval from the respective institutes. All the three institutes are tertiary care academic institutes. All three institutes have DM Neuroanesthesia training program and all possess advanced multimodality neuromonitoring facilities. The study was of a prospective, observational, multicentre design, with data collected over a period of two months or 100 cases, whichever is earlier, from each participating institute. The data was collected from all the institutes in the same year, was collected in a paper format and entered into a predesigned Microsoft excel sheet. The excel sheet was designed by the investigators and distributed among all the three centers to maintain uniformity in the data capture. The relevant explanations for the parameters were given in the excel sheet itself. Data confidentiality was assured by excluding any patient identifiers from the worksheet.

All the patients aged 18 years and above of both sexes undergoing elective or emergency craniotomies during the designated month were included in the study. The data included multiple variables collected preoperatively, intraoperatively, and at one hour and 24 hours, postoperatively. In this study, we intended to describe the postoperative neurological complications that occurred within the first 24 hours after surgery and finding out the predictive factors for those complications. The postoperative neurological complications assessed were: 1. Neurological deficit (ND) defined as new focal neurological motor deficit in the immediate postoperative period (24 hours) relative to preoperative status. 2. Deterioration of sensorium (SD) defined as reduction in Glasgow coma score (GCS) by 2 or more points (within 24 hours postoperatively) compared with preoperative GCS. 3. Postoperative seizures (SZs) defined as any seizure activity detected within 24 hours in the postoperative period.

Statistical Analysis

Data was compiled in a Microsoft Excel worksheet and analysis was conducted on R software version 3.5.2.[8] In this study, the analysis was restricted to only neurological complications, that is, postoperative new NDs, postoperative SD (fall in GCS more than 2 points compared with baseline), and postoperative seizures, in the first 24 hours after craniotomy. All possible variables (both preoperative and intraoperative) associated with the above neurological complications were analyzed. They were initially tested using Chi-square/Fisher exact test or Mann–Whitney U test. The predictors which were found statistically significant at $p < 0.2$ for the respective complications were entered into a multiple logistic regression model (using *glm* function of R). Due to high-multicollinearity between multiple variables on account of low-event rates of some factors, the model estimates and confidence intervals were found to be unstable (large standard errors and coefficients). Hence, penalized logistic regression using Firth method was used to run the same models (using package *logistf* for R).[9] This method reduces variability of estimates. The regression estimates were more stable. To improve generalizability of the results, bootstrapping of the dataset was done to obtain 1000 datasets, and variability of coefficients (95% confidence intervals) was inferred, while correcting for bias induced with repeated resampling (using package *boot* for R).[10] Results of both modelling procedures (Firth and bootstrapped Firth) are presented in the form of odds ratios. The nominal data are presented as percentages, and interval/ordinal scale

data presented as median and interquartile range. Alpha error of 5% was taken as significant.

Results

Data was collected from 279 cases (institution 1 = 110, institution 2 = 100, institution 3 = 69). The total number of neurological complications was 53 (19%). There were 28 patients with new postoperative ND (10.04%), 24 patients had SD (8.6%), and 17 patients had seizures (6.1%). There were few patients who had two complications together. However, no patient had all the three complications. The demographic details are given in ►**Table 1**. The univariate tests of association of putative predictors with the outcome variables are provided in ►**Supplementary Table S1** (ND), **S2** (SD) and **S3** (SZ) (available in the online version).

New Neurological Deficits

The factors which were found significant (at $p < 0.2$) on univariate analysis were included in the multivariate model. These included diagnosis, preoperative comorbidities, intraoperative opioid used, intraoperative bradycardia, hypoxia, hypercapnia, potassium level change, coagulopathy, institution, and duration of anesthesia. Of these, intraoperative potassium level change and coagulopathy were excluded due to low-event rate for the dependent variable. The model was found to be significantly better than a model of no effect ($p < 0.001$).

The model coefficients are shown in ►**Table 2**. Factors found significant after bootstrapping were institution and diagnosis. NDs were significantly less in institution 2 compared with institution 1. Diagnosis of traumatic brain injury (TBI) (compared with supratentorial tumor diagnosis) was associated with very low risk of NDs postoperatively. Vascular diagnosis was associated with a higher chance of ND.

Postoperative Deterioration of Sensorium

The factors which were found significant on univariate analysis (at $p < 0.2$) were included into the multivariate model. They are diagnosis, emergency or elective nature of surgery, maintenance anesthetic used, inhalational agent used, antiepileptic use, intraoperative brain swelling, intraoperative hypertension, sodium level change, coagulopathy, hypothermia, and duration of anesthesia. Sodium level change and coagulopathy were excluded from final analysis due to low-event rate for the dependent variable. The model was found to be significantly better than a model of no effect ($p < 0.001$).

