African Journal of Pharmacology and Therapeutics Vol. 5 No. 4 Pages 241-246, 2016
Open Access to full text available at http://journals.uonbi.ac.ke/ajpt

Research Article

Patterns of antimicrobial use in the neurosurgical ward of Kenyatta National Hospital

Sylvia A. Opanga [a,*], Nimrod J. Mwang'ombe [b], Faith A. Okalebo [c], and Kimani A.M. Kuria [a]

[a] *Department of Pharmaceutics and Pharmacy Practice, School of Pharmacy, University of Nairobi, Kenya*
[b] *Division of Neurosurgery, School of Medicine, University of Nairobi, Kenya*
[c] *Department of Pharmacology and Pharmacognosy, School of Pharmacy, University of Nairobi, Kenya*

* **Corresponding author:** Department of Pharmaceutics and Pharmacy Practice, School of Pharmacy, University of Nairobi, P.O. Box 19676-00202, Nairobi, Kenya. **Tel**: +254-72-1296448; **Email**: sopanga@uonbi.ac.ke

Background: Antibiotics in neurosurgery are used for prophylaxis and treatment of already established infection. Guidelines state that prophylactic antibiotics should be given for up to 24 hours. For treatment of already established infections, empiric therapy with intravenous antibiotics for four to eight weeks is indicated. Studies have shown no distinction between antibiotic use for prophylaxis and treatment of established infection in neurosurgery.

Objectives: To identify antibiotic use patterns and medication errors and their association with development of surgical site infections.

Methods: A prospective cohort study involving adult neurosurgical patients was carried out at Kenyatta National Hospital, between April 2015 and July 2015. Patient demographic data as well as data on surgical procedures carried out, antibiotics used and medication errors was collected. Descriptive data analysis was done for all variables. To test for association between antibiotic use patterns and development of surgical site infections, the Fischer exact Chi square test was used.

Results: Out of the 84 participants recruited in the study, 87.2% (n=68) used antibiotics. Ceftriaxone was the most commonly used (63.7%, n= 44), followed by metronidazole (40.4%, n=23). Medication errors that were noted involved inappropriate choice and use of antibiotics. There was no distinction between use of antibiotics for prophylaxis and treatment of infection. There was no statistically significant association between patterns of antibiotic use and development of surgical site infection.

Conclusion: Antibiotic use patterns do not affect the incidence of neurosurgical site infections. Prescribing errors of various types were prominent. An antibiotic use protocol should guide antimicrobial selection and use in neurosurgery.

Key words: antibiotic, prophylaxis, medication errors

Received: July, 2016
Published: December, 2016

1. Introduction

Antibiotic use in neurosurgery serves the purposes of prophylaxis and treatment of already established infections. Antimicrobial prophylaxis should not be done for more than 24 hours. The choice of antibiotic for prophylaxis should be based on the knowledge of causative organisms at the incision site, antimicrobial susceptibility and resistance patterns at the unit, safety and cost effectiveness of the antibiotic (ASHP Therapeutic Guidelines, 2016). Guidelines exist on the presumptive treatment of intracranial infections. For brain abscesses, treatment with intravenous antibiotics is indicated for a period of 4 to 8 weeks, depending on the response of the patient. The long duration of treatment is required because of the long time required for the brain tissue to repair and close the abscess space. The recommended antibiotics should adequately cross the blood brain barrier and achieve adequate concentrations in the brain (Brook, 2015).

Despite existing guidelines, common practice in neurosurgery across studies shows that antibiotics are used to cover for surgical site infections (SSIs) pre and postoperatively (Jiang et al, 2016; Ha et al, 2012). This has led to prolonged prophylaxis, which in turn increases the risk of surgical site infections (Bozkurt et al, 2013; Ha et al, 2012). This is not uncommon in our set up, where antibiotics are generally used with no distinction between antimicrobial prophylaxis and treatment of already established infections. Lack of antimicrobial use protocols has further compounded the problem.

Our study set out to establish the extent of this problem at the neurosurgical unit of Kenyatta National Hospital. The main objective was to identify antibiotic use patterns and their association with development of surgical site infections as well as identify medication errors in antibiotic use.

