Pediatric Infectious Disease Society of the Philippines Journal
Vol 23 No 1, pp. 97-109 January-June 2022
Ho JO, Ong-Lim AL. The Association of Adherence to Antimicrobial Prophylactic Recommendations for Clean Neurosurgeries with Post-operative Surgical Site Infection
https://doi.org/10.56964/pidspj20222301011

ORIGINAL ARTICLE

THE ASSOCIATION OF ADHERENCE TO ANTIMICROBIAL PROPHYLACTIC RECOMMENDATIONS FOR CLEAN NEUROSURGERIES WITH POST-OPERATIVE SURGICAL SITE INFECTION

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ABSTRACT

Objectives: The use of antimicrobial prophylaxis to prevent surgical site infections (SSI) is well established. This study examined the association of adherence to antimicrobial prophylaxis for clean neurosurgeries with post-operative surgical site infection (SSI) rates.

Methods: A retrospective descriptive study was conducted at the Philippine General Hospital (PGH) among pediatric patients who underwent clean neurosurgical procedures between January 1, 2018 – December 31, 2019. The outcome measured was the development of SSI. Univariate and multivariate analysis was performed to show the association of risk factors with SSI. Compliance to existing antibiotic prophylaxis recommendation was assessed.

Results: One hundred eighty-nine (189) medical charts were reviewed. Overall prevalence of SSI was 9.5% and fever was the most common initial symptom of SSI. *Staphylococcus species* was identified from cultures of surgical sites, consistent with existing literature, however gram-negative organisms including multidrug-resistant organisms (MDRO) were noted. All cases received prophylactic antibiotics, but adherence to all parameters (antimicrobial choice, dose, timing, route, re-dosing and duration of prophylaxis) was low at 7.9%. Appropriate antibiotics were prescribed in only 15.9% and antibiotics were discontinued beyond 24 hours post-surgery in 45.5% of cases. Patients who received a regimen fully compliant with antimicrobial prophylaxis recommendations did not develop SSI.

Conclusion: Adherence to existing antimicrobial prophylaxis protocol for neurosurgeries is low at 7.9%. Patients who received a regimen fully compliant with the recommendations did not develop SSI. Interventions to improve compliance to antimicrobial prophylaxis guidelines are needed.

KEYWORDS: *Surgical Site Infection, Adherence, Clean Neurosurgery, Prophylaxis*

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INTRODUCTION

Surgical site infections (SSI) are one of the most feared hospital-acquired infections in neurosurgery because of their potentially serious consequences and complications and increased morbidity & mortality.[1] SSI is associated with a 3% mortality rate, 75% of which are directly attributable to infection. It is also the most expensive type of hospital-acquired infection with an estimated annual expense of 3.3 billion US dollars.[2,3] Cost-effective strategies are continuously being developed to meet these challenges. Among infection control practices that have been implemented to decrease infection rates, surgical antimicrobial prophylaxis (SAP) has been shown to prevent SSI and has the potential to reduce complication rates and costs. Evidence-based recommendations on the use of SAP are still lacking, especially in clean neurosurgeries, where risk of infection is reported to be low (1-2%).[1,4] Current guidelines in the pediatric population were largely derived from adult neurosurgical studies.[1] One study by Korinek, et al. concluded that prophylaxis is effective in preventing SSI in low risk patients.[5] The presence of risk factors, which include age, nutritional status, immunosuppression, length of pre-operative stay and intra-operative factors, have also been cited as reasons for antimicrobial prophylaxis.[6]

A study conducted at the Philippine General Hospital (PGH) by Dy-Pasco, et al. in 2014 looked at surgical site infection among pediatric patients after clean neurosurgeries. Overall prevalence rate of SSI was 11.26%. Recommendations for antimicrobial prophylaxis for clean neurosurgeries were implemented at PGH last October 2013 by the sections of Neurosurgery and Infectious and Tropical Diseases in Pediatrics. Adherence to this guideline for pre-operative antibiotic use was low at 23.5%.[7] There is increasing concern about clinicians' compliance with current SAP recommendations. Adherence rates were unsatisfactory in industrialized countries like Japan, United Kingdom and the Netherlands.

Inappropriate timing, antibiotic selection and prolonged duration of antibiotic administration have been described. It was also noted that surgeons were accustomed to making decisions based on their own experiences and was counterintuitive for them to accept guidelines.[8]

Data obtained from this study may aid in identifying patients at risk for surgical site infection. Prevalence of surgical site infection in clean neurosurgical procedures and adherence to existing antimicrobial prophylaxis guidelines in the institution as part of continuing surveillance for hospital-acquired infection (HAI) was likewise evaluated.

