Follow-up Study on the Effect of Risk-Stratified, Protocol-Based Perioperative Antibiotic Prophylaxis on Postoperative Infections in a Tertiary Care Neurosurgical Department over 10 Years (2007–2016)

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Abstract

Objective To study the effectiveness of risk-stratified prophylactic antibiotic policy on meningitis, surgical site, and extraneurosurgical site infections among postoperative neurosurgical patients from the year 2007 to 2016. This is a follow-up study for a similar analysis done from 1994 to 2006, which is published in *Neurosurgery*.

Methods Retrospective audit of 30,251 consecutive neurosurgical cases from January 2007 through December 2016 at a tertiary care center with culture positivity in samples taken from patients showing clinical/radiologic evidence of infection as an objective marker of postoperative infection. Risk-stratified, variable-duration antibiotic prophylaxis policy was followed over 10 years; it was modified in the year 2014, and infections from 2007 to 2013 were compared with 2014 to 2016.

Results Over 10 years, there were 2,782 infections in 2,193 (9.45%) patients with meningitis in 281 (0.96%), bloodstream infections in 596 (2.05%), respiratory infections in 913 (3.11%), urinary tract infections (UTIs) in 697 (2.30%), and wound infections in 295 (1.02%) patients. On comparison, the proportion of infections between 2014 and 2016 was significantly lower than that between 2007 and 2013 (4.61 ± 0.14% vs. 11.52 ± 2.2%, $p = 0.001$). The most common microorganisms were non–lactose-fermenting gram-negative bacilli, followed by *Klebsiella* and *Escherichia coli*. The proportion of gram-positive cocci (GPC) was 16.2% with methicillin-resistant *Staphylococcus aureus* (MRSA) accounting for 5.5% cases.

Conclusion A risk-stratified, variable-duration prophylactic antibiotic protocol helps in reducing postoperative meningitis, surgical site, and extraneurosurgical site infections in neurosurgical patients, and prophylaxis with first-generation cephalosporin and aminoglycoside is effective.

Keywords
► antibiotic prophylaxis
► meningitis
► wound infection

Introduction

Postoperative infections are the cause of great morbidity and mortality in a neurosurgical unit, especially in a developing country such as India. Many risk factors for infection have been previously described, which include altered sensorium, preexisting infection, poor nutritional status, emergency surgery, multiple operations, duration of surgery for more than 4 to 6 hours, entering a sinus, use of implants, urinary catheterization, cerebrospinal fluid (CSF) leak, external ventricular drainage, and ventilator support.[1-5]

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The benefit of perioperative antibiotic prophylaxis on decreasing neurosurgical site infection/meningitis is well known.[6–8] However, few studies report the data on extraneurosurgical site nosocomial infections,[4,9,10] and many are limited to an intensive care unit (ICU) setting including several studies from our own institute.[1,2] Various antibiotic prophylaxis regimens have evolved and been in use over the years.

This study's aim was to assess the current load of postoperative infections in a dedicated neurosurgical unit and whether they were significantly decreased by appropriate risk-stratified perioperative variable-duration antibiotic prophylaxis.

Material and Methods

This retrospective analysis was conducted at our institute from January 1, 2007 through December 31, 2016. All patients undergoing routine, emergency, or redo neurosurgical procedures at our center during the study period who developed a postoperative culture-proven infection within 1 month of surgery as identified by the hospital infection control records were included in the study.

In the postoperative period when patients showed clinical/radiologic signs of infection, for example, fever greater than 100.4°F, wound site inflammation, CSF leak, neck rigidity, dysuria, cough with expectoration, leukocytosis more than 11,000, and infiltrates on chest X-rays, appropriate bodily fluids were sent for culture. Bacterial organism(s) grown on culture from CSF, blood, endotracheal aspirate, urine, and wound swab/pus was taken as an objective marker of postoperative infection. A dedicated staff nurse designated as the infection control nurse visited the Department of Microbiology on a daily basis and recorded all positive cultures from patients in dedicated neurosurgical wards and ICUs. These were then compared (name and registration numbers) with the previous month's operation lists so as to exclude patients who were admitted for prolonged conservative management. Every month a team of consultants from the Departments of Neurosurgery and Microbiology reviewed the compiled statistics.