2. Methodology

2.1 Study Design and Population

We conducted a prospective cohort which followed up trauma surgical patients admitted in the Neurosurgical wards of KNH between April 2015 and July 2015 for antibiotic use and development of surgical site infections.

2.2 Inclusion and Exclusion Criteria

Adult patients over 18 years old, who sustained traumatic injuries, were admitted at the neurosurgical unit for elective and emergency neurosurgery in the study period were included.

Patients who underwent neurosurgery for reasons other than trauma were excluded.

2.3 Sampling and Participant Recruitment

The sample size was calculated using the formula for prospective incidence studies (Daniel, 2010).

A study carried out by Njiru et al, (2015) reported an incidence of SSIs of 7.5% in patients who were undergoing elective craniotomy at the neurosurgical unit of Kenyatta National Hospital. Using this incidence and the estimated patient population of Kenyatta National Hospital to be 1800, a sample size of 100 patients was estimated.

2.4 Sampling

The investigator perused through patient files in the neurosurgical ward to identify eligible patients. Universal sampling was used to include all patients who met the inclusion criteria.

2.5 Data Collection

Patients were followed up in the ward daily and the following information abstracted and recorded in predesigned data collection forms: patient biodata, surgical procedure, antibiotics administered and the patterns of use in terms of dosing, frequency and duration of administration; medication errors, and development of surgical site infections.

2.6 Data Analysis

All variables were subjected to descriptive analysis. The Fischer exact Chi Square test was used to test for association between antibiotic use patterns and development of surgical site infections. Data analysis was done using STATA version 13 software. The level of significance was set at 0.05.

2.7 Ethical Considerations

Approval to carry out the study was sought from the University of Nairobi/ Kenyatta National Hospital Research and Ethics Committee, approval number **P76/02/2014**. Informed consent was sought from patients and/or their caregivers before enrolment into the study. All the patient information was treated with confidentiality. Serial numbers were used instead of patient names and admission numbers. All the data was password protected and accessible only to the investigator and data analyst.

3. Results

The study recruited 84 adult patients 18 years and older, who sustained neurotrauma through road traffic accidents, assault, falls and other unidentified forms of trauma.

The males formed 93% of the study population (n=78) with the females being 7% (n=8) of the study population. The median age of the patients was 35 years.

3.1 Prevalence and types of antibiotics used in surgical and non-surgical patients

The total number of patients who were on antibiotics was 68 (87.2%). Of those who underwent surgery, 89.5% (n=51) used antibiotics. Ceftriaxone was the most commonly prescribed antibiotic (78.9%, n=45), followed by metronidazole, amoxicillin clavulanate, cefuroxime and meropenem (**Figure 1**).

The number of antibiotics prescribed per patient varied between one and four. Those who were put on one antibiotic were 20.3%, (n=14) while 26.1% (n=18) received two antibiotics. Fourteen patients (20.3%) received three antibiotics while 5.8% (n=4) were on four antibiotics during the time of hospitalization. As the number of antibiotics used increased, the likelihood of development of infection increased, and this was statistically significant (p=0.015).

3.2 Patterns of antibiotic prescription

Thirty one patients had one ceftriaxone prescription. The daily defined dose for Ceftriaxone is 2g according to the WHO ATC DDD Classification, 2016.

Slightly over half of the patients (54.8%) received the daily recommended dose of Ceftriaxone (2g), while 30% received more than the daily recommended dose of ceftriaxone (3-4g). 3.2% of the patients on ceftriaxone were on an unspecified dose.

Twelve patients had a second prescription of ceftriaxone (17.4%). For eleven of these patients (91.7%), the duration of use was not indicated. Of the patients on only

 ISSN 2303-9841

one prescription of ceftriaxone, 38.6% (n=17) developed surgical site infection, while for those on the second prescription, 91.7% (n=11) developed surgical site infection.