METHODOLOGY

Study Design

This was a two year retrospective chart review of clean neurosurgeries done at the Departments of Pediatrics and Neurosurgery of the Philippine General Hospital from January 1, 2018 to December 31, 2019.

Study Population and Sample Size

Pediatric patients less than 19 years old who underwent elective clean neurosurgical procedures were included. Patients with a previous operation with an interval of more than 90 days from last operation were also included. Excluded were those admitted for an operation but with documented infection, those with multiple surgeries involving other organ systems, and those with a diagnosis of SSI from another hospital. Sample size was based on an 11.26% overall prevalence as reported by Dy-Pasco in 2014.[7] A minimum of 69 patients was required for the study.

Data Collection

A list of pediatric patients who underwent clean neurosurgical procedures (such as placement of ventriculo-peritoneal shunt, ommaya reservoir, craniotomy, craniectomy, tumor excision & spinal surgery) was obtained from the Department of Neurosurgery.

Clinical profile, risk factors and outcomes were collected for each patient. Demographic data obtained were age, gender, weight and nutritional status. Other risk factors were categorized as follows:

(1) Pre-operative Factors included location prior to surgery, number of pre-operative hospital stay before operation, diagnosis, previous neurosurgical operation, co-morbidities, ASA score, past infections, use of pre-operative steroids and previous chemotherapy or radiotherapy; and
(2) Intra-operative Factors included type of surgery, intra-operative antibiotic doses given, location of surgery and total duration of surgery from cutting time to finish time.

Surgical site infection was identified based on symptom onset from date of surgery where date of procedure was counted as day 1. Symptoms evaluated were fever, shunt tract swelling, vomiting, mental status changes, purulent discharge from the surgical site and shunt erosion through the wound or skin. It was classified as superficial incisional, deep incisional and organ/space SSI according to the criteria set by the Centers for Disease Control and Prevention (CDC).[2,7]

Microorganisms isolated in CSF cultures of patients with SSI were identified. For those with absence of growth from CSF, SSI was considered if there was presence of purulent discharge, abscess or erosion from the wound and signs and symptoms as previously mentioned. Outcome of patients with SSI was determined as either 1) discharged improved or 2) expired.

Adherence to antimicrobial prophylaxis was evaluated and classified as compliant if the case satisfied all conditions as listed in the current institutional guidelines and non-compliant if the case did not satisfy all conditions. Specific components of the guidelines are the following:

(1) Oxacillin is recommended for patients admitted for <3 days with no infection before operation; for patients who stayed in the hospital for ≥3 days, or were previously treated for a hospital-acquired infection, either cefuroxime plus amikacin or cefazolin plus amikacin are recommended.
(2) Antibiotics should be administered within 60 minutes before skin incision, with re-dosing administered for procedures longer than 4 hours.
(3) The recommended prophylaxis is either a single dose or continuation of the antibiotic for less than 24 hours.[7,9]

Data Analysis

Data was gathered using standard data collection forms, entered into an Excel database and subjected to descriptive analysis. Frequency and proportion were used for categorical variables; median and inter quartile range were used for non-normally distributed continuous variables. Mann-Whitney U test and Fisher's exact/chi-square test were used to determine the difference of rank and frequency respectively, between patients with and without surgical site infection. Odds ratios and corresponding 95% confidence intervals from binary logistic regression were computed to determine significant factors for surgical site infection. All statistical tests were two tailed tests. The Shapiro-Wilk test was used to test the normality of continuous variables. Missing variables were neither replaced nor estimated. Null hypotheses were rejected at 0.05 α-level of significance. STATA 13.1 was used for data analysis. The study was submitted and approved by the University of the Philippines Manila Research Ethics Board (UPMREB).

RESULTS

Demographics of the Target Population

A total of 189 pediatric patients were admitted at the PGH between January 1, 2018 to December 31, 2019 who fulfilled the inclusion criteria. Demographic data are presented in Table 1. Majority of patients in this series were infants between 1 month to 1 year of age, with a median age of 5 years old.

Most patients who developed SSI were children 2-9 years old and most had normal nutritional status. Malnutrition did not seem to pose an additional risk for the development of infection as 50 of 57 patients (88%) who were underweight/wasted or overweight/obese did not develop SSI.

