Perioperative Factors Associated with Prolonged Intensive Care Unit and Hospital Length of Stay after Pediatric Neurosurgery

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Key Words

Morbidity · Mortality · Neurosurgery · Pediatrics · Intensive care units · Risk factors

Abstract

Objectives: This study aims to describe the association between different postoperative complications and the length of hospital stay among children undergoing neurosurgical procedures. **Methods:** A retrospective cohort study was carried out between May 2004 and May 2009 in a tertiary community hospital. All postoperative complications following neurosurgical procedures and their association with the main outcomes [length of intensive care unit (ICU) and hospital stay] were investigated in a univariate and multivariate analysis. **Results:** The medical records of 198 patients treated during the study period were reviewed. The most frequently performed surgeries were ventriculoperitoneal shunting (16.7%), correction of craniosynostosis (30%) and brain tumor resections (28.3%). Of the 198 patients eligible for this analysis, 79 (39.9%) suffered from at least one complication. The most frequent complications were fever (30.3%), hypothermia (16%), postextubation laryngitis (15.1%) and postoperative bleeding (7%). Factors independently associated with a longer pediatric ICU stay were fever (odds ratio 1.39, 95% confidence interval 1.1–3.2; $p = 0.001$), laryngitis (odds

ratio 2.24, 95% confidence interval 1.8–5.2; $p = 0.001$), postoperative bleeding requiring reoperation (odds ratio 1.8, 95% confidence interval 1.4–3.9; $p < 0.001$) and infection (odds ratio 3.71, 95% confidence interval 1.8–12.4; $p = 0.033$). Fever (odds ratio 2.54, 95% confidence interval 2–7.4; $p = 0.001$) and infection (odds ratio 11.23, 95% confidence interval 4–22.4; $p = 0.003$) were related to the total length of the patient's hospital stay. **Conclusions:** In this study population, most elective neurosurgical procedures were not associated with significant complications, and morbidity and mortality were low. Some complications significantly influenced patients' outcomes and should be monitored for early diagnosis. This study may improve our understanding and identification of postoperative outcomes in pediatric neurosurgery.

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Introduction

Remarkable technical advances and safety improvements in the care and monitoring of children undergoing neurosurgical procedures have taken place in recent years [1]. However, little is known about morbidity and mortality during the postoperative period and the risk factors associated with poor outcomes.

Isolated reports of complications in some surgical procedures, such as postoperative infection and ventilator-associated pneumonia, are well known [2, 3] but have not been studied in the specific context of pediatric neurosurgery. Various clinical and surgical factors can influence the anesthesiological and surgical complication rates in pediatric neurosurgery. Preoperative knowledge of these factors is of great importance for the application of safe anesthesia and surgical techniques and for a favorable surgical outcome.

The care of neurosurgery patients is generally complex, and virtually all patients require monitoring in intensive care units (ICUs) during the postoperative period. Recent studies [4–6] have reported rates for complications related to anesthesia and surgical procedures of 5.5–40%; the most frequent complications are cerebrospinal fluid leaks, new neurological deficits, obstruction and infection of ventriculoperitoneal shunts, significant bleeding and bradyarrhythmia during the initiation of anesthesia. These studies listed the major complications according to the type of surgery; however, the magnitude of their impact on the progress of the patients remains unknown.

The objectives of this study were to establish the frequency of general complications in pediatric neurosurgery at our institution and to describe the various risk factors associated with the length of hospitalization and ICU stay.

Materials and Methods

Study Design

The study was designed as a retrospective, single-center, observational study.

Patients and Setting

After approval by the Santa Catarina Hospital's Institutional Review Board, all medical records from patients aged 1–16 years who underwent neurosurgical procedures involving the central or peripheral nervous system, as well as those exhibiting cranial congenital malformations who underwent surgery upon admission or during hospitalization, were reviewed. Patients whose clinical records could not be fully retrieved or were illegible or incomplete were excluded.

Data Collection

For each patient, demographical and clinical data, including surgical diagnosis before the procedure, duration of mechanical lung ventilation and length of hospital and pediatric ICU (PICU) stay, were collected. The clinical records were reviewed to collect information about the complications that patients suffered during their hospital stay.