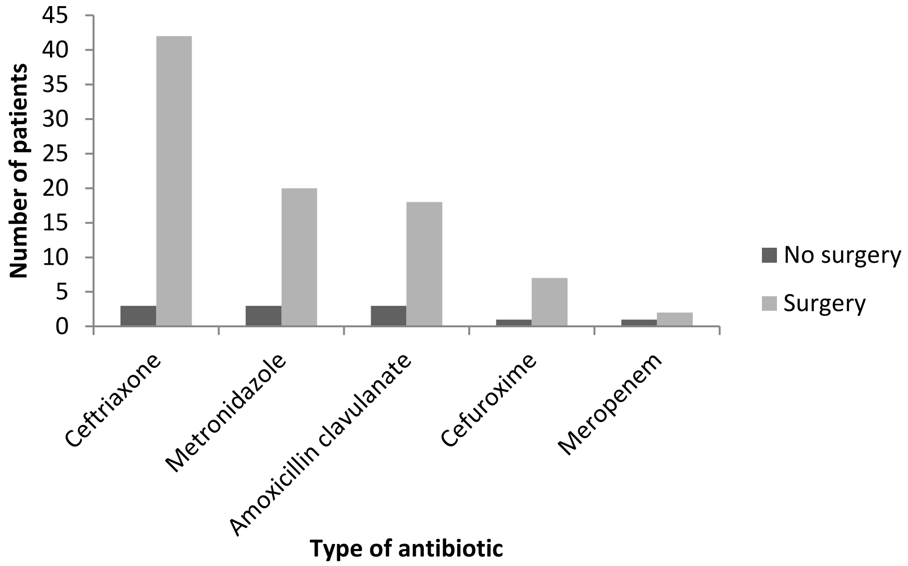

Figure 1: Types of antibiotics used with or without surgery

There was no statistically significant association between administration of the first prescription of ceftriaxone and development of surgical site infection (p=0.478). Similarly, there was no statistically significant association between the second prescription of ceftriaxone and development of surgical site infection (p=0.720).

Metronidazole was used by 40.4% (n=23) of the patients who were on antibiotics, of which 87.0% (n=20) underwent surgery. All the patients received 500 mg of metronidazole 8 hourly. This translates to a daily dose of 1.5g, which is the recommended daily dose for metronidazole (WHO ATC DDD). Of the patients on metronidazole who underwent surgery, 57.9% developed infection (n=11). There was no statistically significant association between metronidazole use and development of infection (p=0.121).

Amoxicillin clavulanate was prescribed for 23 patients. Of these, 78.3% (n=18) underwent surgery. There was no statistically significant association between the dose (p=0.695), frequency (p=0.801) and duration of amoxicillin clavulanate use (p=0.770) and surgical procedure.

According to the WHO ATC DDD Classification, the daily recommended dose for this drug is 1000mg of the amoxicillin component for the oral drug and 3g for the intravenous form. Only two patients were on the oral formulation while 19 were on the intravenous form. Assuming the two were on 1000mg of amoxicillin, it could imply that they exceeded the recommended dose two fold. This assumption of dose is made because the formulations available at the hospital contain 1000mg of amoxicillin.

Ten patients who were on amoxicillin clavulanate developed surgical site infection. There was no statistically significant association between the route, dose, frequency and duration of use of the drug and development of surgical site infection.

Eight patients received cefuroxime during the study period and 87.5% (n=7) of them underwent surgery. There was no statistically significant association between the cefuroxime use patterns and surgical procedure (p=0.450).

The daily recommended dose for oral cefuroxime is 0.5g while that of the parenteral version is 3g. Only two patients were on oral cefuroxime while the rest were on an unspecified route of administration. Assuming two of those on oral cefuroxime were on 500mg, both given twice daily, it shows that they could have exceeded the dose by twice the recommended dose. Four of the patients who received cefuroxime (57.1%) developed surgical site infection. There was no statistically significant association between infection rates and the daily recommended dose of cefuroxime (p=0.714).

Three patients were on meropenem and two of them underwent surgery. There was a statistically significant association between the frequency of administration of meropenem and surgical procedure (p=0.028), as well as the duration of use (p=0.068).The association between the use patterns of meropenem and development of infection was not statistically significant (p=0.103).

3.3. Medication Errors in Antibiotic Use at the Neurosurgical Unit

The most common medication errors in antibiotic use were prescribing errors. According to the National co-ordinating council for medication error reporting and prevention (NCC-MERP, 2001), prescribing errors can occur in form of: dose omission, improper dosage (under dose or overdose), wrong strength, wrong drug, wrong dosage form, wrong route of administration, wrong duration, inappropriate drug selection, lack of a clear purpose of a drug on a prescription and medication

 ISSN 2303-9841

prescribed to the wrong patients. Several prescribing errors were recorded in this study.