Table 1. Demographic and Clinical Profile of Pediatric Patients who underwent Clean Neurosurgical Procedures

Parameter	With SSI (n=18)	Without SSI (n=171)	Total (n= 189)
Median age in years, IQR	6.5, IQR = 4 to 13	5, IQR = 0.58 to 12	5, IQR = 0.58 to 12
Neonates (0-30 days)	0	12 (7.0)	12 (6.4)
Infants (1mo-1 year old)	3 (16.7)	60 (35.1)	63 (33.3)
Children (2-9 years old)	9 (50.0)	45 (26.3)	54 (28.6)
Adolescent (10-18 years old)	6 (33.3)	54 (31.6)	60 (31.8)
Sex, in frequency (%)			
Male	10 (55.6)	88 (51.5)	98 (51.8)
Female	8 (44.4)	83 (48.5)	91 (48.2)
Median weight in kg, IQR	20.8, IQR = 13.5 to 29	14.8, IQR = 8.7 to 33	16.5, IQR = 8.8 to 32.6
Median height in cm, IQR	118, IQR = 102 to 148	108, IQR = 8 to 140	108.5, IQR = 70 to 140
Median BMI, IQR	15.6, IQR = 13.9 to 17.4	17.2, IQR = 14.3 to 20.4	16.8, IQR = 14.1 to 20.1
Nutritional status, in frequency (%)			
Normal	11 (61.1)	108 (63.2)	119 (63.0)
Underweight	0	3 (1.8)	3 (1.6)
Wasted	5 (27.8)	23 (13.4)	28 (14.8)
Overweight	1 (5.6)	14 (8.2)	15 (7.9)
Obese	1 (5.6)	10 (5.8)	11 (5.8)
Incomplete/inconclusive	0	13 (7.6)	13 (6.9)

Pre-operative Risk Factors

Pre-operative risk factors are shown in Table 2. The most common area where patients were admitted prior to surgery was at the Neurosurgery Ward (Ward 6).

This was also where most SSI cases developed. Of the 23 patients who were admitted at the ER prior to their procedure, four (17%) developed SSI, unlike in other areas where rates were all under 10%. There is no marked difference between the SSI and non-SSI groups with respect to this variable (p-value of 0.543).

Pre-operative hospital stay was greater than 7 days in majority (36.5%) of cases, while an almost similar proportion (34.4%) were admitted between 3 to 7 days prior to the procedure. Those who stayed between 3 to 7 days in the hospital pre-operatively seemed to develop infection twice more frequently (9/65 or 14%) compared to those who stayed less than 3 days (4/55 or 7%) or more than 7 days (5/69 or 7%). However, a p-value of 0.369 for this variable indicates that there is no significant difference between groups. Most patients were diagnosed with intracranial mass, which comprised 53.7% of all cases. Majority of those who developed surgical site infection also belonged to this group, comprising 88.9% of eighteen SSI cases. There is a higher percentage of SSI cases among patients with intracranial mass (15.8%) compared to those with congenital hydrocephalus (3.1%), but the p-value (p = 0.126) for this variable is not significant.

Twenty-seven patients had a history of prior neurosurgical procedure and majority (25 patients) did not develop SSI. Of the five patients with co-morbidities, only one patient (with Cushing syndrome) developed SSI. Most cases (54.5%) had an ASA score of 2 and nine of the 18 cases who developed SSI belonged to this category. However a higher ASA score did not seem to predispose to the development of SSI, as the single patient with SSI with ASA score of 3 represented only 7.7% of the 13 patients in the group; this ratio was fairly similar to the ASA 1 (4/37 or 10.8%) and ASA 2 (9/103 or 8.7%) groups. The p-value for this variable is not significant (0.933).

Only 7 of 189 patients had infections prior to surgery and 2 of 18 patients who developed SSI also had a previous episode of pneumonia. Pre-operative steroids were given in 24.3% of the 189 cases included in this series. Of the 46 patients who received steroids, only five (10.9%) developed SSI.

However this group also represented 27.8% of the 18 cases who developed SSI. None of the four cases who previously received chemotherapy or radiotherapy developed SSI. For the rest of the mentioned variables, the p-values were not significant.