Table 1 Demographic variables

Variable	Descriptive
Age (yrs)	39 ± 17
Weight (kg)	57 ± 15
Sex (F/M) (%)	37.6/62.4
Diagnosis (infectious/infratentorial/tumor/supratentorial/tumor/TBI/vascular) (%)	1.1/15.8/55.9/10.4/16.8
Procedure type (elective/emergency) (%)	64.9/35.1
Comorbidities (cardiovascular/endocrine/neurological/none/respiratory) (%)	15.4/6.5/9.3/63.4/5.4
Previous Surgery (no/yes) (%)	87.5/12.5
GCS (IQR)	15 (15–15)

Abbreviations: GCS, Glasgow coma scale' IQR, interquartile range; TBI, traumatic brain injury.
Note: Age and weight as means ± standard deviation (SD), GCS as median (IQR) and sex, diagnosis, procedure type, comorbidities, previous surgery as percentages.

Table 2 Coefficients for variables entered into the multiple regression model for postoperative new NDs

Factors	Firth OR (95% CL)	*p*-Value	Boot OR (95% CL)	*p*-Value
Intercept	0.03 (0–0.22)	< 0.05	0.03 (0–0.83)	< 0.05
Institution 2	0.15 (0.04–0.47)	< 0.05	0.15 (0.06–0.71)	< 0.05
Institution 3	0.12 (0–1.77)	NS	0.12 (0.01–2.45)	NS
Diagnosis infratentorial tumor	0.42 (0.07–2.06)	NS	0.42 (0.03–3.89)	NS
Diagnosis TBI	0.08 (0–0.8)	< 0.05	0.08 (0.01–0.31)	< 0.05
Diagnosis vascular	8.35 (2.26–35.84)	< 0.05	8.36 (1.19–25)	< 0.05
Comorbidity cardiovascular	1.83 (0.5–6.17)	NS	1.83 (0.25–8.84)	NS
Comorbidity endocrine	0.13 (0–1.63)	NS	0.13 (0.01–1.89)	NS
Comorbidity neurological	4.25 (0.92–17.3)	NS	4.25 (0.49–17.73)	NS
Comorbidity respiratory	2.62 (0.41–13.86)	NS	2.62 (0.12–16.83)	NS
Opioid (morphine)	0.41 (0.02–10.15)	NS	0.41 (0.06–6.26)	NS
IO bradycardia present	5.85 (1.3–26.31)	< 0.05	5.85 (0.31–49.5)	NS
IO hypoxia present	4.44 (0.58–26.85)	NS	4.44 (0.04–29.7)	NS
IO hypercarbia present	5.62 (0.89–45.65)	NS	5.62 (0.23–35.48)	NS
Anesthesia duration	1.01 (1–1.01)	NS	1.01 (1–1.01)	NS

Abbreviations: IO, intraoperative; NDs, neurological deficits; NS, not significant.
Note: Reference levels: for institution–institution 1, for diagnosis–supratentorial tumor, for comorbidity–no comorbidity, for opioid–fentanyl. $p < 0.05$ is statistical level of significance.

The model coefficients are shown in ►**Table 3**. The duration of anesthesia was found to be significantly predictive of SD (OR/CI = 1.01 / 1–1.02).

Postoperative Seizures

The factors which were found significant on univariate analysis (at $p < 0.2$) were included into the multivariate model. They are emergency or elective nature of surgery, preoperative neurological deficits, nitrous oxide use, antiepileptic use, steroid use, opioid used, intraoperative hypertension, arrhythmia, hypothermia, institute factor, anesthesia duration, and total GCS score. The final model was significantly better than a null model ($p = 0.004$). ►**Table 4** shows the coefficients for variables in the final model.

Discussion

This study assessed the postoperative neurological complications within 24 hours after a cranial surgery. The incidence of all neurological complications was 19%. The incidence of postoperative NDs was 10%, SD was 8.6%, and seizures was 6.1%. This study also tried to assess the independent predictors for the above neurological complications.