Prescribing in trade names

Metronidazole (64.0%, n=23), Amoxicillin clavulanate (42.0%, n=21) and cefuroxime (16.0%, n=8) were prescribed in trade names (Flagyl, Augmentin and Power-cef respectively). Although this is not in itself a medication error, it could potentially lead to medication errors.

Unspecified dose, route, frequency and duration of administration

For most prescriptions, the dose, frequency and duration of administration was not specified. This could have led to errors in administration of the antibiotics. This is illustrated in **Table 1**. There were more medication errors among patients who underwent surgery compared to those who did not undergo surgery.

Prolonged duration of administration

Prolonged use of antibiotics was defined as antibiotics administered for more a period of 14 days and more. The caveat to this is that intracranial abscesses require to be treated with intravenous antibiotics for up to 4 weeks.

Thirty five per cent of the patients (n=24) received antibiotics for a prolonged period, and they all developed surgical site infections (**Table 2**).

Table 1: Unspecified dose, route and frequency of administration of antibiotics

Unspecified dose	**No Surgery (%)**	**Surgery, n (%)**
Gentamicin qidx7days	0 (0.0%)	1(100.0%)
Unspecified route	**No Surgery (%)**	**Surgery, n (%)**
Metronidazole	3 (27.3%)	8(72.7%)
Amoxicillin clavulanate	3(23.1%)	10 (76.9%)
Cefuroxime	1 (16.7%)	5 (83.3%)
Meropenem	1 (50.0%)	1 (50.0%)
Gentamicin	0 (0.0%)	1(100.0%)
Flucloxacillin	0(0.0%)	1(100.0%)
Amikacin	0(0.0%)	1(100.0%)
Unspecified frequency	**No Surgery (%)**	**Surgery, n (%)**
Ceftriaxone		
Metronidazole	0(0.0%)	1(100.0%)
Amoxicillin clavulanate	0(0.0%)	2(100.0%)
Cefuroxime	0(0.0%)	1 (100.0%)
Meropenem	1 (100.0%)	0(0.0%)
Unspecified duration	**No Surgery, n (%)**	**Surgery, n (%)**
Metronidazole	1(25.0%)	3 (75.0%)
Amoxicillin clavulanate	0 (0.0%)	1 (100.0%)
Cefuroxime	0 (0.0%)	1(100.0%)
Meropenem	0 (0.0%)	1(100.0%)
Flucloxacillin	1(100.0%)	0 (0.0%)
Wrong dose		
Amikacin 50mg	0 (0.0%)	1(100.0%)
Abbreviations		
TEO	1(100.0%)	0 (0.0%)

Table 2: Number of patients who received antibiotics for a prolonged period

	Ceftriaxone	Metronidazole	Coamoxiclav	Cefuroxime	Clindamycin	Amikacin	Meropenem
14 days	12	3	2	1	1	-	-
21 days	1	2	-	-	-	-	-
Indefinite	-	-	-	-	-	1	1

 ISSN 2303-9841

Inappropriate combinations of antibiotics

Inappropriate antibiotic combinations refer to a combination of two or more antibiotics from the same or related class, with the same antimicrobial spectrum. In this case, nineteen patients received inappropriate combinations of amoxicillin clavulanate and cephalosporins. The caveat to this observation is that the antibiotics could have been switched following poor clinical response or using culture and sensitivity reports.

Inappropriate Antibiotic Selection

Prescription of antibiotics was not based on any guidelines, evidence or antimicrobial susceptibility patterns for patients who underwent surgery as well as those who developed infection. A study done by Njiru et al, (2015) on antimicrobial resistance patterns in this neurosurgical unit reported high antimicrobial resistance patterns to commonly used antimicrobials. To illustrate this, we obtained resistance data from the said study, and using *Staphylococcus aureus* and Klebsiella as our reference organisms, we postulated that all patients on Amoxicillin clavulanate, cefuroxime and meropenem were unlikely to benefit from the antibiotics.