Table 2. Pre-operative risk factors of patients with and without SSI

Parameter	With SSI (n=18)	Without SSI (n=171)	Total (n= 189)	P-value
	Frequency (%)			
Location prior to surgery				0.543
Ward 6	11 (61.1)	103 (60.2)	114 (60.3)	
Emergency room	4 (22.2)	19 (11.1)	23 (12.2)	
Ward 11	3 (16.7)	30 (17.5)	33 (17.5)	
Ward 9	0	4 (2.3)	4 (2.2)	
NICU	0	15 (8.8)	15 (7.9)	
Pre-operative hospital stay				0.369
< 3 days	4 (22.2)	51 (29.8)	55 (29.1)	
3 to 7 days	9 (50)	56 (32.8)	65 (34.4)	
≥7 days	5 (27.8)	64 (37.4)	69 (36.5)	
Diagnosis				0.126
Intracranial mass	16 (88.9)	85 (49.1)	101 (53.7)	
Congenital hydrocephalus	2 (11.1)	63 (36.8)	65 (34.2)	
Open lip schizencephaly	0	2 (1.2)	2 (1.1)	
Nasoethmoidal meningocele	0	1 (0.6)	1 (0.5)	
Postmeningitic hydrocephalus	0	4 (2.3)	4 (2.1)	
Shunt malfunction	0	8 (4.7)	8 (4.2)	
Tethered cord	0	4 (2.3)	4 (2.1)	
Syringomyelia	0	1 (0.6)	1 (0.5)	
Ruptured aneurysm	0	1 (0.6)	1 (0.5)	
Neurocutaneous melanosis	0	1 (0.6)	1 (0.5)	
Craniosynostosis	0	1 (0.6)	1 (0.5)	
Previous neurosurgical operation	2 (11.1)	25 (14.6)	27 (14.3)	1.000
Co-morbidities				0.500
Epilepsy	0	3 (1.8)	3 (1.6)	
Bronchial Asthma	0	1 (0.6)	1 (0.5)	
Cushing Syndrome	1 (5.6)	1 (0.6)	2 (1.1)	
ASA score				0.933
1	4 (22.2)	33 (19.3)	37 (19.6)	
2	9 (50)	94 (55.0)	103 (54.5)	
3	1 (5.6)	12 (7.0)	13 (6.9)	
No entry	4 (22.2)	32 (18.7)	36 (19.0)	
Past infections				1.000
Pneumonia	2 (11.1)	3 (1.8)	5 (2.6)	
Urinary Tract Infection	0	1 (0.6)	1 (0.5)	
Shunt infection	0	1 (0.6)	1 (0.5)	
Use of pre-operative steroids	5 (27.8)	41 (24.0)	46 (24.3)	0.774
Previous Chemotherapy or radiotherapy	0	4 (2.4)	4 (2.1)	1.000

Intra-operative Details and Risk Factors

Craniotomy/craniectomy/burrholing with placement of a medical device comprised 50.3% of the clean neurosurgical procedures, as seen in Table 3. Ventriculoperitoneal shunt insertion (VPS) was the most commonly inserted medical device, accounting for 46.6% of total cases and 16.7% of SSI cases. Craniotomy/craniectomy/burrholing procedures without a medical device were performed for 83 out of 189 cases (43.9%), of which majority (65 out of 83 cases, or 78.3%) were tumor excisions. Of the 18 patients who developed SSI in this series, fourteen underwent tumor excision, three underwent VPS insertion, and one had tube ventriculostomy placement. Among the types of surgeries, there is a significant difference between the SSI and non-SSI groups (p = 0.023) and the proportion of SSI for procedures without a medical device was significantly higher (16.9%) compared with those with a medical device (4.2%).

Majority of procedures (50.8%) were performed in the Neurological and Spinal Surgery 2 (NSS 2) operating room and of the 18 cases with SSI, ten also had procedures performed in this area. There is a higher proportion of SSI in neurosurgeries done in other areas (1 in 4 cases). There is no significant difference between the two groups with respect to location or area of surgery (p-value = 0.643).

Most of the surgical procedures (79.9%) done in this series were completed within 4 hours or less. Among the 38 surgeries that took at least 4 hours to perform, seven (18.4%) developed SSI, a larger proportion compared to the 7.3% who developed SSI in the other group. Nevertheless, there is no significant difference between the two groups (p-value = 0.058).

Table 3. Intra-operative Details and Risk Factors

Parameter	With SSI (n=18)	Without SSI (n=171)	Total (n= 189)	P-value
	Frequency (%)			
Type of surgery				0.023
Craniotomy/Craniectomy/ Burrholing without medical device*	14 (77.8)	69 (40.4)	83 (43.9)	
Tumor excision	14	51	65	
Endoscopic third ventriculostomy and other biopsy procedures	0	18	18	
Craniotomy/Craniectomy/ Burrholing with a medical device	4 (22.2)	91 (53.2)	95 (50.3)	
VPS	3	85	88	
Ommaya/Becker	0	4	4	
Tube ventriculostomy	1	2	3	
Cranioplasty	0	1 (0.6)	1 (0.5)	
Spine surgery	0	10 (5.9)	10 (5.3)	
Location of Surgery				0.643
Neurological&SpinalSurgery(NSS 2)	10 (55.6)	86 (50.3)	96 (50.8)	
Pediatric Neurosurgical Craniomaxillofacial Operating Unit (PNCOU)	6 (33.3)	65 (38.0)	71 (37.6)	
Left Central Block (LCB)	1 (5.6)	7 (4.1)	8 (4.2)	
Others	1 (5.6)	4 (2.3)	5 (2.7)	
No entry	0	9 (5.3)	9 (4.8)	
Surgical time				0.058
≤ 4hrs	11 (61.1)	140 (81.9)	151 (79.9)	
> 4 hrs	7 (38.9)	31(18.1)	38 (20.1)	