Definition of Outcomes and Complications

The primary outcomes were length of stay in the PICU and in the hospital. Complications were defined as follows: fever (axillary temperature above 37.8°C, independent of infection or intracranial hypertension, any time between admission and discharge; axillary temperature, while less accurate than other temperature measurement methods, is the standard method used in the ICU), relevant bleeding requiring reoperation or the need of 40 ml/kg or more of packed red blood cells during the entire hospitalization, clinically diagnosed postextubation laryngitis (clinically relevant upper stridor after extubation in the ICU, regardless of whether or not reintubation was required), hypothermia upon ICU admission (axillary temperature below 35°C upon admission to the PICU), diabetes insipidus (hypernatremia, polyuria and low concentrations of urinary sodium), syndrome of inappropriate antidiuretic hormone secretion (low urinary output, hyponatremia and high concentrations of urinary sodium), infection (diagnosed by positive blood, urine, cerebrospinal fluid or other cultures or other exams) and seizures.

Table 1. Surgical procedures and patient demographics

Variable	
Type of surgery, n	
Ventriculoperitoneal shunting	33 (16.7)
Craniosynostosis	62 (31.3)
Supratentorial brain tumors	39 (19.7)
Infratentorial brain tumors	17 (8.6)
Dysostosis syndromes	9 (4.5)
Epilepsy surgery	4 (2)
Medullary tumors	18 (9.1)
Others	16 (8.1)
Gender, n	
Male	112 (56.6)
Female	86 (43.4)
Age, months	
Mean $\pm$ SD	50.31 $\pm$ 52.68
Median	24.5
Minimum/maximum	1/187
PICU length of stay, days	
Mean $\pm$ SD	3.42 $\pm$ 4.84
Median	2
Minimum/maximum	0/59
Hospital length of stay, days	
Mean $\pm$ SD	7.16 $\pm$ 7.35
Median	5
Minimum/maximum	2/70
MV duration, h	
Mean $\pm$ SD	6.63 $\pm$ 9.57
Median	5
Minimum/maximum	1/90
Mortality, n	2 (1)

Figures in parentheses represent percentages. MV = Mechanical ventilation.

Statistical Analysis

In the univariate analysis, the primary outcomes were compared between patients who had one of the complications listed above and those who did not. For continuous variables, the Mann-Whitney U test was used, and for categorical variables, the χ^2 test or Fisher's exact test was used. The independent contribution of each complication to each outcome parameter (PICU and hospital length of stay) was assessed by multiple logistic regression analysis. All statistical analyses were performed with SPSS 13 (Chicago, Ill., USA). *p* values below 0.05 were considered statistically significant.

Results

During the study period, the clinical records of 198 patients were analyzed. Records for 13 patients were excluded (4 under palliative care and 9 with unclear medical records). Overall data and demographic characteristics of the patients are shown in table 1.

Table 2 summarizes the distribution of each procedure in the study. In total, 171 complications occurred in 79 patients (39.9%). The other 121 patients (61.1%) had no reported complications. Repair of craniosynostosis (41.7%) and supratentorial brain tumor surgeries (9.1%) were found to have the most complications per procedure. Table 3 lists the specific complications for our pediatric neurosurgical service. The most common complications were fever (60 cases), hypothermia (32 cases), laryngitis (30 cases) and postoperative hemorrhage requiring a repeat operation (14 cases). Seizures occurred in 8 cases. Infections occurred in 9 children, with equal proportions of pneumonia and urinary tract infection, and only 1 patient (0.5%) did not receive any antibiotic prophylaxis in

the postoperative period. Deaths were counted separately, and there were 2 deaths during the study period, both as a result of untreatable postoperative intracranial hypertension due to cerebral edema after craniotomy. Four patients (2%) required postoperative mechanical ventilation, and 3 children (1.5%) required more than one surgical procedure.

The group of patients who suffered each complication were examined by determining their average length of stay in the PICU and in the hospital. First, these outcomes were studied by comparing patients with and without the listed complications. Then, we conducted a multivariate analysis to identify risk factors that were independently associated with these outcomes and to determine the extent to which they tended to increase the length of stay in the PICU and hospital. Tables 4 and 5 show the results of the univariate and multivariate analyses with the respec-

Table 2. Number of cases and complications by procedure

Procedure type	Patients with complications, n
Ventriculoperitoneal shunting (n = 33)	10 (5%)
Craniosynostosis (n = 62)	28 (14.1%)
Supratentorial brain tumors (n = 39)	18 (9.1%)
Infratentorial brain tumors (n = 17)	8 (4%)
Dysostosis syndromes (n = 9)	2 (1%)
Epilepsy surgery (n = 4)	1 (0.5%)
Medullary tumors (n = 18)	8 (4%)
Others	4 (2%)
Total	79 (39.9%)