Infections were classified as CSF, blood, pulmonary, urinary, and wound. The total number of hospital acquired infections and the number of infected patients were recorded along with the type of different microorganisms in the grown cultures. The year 2007 was chosen as the starting point for this study as before that time neurotrauma was also catered to at the main institute and it was in 2007 when it was shifted to a separate dedicated trauma center, away from the main hospital. Therefore, this study does not include trauma patients who are at a higher risk of developing infections in the postoperative period.

From 2007 onward through 2013, the neurosurgical patients at our institute were categorized in three groups and the antibiotics used for prophylaxis were cloxacillin and amikacin.

- Class 1: Uncomplicated surgery of less than 4-hour duration—24 hours of intravenously administered cloxacillin and amikacin.
- Class 2: Surgery lasting 4 to 6 hours or in whom a breach in sterility was suspected—48 hours of intravenously administered cloxacillin and amikacin.
- Class 3: Procedures lasting longer than 6 hours, breach of paranasal sinuses, redo or emergency operations or implants, or immunocompromising conditions such as diabetes mellitus—48 hours of intravenously administered cloxacillin and amikacin followed by cefuroxime 500 mg administered orally every 12 hours and amikacin 500 mg administered intramuscularly/intravenously every 12 hours for 3 days.

In 2014, the policy was modified with categorization of neurosurgical cases into four classes and the change of cloxacillin to cefazolin based on input from culture-sensitivity reports from the Department of Microbiology. The newer classes were as follows:

- Class 1: Clean cases (< 6 hours)—injectable cefazolin and amikacin at induction with postoperative cefazolin and amikacin for 24 hours.
- Class 2: Clean-contaminated cases (> 6 hours or breach in sterility, e.g., ventriculoperitoneal [VP] shunt, Ommaya, spinal implants, deep brain stimulation [DBS] implants, electrocorticography [ECoG] implants, transsphenoidal surgeries, cases in which frontal or mastoid air cells have been opened)—injectable cefazolin and amikacin at induction with postoperative cefazolin and amikacin for 48 hours followed by oral cefuroxime for 3 days.
- Class 3: Contaminated cases (emergency cases except penetrating head injury, external ventricular drains, redo surgeries, osteomyelitis)—injectable cefazolin, amikacin, and Metrogyl at induction with postoperative cefazolin, amikacin, and Metrogyl for 48 hours followed by cefazolin and amikacin for 3 days.
- Class 4: Dirty cases (penetrating head injury, abscesses, suspected meningitis)—Cefoperazone-sulbactam, amikacin, and Metrogyl at induction followed by cefoperazone-sulbactam, amikacin, and Metrogyl for 7 days with review of culture reports.

We combined the data from 2007 through 2013 and compared them to the infection rates prevailing over 2014 through 2016.

Over the entire study period from 2007 through 2016, the operating theaters, dedicated neurosurgical ICUs and wards, and a number of beds have remained the same and neurosurgical residents rotated equally between two neurosurgical units on a 6 monthly basis. The types of surgeries, basic preoperative preparations, draping, surgical techniques, sterilization, and fumigation protocols, etc. were similar over the study period. Intraoperative normothermia was maintained, and for surgeries lasting more than 6 hours, a single dose of prophylactic antibiotic was repeated.

The institute ethics committee reviewed and permitted this study. Individual patient consent was not sought as this was a retrospective data audit from the hospital records.

Data were collected from hand-written and later electronic records and entered by the principal investigator in Microsoft Excel 2016 (Microsoft Corp.). Statistical analysis was performed using IBM SPSS Statistics Version 23 (IBM Inc.). Continuous variables were compared with Student's unpaired *t*-test. A $p < 0.05$ was considered significant.