Results of Univariate Analysis

The independent variables were assessed by univariate analysis as seen in Table 4. The association between these identified factors and surgical site infection was expressed as odds ratios (OR) as well as 95% confidence intervals. For risk factors with more than two categories, odds ratios were computed relative to the reference category (for example, in pre-operative hospital stay, <3 days was used as reference to the other 2 groups: 3 to 7 days and >7days).

Other odds ratios were computed based on presence or absence of specific variables, such as diagnosis, presence of medical device and pre-operative antibiotics. Univariate test of any variable resulting in a p-value of <0.05 was used as a candidate for multivariate analysis. It was determined that intracranial mass, type of surgery and duration of surgery were significant factors in the univariate analysis.

Based on the odds ratios and statistically significant p-values obtained, patients diagnosed with intracranial mass were 9 times more likely to have surgical site infection (OR 9.3, 95% CI 1.85 to 37.14, p = 0.006) as compared to those who were not diagnosed to have intracranial mass. Moreover, patients with >4 hours of surgery time were 2.9 times more likely to have surgical site infection (OR 2.9, 95% CI 1.03 to 8.00, p = 0.043) as compared to those who had a surgical time of ≤4 hours.

Presence of VPS may be a protective factor for SSI (OR 0.20, 95% CI 0.06 to 0.72, p = 0.014) as shown in the univariate analysis. This is consistent with the results in those who underwent craniotomy/craniectomy/burrholing with medical devices (OR 0.22, 95% CI 0.07 to 0.69, p = 0.009). Results from multivariate analysis was not significant due to lack of significant covariates left within the model. Other factors such as age, pre-operative hospital stay, previous neurosurgical operation, ASA score, use of pre-operative steroids, pre-operative antibiotics and location of surgery did not reach any significance.

Patients with Surgical Site Infection

Eighteen of 189 patients had post-operative surgical site infection and fever was the most common presenting symptom in 13 (72.2%) patients, occurring at a median time of 6 days post-surgery. Two cases presented with cerebrospinal fluid leakage, one case initially presented with vomiting, while the other case presented with erythema and purulent discharge on the surgical site.

Table 4. Risk Factors with Univariate Analysis

Parameter	Crude Odds ratio	95% CI	P- value
Age (years)			
Neonates (0-30 days)	(reference)		
Infants (1mo-1year old)	0.45	0.11 to 1.89	0.275
Children (2-9)	1.8	0.60 to 5.44	0.298
Adolescent (10-18)	-	-	-
Pre-operative hospital stay			
< 3 days	(reference)		
3 to 7 days	2.05	0.59 to 7.06	0.256
> 7 days	1.00	0.25 to 3.90	0.996
Diagnosis			
Congenital hydrocephalus	0.21	0.05 to 0.96	**0.044**
Intracranial mass	9.29	1.85 to 37.14	**0.006**
Previous neurosurgical operation	0.73	0.16 to 3.37	0.687
ASA score			
1	(reference)		
2	0.79	0.23 to 2.74	0.710
3	0.69	0.07 to 6.78	0.748
No entry	1.03	0.24 to 4.48	0.967
Use of preoperative steroids	1.22	0.41 to 3.63	0.721
Pre-operative antibiotics			
Cefuroxime	1.35	0.48 to 3.78	0.564
Cefuroxime + Amikacin	0.61	0.17 to 2.23	0.458
Ceftriaxone	1.70	0.45 to 6.44	0.435
Type of surgery			
Craniotomy/Craniectomy/ Burrholing without a medical device	(reference)	-	-
Craniotomy/Craniectomy/ Burrholing with a medical device	0.22	0.07 to 0.69	**0.009**
Presence of VPS	0.20	0.06 to 0.72	**0.014**
Location of surgery			
NSS2	1.24	0.46 to 3.28	0.671
PNCOU	0.82	0.29 to 2.28	0.697
LCB	1.38	0.16 to 11.88	0.770
Others	2.46	0.26 to 23.24	0.433
Surgical time			
≤ 4hrs	(reference)	-	-
> 4 hrs	2.87	1.03 to 8.00	**0.043**

Outcomes of SSI

Majority of patients had organ/space SSI such as meningitis (7 cases) and ventriculitis (9 cases). There was one case of superficial incisional SSI and another case of deep incisional SSI where MRSA was identified from an abscess at the surgical site. Nine cases were readmitted due to SSI. Eight cases had nosocomial infections post-operatively (pneumonia, sepsis and urinary tract infections).