Table 3. Complications according to the surgical diagnosis

Procedure type	Fever	Bleeding	Laryngitis	IADH	Seizures	Hypothermia	CSF leakage	ICH	Infection
Ventriculoperitoneal shunting (n = 33)	3 (9.1)	0	2 (6)	0	0	12 (36.4)	0	2 (6)	1 (3)
Craniosynostosis (n = 62)	24 (38.7)	10 (16.1)	15 (24.2)	0	0	12 (19.4)	0	0	0
Supratentorial brain tumors (n = 39)	17 (43.6)	2 (5.1)	3 (7.7)	2 (5.1)	4 (10.2)	5 (12.8)	2 (5.1)	6 (15.3)	3 (7.7)
Infratentorial brain tumors (n = 17)	8 (47.1)	2 (11.8)	4 (23.5)	1 (5.9)	1 (5.9)	1 (5.9)	2 (11.8)	0	2 (11.8)
Dysostosis syndromes (n = 9)	2 (22.2)	0	2 (22.2)	0	1 (11.1)	0	1 (11.1)	0	0
Epilepsy surgery (n = 4)	4 (100)	0	2 (50)	0	2 (50)	1 (25)	0	0	3 (75)
Medullary tumors (n = 18)	2 (11.1)	0	2 (11.1)	0	0	1 (5.6)	1 (5.6)	0	0
Total	60	14	30	3	8	32	6	8	9

Values represent numbers of patients (percentage). IADH = Inappropriate antidiuretic hormone syndrome; CSF = cerebrospinal fluid; ICH = intracranial hypertension.

Table 4. Mean durations of PICU and hospital stay by type of complication based on univariate analysis

Outcome	Variable	Mean time days	SD	n	p
<i>Fever</i>					
PICU LOS	no	2.7	1.9	138	0.006
	yes	5.08	8.11	60	
Hospital LOS	no	5.96	4.61	138	0.001
	yes	9.9	10.97	60	
<i>Bleeding</i>					
PICU LOS	no	3.13	2.94	184	0.001
	yes	5.73	2.26	14	
Hospital LOS	no	6.13	6.79	184	<0.001
	yes	8.22	3.95	14	
<i>Laryngitis</i>					
PICU LOS	no	2.9	2.29	168	0.027
	yes	6.33	10.89	30	
Hospital LOS	no	6.6	5.66	168	0.059
	yes	10.3	13.06	30	
<i>Coagulation disorders</i>					
PICU LOS	no	3.32	4.82	189	0.065
	yes	5.44	5.05	9	
Hospital LOS	no	7.08	7.4	189	0.247
	yes	8.78	6.4	9	
<i>IADH</i>					
PICU LOS	no	3.4	4.87	195	0.037
	yes	4.67	1.15	3	
Hospital LOS	no	7.16	7.41	195	0.214
	yes	6.67	0.58	3	
<i>Seizures</i>					
PICU LOS	no	3.03	2.62	190	0.003
	yes	12.63	19.33	8	
Hospital LOS	no	6.65	5.79	190	<0.001
	yes	19.25	21.07	8	
<i>Hypothermia</i>					
PICU LOS	no	3.5	5.14	166	0.65
	yes	3	2.86	32	
Hospital LOS	no	7.37	7.8	166	0.365
	yes	6.06	4.28	32	
<i>CSF leakage</i>					
PICU LOS	no	3.24	4.72	192	0.001
	yes	9.17	5.6	6	
Hospital LOS	no	6.7	6.75	192	<0.001
	yes	21.67	11.47	6	
<i>ICH</i>					
PICU LOS	no	2.97	2.54	189	<0.001
	yes	12.78	17.95	9	
Hospital LOS	no	6.72	5.78	189	0.011
	yes	16.33	21.14	9	
<i>Infection</i>					
PICU LOS	no	3.17	4.7	189	<0.001
	yes	8.56	5.22	9	
Hospital LOS	no	6.58	6.74	189	<0.001
	yes	19.33	9.46	9	

LOS = Length of stay; IADH = inappropriate antidiuretic hormone syndrome; CSF = cerebrospinal fluid; ICH = intracranial hypertension.

tive odds ratios for the complications mentioned. In our study, factors independently associated with longer PICU length of stay were fever and laryngitis ($p = 0.001$), clinically relevant bleeding requiring reoperation ($p < 0.001$) and infection ($p = 0.033$). Fever ($p = 0.001$) and infection ($p = 0.003$) were significantly related to the length of the patients' hospital stay.