Many studies have assessed complications in specific groups of patients. In our study, we have assessed

Table 3 Coefficients for variables entered into the multiple regression model for postoperative SD

Factors	Firth OR (95% CL)	*p*-Value	Boot OR (95% CL)	*p*-Value
Intercept	0 (0–0.01)	< 0.05	0 (0–0.03)	< 0.05
Diagnosis infratentorial tumor	0.58 (0.104–2.56)	NS	0.58 (0.13–2.83)	NS
TBI	1.22 (0.08–13.03)	NS	1.22 (0.17–20.09)	NS
Vascular	2.28 (0.61–8.21)	NS	2.27 (0.21–10.7)	NS
Procedure status - emergency	2.52 (0.68–9.61)	NS	2.51 (0.31–14.59)	NS
N2O used	1.58 (0.31–12.22)	NS	1.57 (0.14–8)	NS
Inhalational agent–desflurane	1.56 (0.22–8.28)	NS	1.55 (0.11–15.33)	NS
Inhalational agent–sevoflurane	2.13 (0.66–7.15)	NS	2.14 (0.55–9.87)	NS
IO antiepileptic used	0.89 (0.22–3.22)	NS	0.89 (0.12–6.96)	NS
Brain swelling present	5.48 (1.67–17.95)	< 0.05	5.47 (0.86–21.76)	NS
Hypertension present	2.62 (0.66–9.16)	NS	2.61 (0.21–8.5)	NS
Hypothermia present	1.99 (0.31–10.52)	NS	1.99 (0.08–20.09)	NS
Duration of anesthesia	1.01 (1.01–1.02)	< 0.05	1.01 (1–1.02)	< 0.05

Abbreviations: IO, Intraoperative; NS, Not significant; SD, sensorium deterioration; TBI, traumatic brain injury.
Note: Reference levels: for diagnosis–supratentorial tumor, for procedure status–elective, for inhalational agent–isoflurane. $p < 0.05$ is statistical level of significance.

Table 4 Coefficients for variables entered into the multiple regression model for postoperative seizures

Factors	Firth OR (95% CL)	*p*-Value	Boot OR (95% CL)	*p*-Value
Intercept	0.09 (0–1.83)	NS	0.09 (0–2.28)	NS
Institution 2	2.42 (0.46–17.55)	NS	2.42 (0.31–20.57)	NS
Institution 3	0 (0–0.08)	< 0.05	0 (0–21.16)	NS
Procedure status–emergency	1.35 (0.3–5.25)	NS	1.35 (0.31–6.16)	NS
Preoperative Neurological deficit present	2.23 (0.7–7.3)	NS	2.23 (0.47–8.86)	NS
Opioid–morphine	156.17 ($5.3–2.9^{*}10^{4}$)	< 0.05	156.18 ($0.02–1.26^{*}10^{7}$)	NS
N2O used	0.38 (0.05–2.45)	NS	0.38 (0.03–8.42)	NS
Antiepileptic used	2.41 (0.51–9.83)	NS	2.41 (0.16–12.85)	NS
Steroid used	0.22 (0–2.26)	NS	0.22 (0.06–1.29)	NS
Hypertension	1.31 (0.21–5.97)	NS	1.31 (0.26–6.89)	NS
IO arrythmia present	2.02 (0.41–8.12)	NS	2.02 (0.29–8.04)	NS
Hypothermia	6.23 (1.02–34)	< 0.05	6.23 (0.68–39.49)	NS
Preop GCS	0.96 (0.77–1.2)	NS	0.96 (0.77–1.3)	NS

Abbreviations: GCS, Glasgow coma scale; IO, intraoperative; NS, not significant; SZs, seizures.
Note: Reference levels: for institution–institution 1; for procedure status–elective; for opioid–fentanyl. $p < 0.05$ is statistical level of significance.

complications in all types of cranial surgeries within 24 hours. It is important that all the neurological setups should be prepared to handle the possible complications. There is a need to assess whether these neurological complications can be prevented. Toward this end, we tried to assess the independent predictors of these neurological complications. With an understanding of these predictors, one should be able to decrease these complications and improve the outcomes of the patients. Pooling of data from multiple institutions should help in applicability of the results across multiple institutions.

Postoperative New Neurological Deficits

Postoperative ND is a matter of concern and new or worsened ND following neurosurgery is known to influence patient outcome following neurosurgery. In a retrospective study, Rehman et al [11] reported that development of a postoperative ND following glioblastoma resection significantly affected survival. The authors observed that development of a permanent ND postoperatively had ominous prognosis with reduced survival time. However, patients who had temporary deficits had improved survival.