Outcomes of SSI are presented in Table 5. One case of SSI expired due to brain herniation secondary to acute parenchymal hemorrhage, *Acinetobacter baumanii* multidrug-resistant organism *(*MDRO) ventriculitis and sepsis. The rest improved with antibiotics and were all discharged.

Table 5. Outcomes of Surgical Site Infection

Outcome	**Frequency (%) (n = 18)**
Discharged, improved	17 (94.4%)
Expired	1 (5.6%)

The characteristics of infecting microorganisms are presented in Table 6 together with their corresponding culture sites. In three cases, *Staphylococcus* species was seen on cultures obtained on initial operation, while gram-negative microorganisms and MDROs were seen on succeeding operations. Three patients had 2 microorganisms isolated (*Staphylococcus hemolyticus and Acinetobacter baumanii* (MDRO), *Staphylococcus epidermidis* and *Stenotrophomonas maltophilia,* and *Staphylococcus epidermidis* and *Klebsiella pneumoniae* (MDRO)) in their cultures. Fifty percent of cases were culture-negative.

Prevalence of SSI and Adherence to Antibiotic Prophylaxis

The overall prevalence of SSI in this study is 9.5% (Table 7). Cases were considered fully compliant if parameters such as choice of antibiotic, dose, route, timing, re-dosing and duration of prophylaxis were followed based on the current recommendations.[7] All patients who received an antibiotic regimen fully compliant with the recommendations did not develop SSI.

Table 6. Characteristics of Infecting Organisms

Organism	**Site**	**No. of organisms***
Initial operation during time of admission		
Staphylococcus aureus (methicillin-sensitive) -- 1 (methicillin-resistant) -- 1	Subgaleal fluid Abscess	2
Staphylococcus hemolyticus (methicillin-resistant)	Subgaleal fluid	1
Succeeding operations during time of admission		
Staphylococcus epidermidis (methicillin-resistant)	Cerebrospinal fluid	2
Klebsiella pneumoniae (MDRO)	Cerebrospinal fluid	3
Acinetobacter baumanii (MDRO)	Cerebrospinal fluid	1
Stenotrophomonas maltophilia	Cerebrospinal fluid	1
Pseudomonas aeruginosa	Cerebrospinal fluid	1
Burkholderia cepacia	Cerebrospinal fluid	1
Culture – negative		9

*Three patients had 2 microorganisms isolated in their cultures.

Table 7. Surgical Site Infections According to Adherence to Recommended Regimen

Compliance	**Number of surgeries**	**SSI cases**	**Infection rate (%)**
Compliant	15	0	0%
Non-compliant	174	18	10.3%
Total	**189**	**18**	**9.5%**

Several parameters were assessed between those with and without SSI with respect to adherence to antibiotic prophylaxis (Table 8). All patients were given antibiotic prophylaxis intravenously.

Only 15.9% of cases were given appropriate pre-operative antibiotics based on existing institutional recommendations. Cefuroxime and ceftriaxone were the two most commonly used antibiotics among non-compliant cases. The rest were given antibiotics such as cefotaxime, meropenem or a combination of ceftazidime and oxacillin, ceftriaxone and metronidazole, or cefuroxime and oxacillin.

With regards to dosage, majority were given the correct dose; however, there were some cases where antibiotics were underdosed or overdosed.

Pre-operative antibiotics were also given at the appropriate time (within 60 minutes prior to surgical incision) in 88.4% of cases. Administration of appropriate intra-operative doses was also noted in most cases. Post-operatively, antibiotics were discontinued within 24 hours of surgery in 45.5% of cases. The most common duration of antibiotics was 2 days, followed by 3 and 7 days, respectively. Except for overall compliance rate, there were no significant differences seen in all parameters between those with SSI and those without. Adherence to pre-operative antibiotic recommendations for clean neurosurgery was low at 7.9%.