Results

Between 2007 and 2016, our department performed nearly 3,000 surgical procedures per year with nearly a quarter of them being emergency procedures (►**Fig. 1**). In this 10-year period, out of a total of 30,251 neurosurgical procedures, 2,193 patients had 2,782 culture-proven hospital-acquired infections (HAIs) in the postoperative period with increasing number of surgical procedures and decreasing infections over the years (►**Fig. 2**).

The percentage of postoperative infections varied form 12.12% in 2007 to 4.46% in 2016 with a mean rate of 9.45% over 10 years (►**Fig. 3**). This included meningitis, surgical site, and extraneurosurgical site infections. The percentage of patients who had culture-proven meningitis after a neurosurgical procedure came down from 1.58% in 2007 to 0.48% in 2016 with a mean of 0.96% over 10 years (►**Fig. 3**). The percentage of extraneurosurgical site infections also decreased over the years. While in 2007 we saw 2.1% bloodstream infections, 2.92% pulmonary infections, 2.95% urinary tract infections (UTIs), and 2.57% wound infections, they had dropped to 0.69%, 1.17%, 2.08%, and 0.03%, respectively, in 2016 (►**Table 1**).

Comparison Between 2007–2013 and 2014–2016

We found that the rates of culture-proven meningitis, bloodstream infections, pulmonary infections, wound infections, and overall HAIs were significantly lower in 2014 to 2016 as compared with 2007 to 2013 (►**Table 2**). However, the percentage of UTIs, although decreased, was not significantly different between the two time periods.

Distribution of Microorganisms Grown on Culture

As seen in ►**Fig. 4**, the most common organisms grown on culture have been non–lactose-fermenting gram-negative bacilli (GNB), including *Acinetobacter*, *Pseudomonas* (combined 42%), followed by Enterobacteriaceae (incl. *Klebsiella* 17%, *Escherichia coli* 12.8%, *Enterobacter* 8%, *Proteus* 2%, and others) and *Staphylococcus* spp. 16% (incl. methicillin-susceptible *Staphylococcus aureus* [MSSA], methicillin-resistant *Staphylococcus aureus* [MRSA], and coagulase-negative *Staph*).

While from 2007 to 2009, 24% infections were caused by gram-positive cocci (GPC), this proportion came down to 7.25% in 2014 to 2016. The proportion of MRSA in our study has decreased from 8.8% in 2007 to 2009 to a low of 0.2% in 2014 to 2016, with a mean rate of 5.4% over 10 years from 2007 through 2016.

Discussion

Many studies have reviewed the development of postoperative meningitis and wound infections following neurosurgical procedures with rates ranging from 0.8 to 6%.[1,3,5,8,11] The benefit of antibiotic prophylaxis on decreasing neurosurgical site infection/meningitis is well known.[7,8,10] However, few studies report the data on extraneurosurgical site nosocomial infections.[2,4,9,10]

In 1964, the Committee on Trauma of the National Academy of Sciences—National Research Council in the United States[12] classified the surgical wounds based on the risk of contamination from endogenous sources into four types: clean, clean-contaminated, contaminated, and dirty. These categories have been validated in neurosurgical practice by Narotam et al[13] in 1994 in a prospective study that showed a significant difference in the infection rates ranging from 0.8% in clean cases, 6% in clean cases with foreign materials