Discussion

This study revealed the impact of several common complications that affect the progress of pediatric patients during hospitalization after neurosurgical procedures. Other studies have examined more patients and described the frequencies of such complications, but they did not relate the complications to outcomes, including the unfavorable progress of pediatric neurosurgery patients.

Morbidity is a significant issue in a busy tertiary pediatric neurosurgery unit and should not be unexpected. Pediatric neurosurgery patients may present with life-threatening conditions requiring urgent care and usually have significant related clinical conditions, such as prematurity. Moreover, they have particular issues related to communication, vascular access and sedation, as well as others that may delay or complicate diagnosis and treatment. Craniosynostosis and brain tumors represent a large part of pediatric practice and account for a significant proportion of adverse events.

In our patients, there was great variation in types of surgeries; however, most procedures involved the same, mostly complex diseases (mainly brain tumors and craniosynostosis). Among the 198 patients, 77 (38.9%) exhibited some type of complication, but these tended to be of low severity.

The overall short lengths of stay in the PICU and in the hospital, the short times of mechanical lung ventilation and the low severity of complications must be considered within the context of the study population. In our study, most patients lacked past medical histories, were healthy until surgery, did not have pulmonary diseases and were not considered high risk for anesthesia. Additionally, diagnoses were made very early, particularly in the case of central nervous system tumors, which reduced morbidity during the postoperative period and probably also reduced the duration of mechanical lung ventilation. The retrospective analysis of the severity of illness in the patients, as well as prognostic scores, such as pediatric risk of mortality (PRISM) or pediatric index of mortality

Table 5. Results of the multivariate analysis

Variable	Outcome							
	PICU LOS				hospital LOS			
	χ^2	OR	95% CI	p	χ^2	OR	95% CI	p
Fever	11.56	1.39	1.1–3.2	0.001	11.8	2.54	2–7.4	0.001
Bleeding	12.2	1.8	1.4–3.9	<0.001	NS	NS	NS	NS
Laryngitis	10.3	2.24	1.8–5.2	0.001	NS	NS	NS	NS
Infection	4.53	3.71	1.8–12.4	0.033	8.73	11.23	4–22.4	0.003

LOS = Length of stay; OR = odds ratio; CI = confidence interval; NS = not significant.

(PIM), was not possible; however, due to the fact that most procedures were performed electively and in children with a low anesthetic risk, this probably did not influence the interpretation of the results.

Clinical Complications

Among the craniosynostosis patients, 60 (96.8%) required transfusions of blood components, primarily during surgery, with an average volume of red blood cell concentrate transfused of 25 ml/kg. In fact, the main complication in the surgical management of these patients is the unavoidable and occasionally significant loss of blood that sometimes occurs during the procedures. This phenomenon is even more significant in light of the fact that the majority of these surgeries are performed in young toddlers. A nonsystematic review of the surgical management of craniosynostosis [7] retrieved studies in which the surgical loss of blood was estimated. Meyer et al. [8] reported blood loss of $91 \pm 66\%$ of total volemia during the postoperative period, and Kearney et al. [9] reported average losses of 24, 12, 65 and 42% of the blood mass in sagittal suture repair, unicoronal repair, bicoronal repair and metopic suture repair, respectively. The transfusion of blood during craniosynostosis surgery is virtually inevitable and is required in 96.3% of cases [10]. By contrast, the occurrence of severe hemorrhage requiring reoperation in our patients was low (14 patients, i.e. 7% of the total).

The overall incidence of postoperative infection was 4.5% for all of the surgical groups. Cefuroxime was the most frequently used prophylactic antibiotic, with doses of 100 mg/kg/day for about 48–72 h (81% of patients). Postoperative meningitis causes greater mortality and more neurological sequelae than do extradural infections. When meningitis occurs despite treatment with

antibiotics, it usually involves resistant, difficult-to-treat microorganisms. Postoperative neurosurgical infections result in high morbidity rates and are among the most severe and life-threatening infections [11]. No infections were associated with ventriculoperitoneal shunts. The catheters employed were conventional and were not impregnated with antibiotics, a practice that has reduced the incidence of shunt infections but is quite expensive [12–14]. Sepsis has been reported as one of the most frequent and severe complications of ventriculoperitoneal shunts and first develops during surgery in most cases [15].

Approximately 30% of patients developed fever without an identifiable source during the postoperative period. In fact, for most patients presenting fever during the postoperative period, an etiological or topographical diagnosis of infection was not established. This uncertainty is a sign for caution and highlights the need to conduct a thorough clinical and laboratory investigation to improve our understanding of recovery. In our study, fever and infection were not correlated, so we maintained them as independent variables. Both clinical presumptive and microbiological confirmatory diagnoses are rare [16]. The use of antibiotic prophylaxis in pediatric neurosurgery is mandatory, and its value has been supported in several randomized controlled trials and is widely described by meta-analyses [17].