Table 8. Parameters of Compliance in Antibiotic Prophylaxis between Patients with or without SSI

Parameters	SSI (N= 18)	Without SSI (N= 171)	Total (N = 189)
	Frequency, (%)		
Prophylaxis given	18 (100%)	171 (100%)	189 (100%)
Antibiotic type			
Correct choice	3 (16.7)	27 (15.8)	30 (15.9)
Dosing			
Correct dose	1	21	22
Under dose	1	2	3
Over dose	1	4	5
Route - Intravenous	18 (100%)	171 (100%)	189 (100%)
Timing			
within 60 minutes	17 (94.4)	150 (87.7)	167 (88.4)
> 60 minutes	1 (5.6)	14 (8.2)	15 (7.9)
At surgical incision time	0	1 (0.6)	1 (0.5)
After incision time	0	6 (3.5)	6 (3.2)
Intra-operative			
Not needed and not given	10 (55.6)	134 (78.4)	144 (76.2)
Needed and given	3 (16.7)	11 (6.4)	14 (7.4)
Needed but not given	4 (22.2)	16 (9.4)	20 (10.6)
Not needed, but still given	1 (5.6)	10 (5.9)	11 (5.8)
Post-operative			
Discontinued antibiotics within 24 hours after end of surgery	7 (38.9)	79 (46.2)	86 (45.5)
Full Compliance	0%	7.9%	7.9%

DISCUSSION

There are published studies on compliance to guidelines on antibiotic prophylaxis from many countries. However, not all considered compliance to all aspects of the guidelines. It remains to be a challenge worldwide to implement proper surgical antimicrobial prophylaxis as it requires knowledge of international recommendations and repeated evaluation of guidelines.[10]

In our study, the presence of fever was the most common symptom seen among SSI patients, consistent with findings from previous studies where fever in the absence of another clear source of infection was suggestive of CSF shunt infection.[11] Fever was the most common symptom for patients who developed post-operative infections.[7,11-12]

Several published studies reported that risk factors for SSI are still unclear and conclusions vary.[12,13] Although this study showed that intracranial mass, duration of operation (in hours) and type of surgery were independent risk factors for the development of SSI in the univariate analysis, these were not statistically significant in the multivariate logistic regression model. Majority of patients with SSI were diagnosed with intracranial mass who also underwent craniotomy, craniectomy or burrholing procedures without a medical device, which were mostly tumor excision cases. Intracranial mass as a risk factor for SSI is also consistent with other studies which show that meningioma, brain metastasis surgery and intracranial malignant lesions are risk factors for SSI.[5,14]

The larger proportion of SSI cases in surgeries done for >4 hours support that duration of surgery is a significant risk factor. In a study by Korinek, et al. which looked at risk factors for neurosurgical site infections after craniotomy, duration of surgery was confirmed to be an independent risk factor which may indicate difficulties in surgery, surgeon expertise and occurrence of intra-operative complications.[5]

Patients with a medical device generally have higher SSI rates as described by Simon, et al. (11%), Kulkarni, et al. (10.4%) and Claus, et al. (1.5% to 38%).[12,15-16] However in this study, presence of VPS appears not to be a risk factor for SSI. It is important to note that congenital hydrocephalus cases accounted for the most number of VPS insertion cases and majority of them also had surgeries in ≤4 hours.

With regards to causative microorganisms, intra-operative cerebrospinal fluid (CSF) sample collection was not done routinely during initial operation in SSI patients, especially in those who underwent tumor excision. The need to obtain samples was driven by clinical judgement, especially when patients showed signs and symptoms of surgical site infection. It was suggested in a study by Chidambaram to perform fixed intervals for CSF analysis post-operatively to more closely follow trends.[17] In some cases, since cultures were only obtained in succeeding operations, it was hard to assess whether the microorganism was already present during the initial operation.

The organisms obtained on initial operation were consistent with pathogens commonly identified as a complication of clean neurosurgical procedures (gram positive organisms such as *Staphylococcus aureus* or other coagulase-negative *Staphylococci*).[5,18] The presence of hospital-acquired gram negative organisms and MDRO can be explained by the occurrence of other nosocomial infections in SSI patients. Prolonged and inappropriate prophylactic antibiotics have been associated with the occurrence of nosocomial infections and the development of multidrug-resistant organisms.[1,19-20]

For outcomes of SSI patients in this study, one expired due to post-operative complications, accounting for a 5.6% SSI-related mortality. The relatively higher rate, compared to 3% as described in other large sample studies, can be attributed to the smaller sample size used in the study.[3] Patients who develop SSI have a 2 to 11 times higher risk of death compared to patients without an SSI.[3]

There is increased morbidity, mortality, length of hospital stay and cost due to SSI, particularly from post-operative infections in neurosurgery.[21]