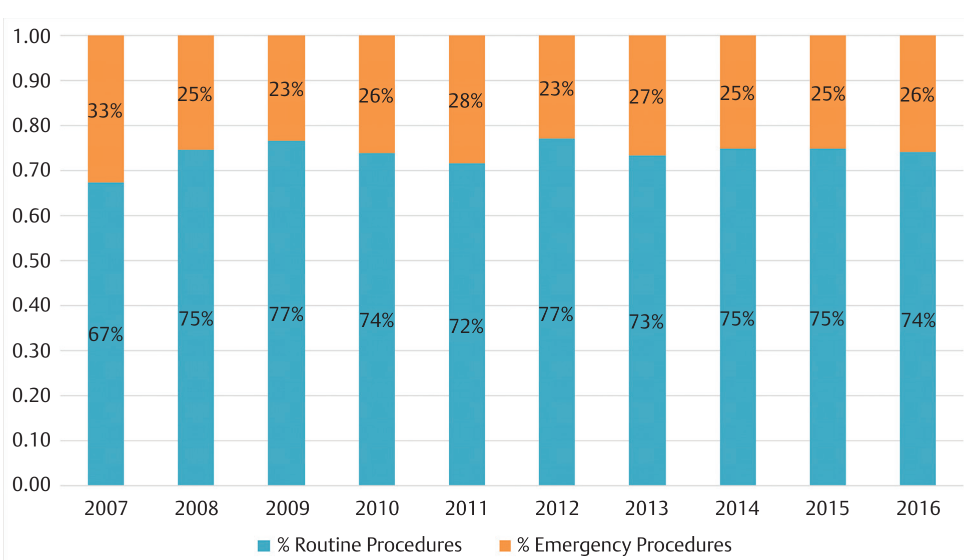

Fig. 1 Stacked bar chart depicting the proportion of routine versus emergency surgical procedures.

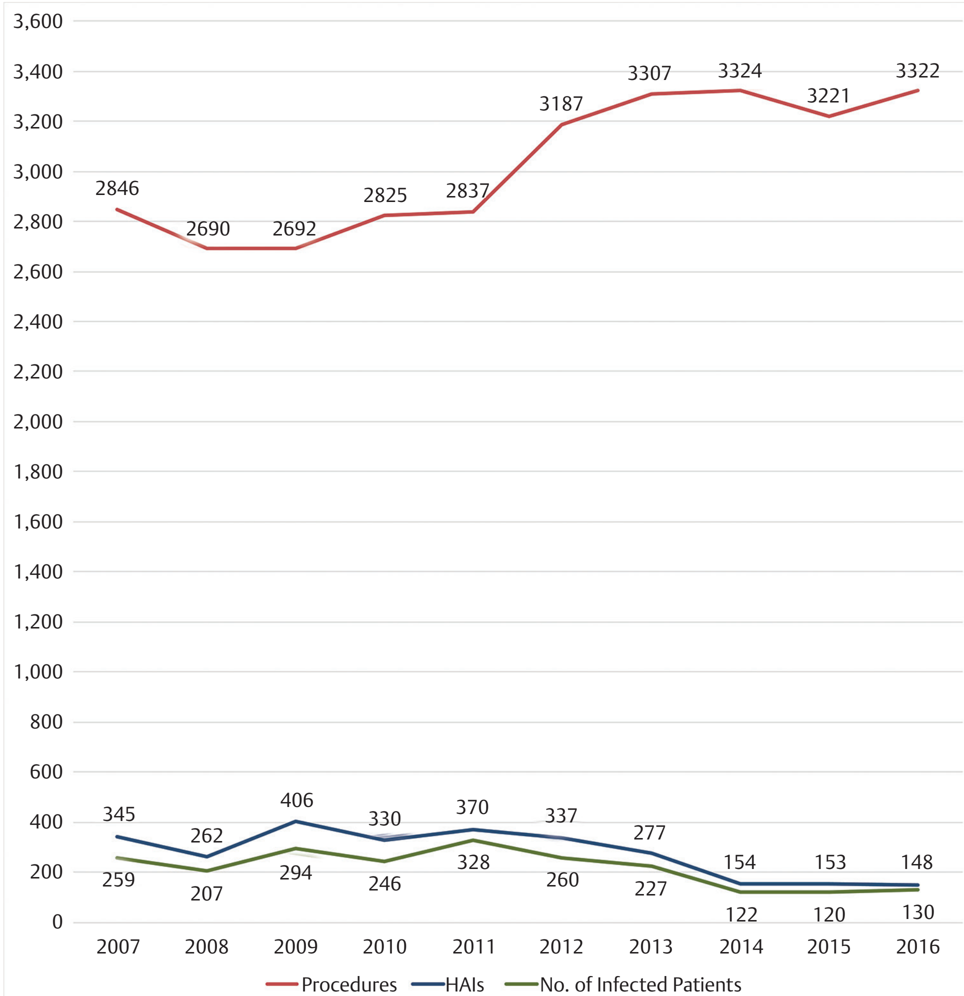

Fig. 2 Line chart depicting the increase in number of procedures over the years compared with the decrease in hospital-acquired infections (HAIs).