In our study, a 4% incidence of seizures (8 patients) was observed, primarily in patients who underwent lobectomy due to epilepsy and who exhibited seizures before surgery. Four patients (2%) had seizures preoperatively, and 1 child (1%) was diagnosed with inappropriate antidiuretic hormone syndrome, along with hyponatremia. Among the patients with supratentorial brain tumors, approximately 56% were given phenytoin to prevent seizures during the postoperative period. The ‘mandatory’

prescription of anticonvulsant prophylaxis in craniotomy arises from studies published nearly 20 years ago. A meta-analysis including 4 randomized controlled studies of phenytoin [18] revealed its tendency to decrease seizures in 3 of the 4 trials. These data contradict the American Academy of Neurology, which does not recommend routine prophylaxis [19]. The most recent meta-analysis published by Cochrane [20] did not reveal any differences between control and intervention groups in the prevention of seizures in patients with brain tumors. However, an epidemiological study demonstrated that more than 70% of surgeons routinely employed anticonvulsant drugs after brain tumor surgery; a similar percentage was observed in our hospital during this study [21].

Results of Univariate and Multivariate Analysis

Unadjusted analyses revealed that most of the studied complications were associated with longer hospitalizations and longer stays in the PICU. Nevertheless, many complications overlapped in several patients (e.g. the same patient may exhibit fever, bleeding and laryngitis), making it necessary to develop a multiple analysis model that can reveal which isolated complications were associated with the indicated outcomes.

Indeed, fever during the postoperative period had the greatest impact on all three outcomes. Fever increased the length of stay in the PICU and the hospital 1.4- and 2.6-fold, respectively. Therefore, its effect is important considering the large number of surgical patients. Additionally, few resources are available to prevent fever, as the only treatment proven to decrease postoperative infection is antibiotic prophylaxis, which is already used almost universally.

The multivariate analysis demonstrated that laryngitis, infection and severe bleeding during the postoperative period, with or without an indication for reoperation, were associated with a longer stay in the PICU, and fever and infection were associated with a longer stay in the hospital.

Infection increased the patient's length of stay in the PICU almost 4-fold and the length of the stay in the hospital almost 11-fold. Although their incidence was low, most infections (pulmonary or urinary) were acquired during hospitalization and required broad-spectrum antibiotics.

The findings quantify the effects of certain complications on patients' progress during hospitalization. Although it was previously suspected that factors such as fever, laryngitis and infection might increase the length of hospitalization, such associations had not been demon-

strated in the pediatric neurosurgical setting. Patients with laryngitis tended to stay 2 additional days in the PICU, mainly because of reintubation. Taking steps to prevent infection during tracheal intubation using rapid sequence intubation and a cannula with the proper diameter can decrease the length of hospitalization and consequently also decrease morbidity, mortality and superfluous expenses related to patient care by avoiding severe laryngitis.

The results of this study helped our ICU team to address risk factors in order to reduce the morbidity and length of stay of pediatric neurosurgical patients. Active fever control has now been introduced by our nursing team, as well as measures to avoid hypothermia upon admission to the PICU, while the child is still in the operating room. Knowing that these two risk factors may contribute to increased morbidity and length of stay, it is important to control them more actively. A schedule for blood tests after admission was introduced in order to control electrolyte disorders and for early diagnosis of inappropriate antidiuretic hormone syndrome, for example.

This study has some limitations. It is retrospective, which makes analysis difficult and subject to error because of the incompleteness of clinical records and illegible or incorrect annotations by the medical and nursing team. Furthermore, the oldest records were missing because the hospital could not locate them; besides, the study is descriptive and had no control group. Although the study sample as a whole is large, the sizes of the various surgical groups were insufficient. Therefore, although comparison tests may yield significant differences within the sample, these differences may have limited external validity.

Conclusions

The surveillance of surgical complications provides important information on the incidence of complications, particularly those common to different procedures, and thus can improve patient care. In the present study population, most elective neurosurgical procedures were not associated with significant complications. The most frequent postoperative complications were bleeding, fever, hypothermia and postextubation laryngitis. Antibiotic prophylaxis was widely used, and the rate of postoperative infection was low (4.5%). Multivariate analysis revealed the main factors that increase the length of stay in the PICU (fever, laryngitis, clinically relevant bleeding and infection) and in the hospital (fever and infection).

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