In this study, the initial univariate tests specified the putative variables which were associated with the incidence of postoperative NDs at a $p < 0.2$. Diagnosis of the patient was found to be predictive of ND. Patients with vascular lesions (aneurysms and arteriovenous malformations) were approximately eight times more susceptible to ND. TBI showed 92% less chance of ND compared with supratentorial tumors. The increased deficits with vascular lesions are easily explainable, as these patients are prone to develop vasospasm/delayed cerebral ischemia and thus the ND. However, in TBI patients, the incidence of postoperative deficits was less. This might be due to the following reasons: 1.Many patients might be having deficits preoperatively 2. The deficits are truly less frequent postoperatively, as there is an improvement in the deficits after the operation rather than worsening of the deficits. 3. Another reason could be that these patients are sedated and ventilated postoperatively; hence, it was difficult to assess the NDs. It also depends on the availability of the dedicated neuro-ICU and availability of the ICU beds.

Institution 2 reported 85% less chance of NDs compared with Institution 1, which may be explained by the differences in hospital policy and expertise of treating surgeons. Surgeon's expertise and attitude toward treatment may play an important role. The hospital policy regarding choice of patients for surgery may also play a role. Some hospitals are very aggressive in their treatment approach, and they may accept even poor grade patients for surgery. Such institutions may have higher incidence of postoperative NDs. In one study, age has been shown to be a risk factor for postoperative ND.[12] However, in our study, age was not seen as a significant factor affecting the NDs.

Postoperative stroke rates vary significantly in various surgical populations. It could be 0.1 to 10%.[13] The high-rates are seen in cardiac surgery, vascular surgery and neurological surgeries. In a review of glioma surgery, the incidence of new NDs was 0 to 20%.[14] Studies with newer advancements in surgical techniques have reported lesser incidence of complications. In another study of meningiomas, an incidence of 14.8% has been reported. In surgery for vestibular schwannoma, the incidence of new NDs was as high as 31%.[15] Compared with these studies, the incidence of postoperative NDs in the current study was relatively low. It may be because our study was limited to only 24 hours.

Postoperative Deterioration of Sensorium

In this study, postoperative SD was observed in 8.6% of patients. Various studies have quoted different incidences of postoperative SD. One Indian study has quoted an incidence of 11%.[16] In the final analysis of the results, anesthesia duration and intraoperative brain swelling were found to be independently predictive of SD. This may be explained by residual sedation of anesthetics due to storage in fat compartments over prolonged exposure. Also, it can be related to the experience of neurosurgeon. A less experienced surgeon takes longer time than the experienced surgeon. Intraoperative brain swelling also can theoretically cause SD due to decrease in the cortical cerebral blood flow. However, the effect did not survive bootstrapping.

Postoperative Seizures

In this study, seizures were observed postoperatively in 6% of patients. Various studies have reported an incidence of postoperative seizures ranging from 1 to 12%.[11,13,17] One Indian study has documented an incidence of 6.3%, which is almost similar to our study. Dorzi et al[18]analyzed the risk factors for seizures following resection of primary brain tumors. The independent risk factors reported in their study were presence of preoperative seizures and small tumor size. Preoperative seizure history is a well-known risk factor for postcraniotomy seizures.[19] Another interesting finding in this study was association of small tumor size and postoperative seizures. The authors explained this association based on the requirement of more brain tissue dissection or manipulation for surgical access in small lesions. In the regression analysis, the Firth model has shown institution 3, usage of morphine and presence of hypothermia as predictive factors. However, the confidence intervals of morphine use were seen to be impossibly large and none of the factors were significant with bootstrapping.

Strengths of Study

Multicentre nature of the data provides a pragmatic view of the topic, with variation in practices and outcomes.

Limitations of Study

In spite of multicentre nature of the study, the event rate for the outcomes was relatively low. Finding the causative factors for the neurological complications became difficult. This study was not designed to assess complication differences between the institutions but to look for differences in the management strategies. Other limitations are as follow: We have not included and evaluated the facilities available

in the institutions, for example, dedicated neuro-ICU, navigation, awake craniotomy, intraoperative neuromonitoring, etc., which can have a bearing on the outcomes. Types of lesions operated at various centers also have not been taken into account.

Conclusion

Overall postoperative neurological complications are 19%. The incidences of postoperative NDs, SD, and postoperative seizures were 10, 8.6, and 6.1%, respectively. There is a large variation in the institutional reporting of the complications. Further well-designed studies with larger sample sizes and better models are required to overcome the limitation of low-event rate for prediction and prognostication of postoperative neurological complications following surgery.

Conflict of Interest

None declared.

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