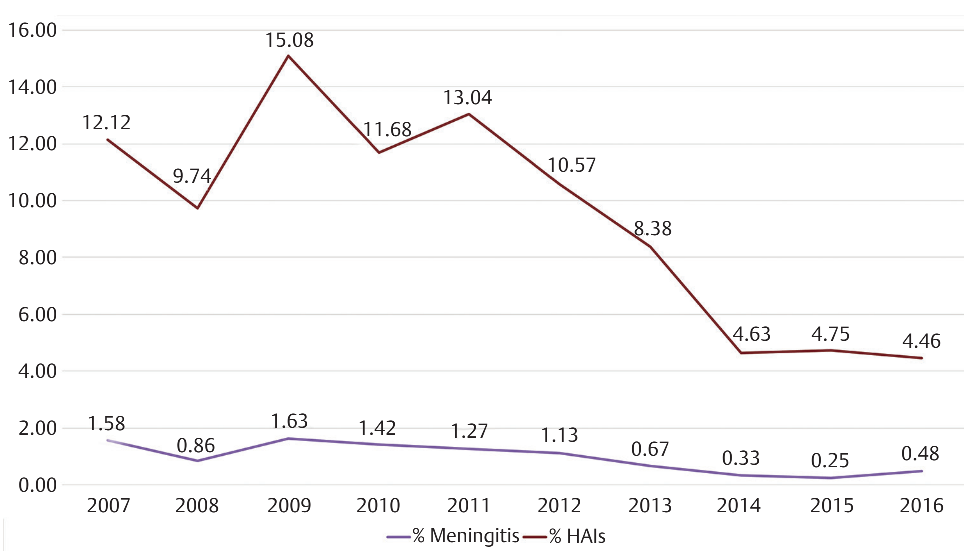

Fig. 3 Line chart depicting the trend of culture-proven meningitis and overall hospital-acquired infections (HAIs) among postoperative patients as a percentage of total surgical procedures every year.

Table 1 Trend of postoperative infections among neurosurgical patients from 2007 to 2016

Year	Procedures	Meningitis	Blood[a]	Pulmonary[b]	Urine[c]	Wound[d]	HAIs[e]
2007	2,846	45 (1.58%)	60 (2.11%)	83 (2.92%)	84 (2.95%)	73 (2.57%)	345 (12.12%)
2008	2,690	23 (0.86%)	59 (2.19%)	98 (3.64%)	42 (1.56%)	40 (1.49%)	262 (9.74%)
2009	2,692	44 (1.63%)	116 (4.31%)	150 (5.57%)	53 (1.97%)	43 (1.60%)	406 (15.08%)
2010	2,825	40 (1.42%)	90 (3.19%)	97 (3.43%)	72 (2.55%)	31 (1.10%)	330 (11.68%)
2011	2,837	36 (1.27%)	86 (3.03%)	133 (4.69%)	74 (2.61%)	41 (1.45%)	370 (13.04%)
2012	3,187	36 (1.13%)	46 (1.44%)	125 (3.92%)	103 (3.23%)	27 (0.85%)	337 (10.57%)
2013	3,307	22 (0.67%)	64 (1.94%)	83 (2.51%)	80 (2.42%)	28 (0.85%)	277 (8.38%)
2014	3,324	11 (0.33%)	26 (0.78%)	47 (1.41%)	62 (1.87%)	8 (0.24%)	154 (4.63%)
2015	3,221	8 (0.25%)	26 (0.81%)	58 (1.80%)	58 (1.80%)	3 (0.09%)	153 (4.75%)
2016	3,322	16 (0.48%)	23 (0.69%)	39 (1.17%)	69 (2.08%)	1 (0.03%)	148 (4.46%)
Total	30,251	281 (0.96%)	596 (2.05%)	913 (3.11%)	697 (2.30%)	295 (1.02%)	2,782 (9.45%)

[a]Blood—bloodstream infections.
[b]Pulmonary—respiratory infections.
[c]Urine—urinary tract infections.
[d]Wound—surgical site infections.
[e]HAIs—hospital-acquired infections.
Note: Percentages are based on proportion of procedures.