Prevalence of SSI

The prevalence of SSI in clean neurosurgical procedures in this study was 9.5%, compared to the 1-2% prevalence rate reported in literature. Other studies report lower prevalence from 1-8% after cranial surgery. No other related large pediatric studies were done correlating efficacy of antibiotics to prevent SSI in low-risk craniotomies. The value we obtained may be higher compared to published literature due to our small sample size, as compared to other studies which involved larger samples who were mostly adults.[1,5] Most SSI patients were also diagnosed with an intracranial mass who had tumor excisions which lasted >4 hours which may explain the calculated rate. The current rate we obtained, however, is slightly lower than the prevalence rate reported by Dy-Pasco, et al. in 2014 at 11.3%.[7]

Adherence

Many factors may affect the low adherence to the recommended antibiotic prophylaxis regimen. In a previous study by Dy-Pasco, et al. in 2014, low adherence to recommended pre-operative antibiotics was also noted at 23.5%, however, the study did not look at other parameters such as dose, route, timing, re-dosing and duration of prophylaxis.[7] A medical records-based, cross-sectional study done in 2015 at Philippine General Hospital by Nabor, et al. looked at compliance with international guidelines on antibiotic prophylaxis and showed that only 13% conformed to all parameters, but this involved other types of elective surgeries.[22] There is a wide variation in overall compliance to guidelines ranging from 0% to 71.9%.[23] According to literature, compliance seems to be lower in neurosurgery than in other procedures.[24-27] Among the various parameters in surgical prophylaxis, inappropriate choice of antibiotic and prolonged duration of administration are the two most common areas for non-compliance seen among the cases analyzed in the study, also consistent with previous studies.[23]

Administration of a single agent cefuroxime accounted for majority of cases demonstrating non-compliance and inappropriate antibiotic use when compared with recommendations, but the use of broad spectrum pre-operative antibiotics, such as ceftriaxone and ceftazidime, were also described.

One study showed that third-generation cephalosporins failed to show superiority over conventional regimens on both incisional and organ related SSI in neurosurgery and mentioned that its use has been associated with resistance to gram negative pathogens.[21] Most studies report an adherence rate of less than 70% with respect to antibiotic selection and the main discord was use of broader spectrum agents than what is recommended.[23]

Post-operatively, most antibiotics were not discontinued within 24 hours after surgery. It was noted that physicians continued antibiotics while awaiting final intra-operative cultures. In majority of cases, reasons for extending antibiotics were not documented. Early post-operative fever is also a concern. This is said to be non-infectious but it is one of the reasons why majority of non-compliant cases continued antibiotics up to 48-72 hours post-surgery.[28] Most studies show less than 50% compliance to duration of antimicrobial prophylaxis but higher compliance to dose and indication.[23,25-26,29] This is consistent with our study which showed a 45.5% compliance rate on this parameter. This poses a huge problem as prolonging antibiotics contributes to antibiotic resistance and predisposes to *Clostridium difficile* infections.[24]

Greater compliance was observed in terms of antimicrobial indication, dose, number of intra-operative doses and timing of prophylaxis, which is also consistent with other studies.[24] Compliance to existing antibiotic prophylaxis recommendation is still encouraged as those who adhered to all parameters did not develop SSI.

This study had several limitations as this involved data collection through chart review. Several sources of bias may be present owing to inaccurate documentation resulting in poor quality of data. A number of patients were also excluded from the data analysis since charts were incomplete or missing. The height of some patients were not documented which affected accurate calculation of BMI.

Patients who had post-operative surgical site infection but were seen at another hospital and those who did not follow up were also not accounted for, which may cause an underestimation of infected cases. Patients who were seen at the outpatient clinic who had SSI were also excluded, as there was no accurate documentation of cases.

CONCLUSION

Adherence to existing pre-operative antimicrobial prophylaxis for neurosurgery is problematic and low in our setting. Except for compliance rates, there were no significant differences in adherence to parameters of antibiotic prophylaxis between patients who had SSI and those who did not. Patients who received an antibiotic regimen fully compliant with the recommendations did not develop SSI. Increased compliance to existing antibiotic prophylaxis recommendation is still desired.

RECOMMENDATIONS

It remains challenging to ensure that surgeons fully adhere with existing guidelines on antibiotic prophylaxis. Interventions to improve compliance are necessary, such as close collaboration with the pediatric infectious disease specialists, hospital infection control unit, neurologists, neurosurgeons and the healthcare staff involved in the neurosurgical operation.

Continuing education on surgical prophylaxis emphasizing rationale use of antibiotics to increase awareness on existing guidelines and updates on local resistance rates, including antimicrobial stewardship, should be regularly done. Studies exploring factors influencing adherence to guidelines may be conducted. Timely follow-up of intra-operative cultures is also necessary to immediately identify SSI and prevent inappropriate use of antibiotics leading to resistant organisms.

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