Table 2 Comparison between postoperative infection rates from 2007–2013 to 2014–2016

Years	Procedures	Meningitis	Blood infections	Pulmonary infections	UTIs	Wound infections	HAIs
2007–2013	20,384	246	521	769	508	283	2,327
Mean (%) ± SD[a]		1.22 ± 0.36	2.60 ± 0.97	3.81 ± 1.04	2.47 ± 0.56	1.41 ± 0.59	11.52 ± 2.2
2014–2016	9,867	35	75	144	189	12	455
Mean (%) ± SD[a]		0.35 ± 0.11	0.76 ± 0.06	1.46 ± 0.32	1.91 ± 0.14	0.12 ± 0.10	4.61 ± 0.14
p Value[b]		0.004	0.002	0.006	0.144	0.007	0.001

Abbreviations: HAI, hospital-acquired infection; UTI, urinary tract infection.
[a]Mean percentages are based on proportion of procedures; SD, standard deviation.
[b]*p* Value as obtained from unpaired *t*-test, < 0.05 was considered significant.

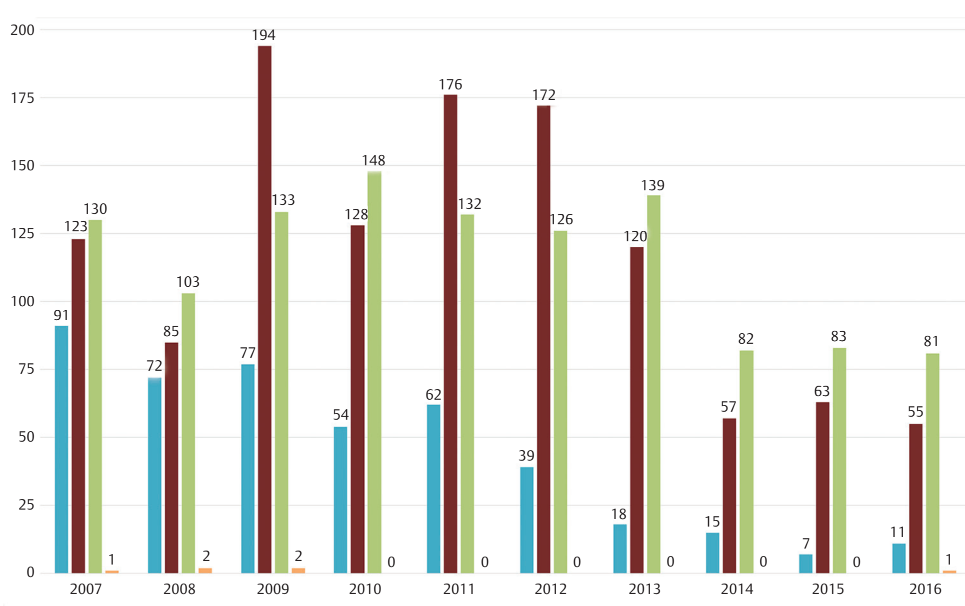

Fig. 4 Bar chart depicting the distribution of microorganisms grown on culture from clinical specimens every year. GNB, gram-negative bacilli; GPS, gram-positive cocci.

as implants, 6.8% in clean-contaminated cases, to 9.7% in the contaminated cases. A stratified chemoprophylactic regimen has been followed in our institute since 2000 with various modifications over the years. After identifying the causative microorganism on culture, the patients were shifted from the empirical prophylactic regimen to specified sensitive antibiotics as per the culture-sensitivity reports.

In a study involving 2,320 postoperative neurosurgical ICU patients between 1995 and 1996, Suri et al[2] identified *Acinetobacter* as a common pathogen (24.6% of all infected patients) and found that it was related significantly to the length of stay in the ICU after surgery. Additional risk factors included ventilation for more than 5 days, ICP monitoring, and prolonged indwelling urinary catheter.

We also found *Acinetobacter* to be a common pathogen among postoperative neurosurgical patients in our study as it was isolated from CSF (26% of meningitis cases), blood (16% of bloodstream infections), respiratory secretions (48% of pulmonary infections), urine (8% of UTIs), and wound cultures (10% of surgical site infections). In our study, the most common organisms causing meningitis were non–lactose-fermenting GNB (47% of meningitis). The proportion of *Staphylococcus* spp. in our study was significantly higher in wound infections (52% in surgical site infections) and was 13% in meningitis, 35% in bloodstream infections, 5% among pulmonary infections, and 29% of UTIs.

During a 12-year study period from 1994 to 2006 at our institute by Sharma et al,[9] out of a total of 31,927 procedures, 3,686 patients developed 5,171 culture-proven infections (16.2%). The most common were pulmonary (4.4%), blood (3.5%) followed by urinary (3%), CSF (2.9%), and wound (2.5%). There was a significant decrease in the infection rate following the introduction of a risk-stratified, variable-duration, written antibiotic protocol in 2000. The percentage of culture-proven meningitis and wound infections were significantly lower in this study compared with the data from 2000 to 2006, as is expected from the exclusion of neurotrauma patients in this study (►**Table 3**). However, despite a decrease in the overall nosocomial infections from 2007 to 2016 as compared with the data from 2000 to 2006, there has been a rise in the UTIs in this study.

Sharma et al[9] identified *Staphylococcus* spp. as the most common pathogen in cases of nosocomial meningitis (27% of cases), followed by non–lactose-fermenting GNB (*Acinetobacter* 15%, *Pseudomonas* 5%) and *Klebsiella* (18%) in 2006.

In this follow-up study, we showed that over the course of 10 years from 2007 to 2016, the proportion of *Staphylococcus* spp. in meningitis decreased from 24% in 2007 to 8% in 2015 to 2016 with a mean of 13% over the 10-year period. This can be seen to concur with the routine use of antistaphylococcal antibiotics in prophylactic regimens. Also, as can be seen by the low prevalence of MRSA infections (5.5% over 10 years), empirical use of broad-spectrum antibiotics would be fallacious.

According to a retrospective study at NIMHANS, Bangalore, over a period of 7 years from 2001 to 2007 by Srinivas et al,[14] out of 18,092 patients undergoing neurosurgical procedures, 2.2% (415) cases developed meningitis in the postoperative period. The most common organisms were non–lactose-fermenting GNB, followed by *Pseudomonas*, *Klebsiella*, and *Staphylococcus* spp.

This study at our institute shows lower infection rates with meningitis in 0.96% cases. However, there was a comparable distribution of pathogens with non–lactose-fermenting GNB (*Acinetobacter*, *Pseudomonas*) being the most common (47%), followed by Enterobacteriaceae (*Klebsiella*, *E. coli*) (39%) and *Staphylococcus* spp. (13%).

Moorthy et al[3] prospectively collected data from 2003 to 2011 on patients undergoing nontrauma cranial surgeries (craniotomies, transsphenoidal procedures, and shunts, excluding preexisting infections) at a tertiary care center with use of 1-day course of intravenous chloramphenicol or single dose of ceftriaxone as prophylaxis. They considered CSF culture positivity in suspected cases as evidence of meningitis that is similar to the criteria used in our study. They showed a postoperative meningitis rate of 0.8%. with the most common organism grown from CSF cultures being *Staphylococcus* spp. (13 out of 27 cases or 48%).

Again, this was contrary to our study wherein the common causative agents for meningitis were GNB—*Acinetobacter* (27%) and *Pseudomonas* (22%) and *Klebsiella* (15%) with *Staphylococcus* spp. accounting for only 13% of meningitis cases.

We found that the rates of meningitis, surgical site infection, and extraneurosurgical site infections from 2014 to 2016 were

Table 3 Comparison between postoperative infection rates[a] from 2000–2006 to 2007–2016

Years	Procedures	Meningitis	Blood infections	Pulmonary infections	UTIs	Wound infections	HAIs
2000–2006[b]	20,339	2.12 ± 0.41	2.29 ± 0.67	3.20 ± 0.74	1.18 ± 0.52	2.26 ± 0.49	11.04 ± 2.24
2007–2016 (present study)	30,251	0.96 ± 0.51	2.05 ± 1.19	3.10 ± 1.42	2.30 ± 0.53	1.03 ± 0.79	9.45 ± 3.79
p Value[c]		0.000	0.633	0.878	0.001	0.002	0.335

[a]Reported as % based on proportion of procedures ± standard deviation.
[b]Data from Sharma et al.[9]
[c]*p* Value as obtained from unpaired *t*-test, < 0.05 was considered significant.

significantly lower than those in 2007 to 2013, as mentioned previously in the results. The main difference between these two groups was the substitution of cefazolin for cloxacillin in the antibiotic prophylaxis regimen, and we hypothesize that the cause of this significant drop in infection rates may be due to the better clinical spectrum of cefazolin (a first-generation cephalosporin) when compared with cloxacillin. Cefazolin has better activity against GNB that are common pathogens in our setting and also methicillin-susceptible *Staphylococcus* spp. The proportion of MRSA in our study was on an average 5.5% over 10 years from 2007 through 2016.

The proportion of different microorganisms grown from the samples is also helpful in identifying the proper empirical prophylactic antibiotics. As can be seen from our data, non–lactose-fermenting GNB were responsible for 47% of meningitis at our center reinforcing that adequate gram-negative coverage is required for prophylaxis. Bloodstream cultures showed nearly equal distribution of GPC and GNB, whereas surgical site infections showed predominance of *Staphylococcus* spp. (52%) as can be expected. Most pulmonary infections were caused by *Acinetobacter* and *Pseudomonas* (combined 66%) that can be seen as due to ventilator-associated pneumonia among postoperative patients. UTIs were commonly caused by Enterobacteriaceae (69%), with *E. coli* and *Klebsiella* being the most common pathogens.

Aminoglycosides are more active against gram-negative than gram-positive organisms. The associated ototoxicity and nephrotoxicity require close monitoring of therapy, and their appeal was thought to be limited.[15] However, in Indian setting majority of postoperative infections are caused by gram-negative organisms.[9,14] This was also confirmed by this study with most of the meningitis, bloodstream, pulmonary, and urinary tract infections being caused by non–lactose-fermenting GNB and Enterobacteriaceae. This warrants an inclusion of an aminoglycoside in the prophylactic regimen.

Cefazolin is a first-generation cephalosporin active against gram-positive bacteria, methicillin-susceptible staphylococci, and nonenterococcal streptococci. Scher[16] found that it provides adequate coverage for many clean and clean-contaminated operations. He also noted correctly that prophylactic antibiotic needs to be repeated in a prolonged surgery for optimal benefit.

Given the rise in antibiotic resistance, physicians have a societal and ethical responsibility to use antibiotics in an appropriate manner. We last reviewed our prophylactic antibiotic policy in 2014 and plan to undertake another revision in 2019 based on the 5-year antibiogram from 2014 to 2018, to select the antibiotics that are effective against prevailing pathogens and reduce the burden of postoperative infections.

Conclusion

Based on this study findings, we can conclude that a risk-stratified, variable-duration chemoprophylactic protocol helps in reducing postoperative meningitis, surgical site, and extraneurosurgical site infections in neurosurgical patients. Non–lactose-fermenting GNB and Enterobacteriaceae are important pathogens among postoperative neurosurgical patients and antibiotic prophylaxis including first-generation cephalosporin, and an aminoglycoside is effective in such a setting.

Conflict of Interest

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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