Unclear Indication of prescription

There was no clear indication for administering antibiotics, whether for prophylaxis or treatment. For purposes of discussion, we made an assumption that any antibiotic given for three days or less was given for prophylaxis and presumptive treatment was for those antibiotics that were given for more than three days.

Inappropriate doses

Using the WHO ATC DDD recommended daily doses of the major antibiotics, it was noted that some patients received more than the daily recommended doses of different antibiotics as shown in **Table 3.**

Table 3: Inappropriate dosing of antibiotics

Drug	Daily recommended dose (DDD),mg	No of patients on inappropriate dose	Comments
Ceftriaxone	2000	9 (20.0%)	Overdose iv
Amoxicillin Clavulanate	1000 oral, 3000 iv	2 (8.7%)	Overdose on oral drug
Cefuroxime	500 oral, 3000 iv	2 (25.0%)	Overdose on oral drug

4. Discussion

Instances of irrational antimicrobial use were identified and prescribing errors were noted in this study. The irrational use stemmed from improper drug selection, unclear indication for antibiotic, inappropriate doses and wrong frequency and duration of administration of antimicrobials. This could be due to lack of antimicrobial use protocols and guidelines at Kenyatta National hospital. Prophylactic use of antibiotics may have been prolonged.

Our findings are similar to other studies in which antibiotic overuse and misuse was noted (Apostolopoulou et al, 2016; Testa et al, 2015; Sharma et al, 2012). As seen in our study, antibiotics to which the infecting microbes were resistant were still given despite the availability of resistance data. The same trend was reported in another study in which 94% of the patients received antibiotics despite antimicrobial resistance data.

Antibiotic overuse has also been reported in another study where, all the patients received prophylaxis despite indication for only half of the patients (Apostolopoulou et al, 2016). Another study reports contrary results where there was underuse of antibiotics (Lundine et al, 2010).

It was difficult to distinguish between antimicrobial prophylaxis and treatment regimens in our study. The same was also seen in other studies (Testa et al, 2015; Sharma 2012). The most common antibiotics used in our study were ceftriaxone, metronidazole, cefuroxime, Amoxicillin clavulanate and meropenem. Other studies also used similar drugs (Apostolopoulou et al, 2016; Hammad et al, 2013; Sharma et al, 2012). Like in our study, combinations of antibiotics were used (Hawnet al, 2013; Lundine et al, 2010). The use of some antibiotic combinations increased the risk of development of infections while some combinations reduced the risk (Hawn et al, 2013). Some combinations were deemed inappropriate just like in our study (Testa et al, 2015).

Several studies reported prolonged antibiotic use beyond the treatment or prophylaxis duration just like in our study (Testa et al, 2015; Lorensia et al, 2012); yet this does not prevent the development of surgical site infections (Sharma et al, 2012).

Similar studies reported that antimicrobial prophylaxis did not conform to guidelines or protocols, and there were variations in compliance regarding the choice of antibiotic, indication for prophylaxis, timing and discontinuation of prophylaxis (Gouveaet al, 2015; Testa et al, 2015). This is unlike in our study where there were no local protocols against which appropriate use of antibiotics could be compared. This calls for development of an antibiotic use protocol (Jiang et al, 2016). The quality of antimicrobial prophylaxis can be improved through continuous training, compliance with available guidelines and supervision of the use of antibiotics (Bozkurt et al, 2013).

5. Conclusion

There was no clear distinction between antimicrobial prophylaxis and treatment of intracranial infections. Some antibiotics were used despite the fact that there was data on resistance to those antibiotics. Guidelines

ISSN 2303-9841

on antibiotics should be developed and adhered to, to reduce surgical site infections and improve outcomes of prophylaxis and treatment of neurosurgical site infections. Clinical pharmacists should be incorporated in the neurosurgical team to guide antimicrobial use. Studies should be conducted to monitor the clinical effectiveness of antimicrobials alongside resistance patterns, to evaluate the overuse of antibiotics at the KNH neurosurgical unit, and to demonstrate the benefit of administration of antibiotics for shorter durations.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgements

The authors acknowledge the Gandhi Smarak Nidhi Fund for financial support.

References

American Society for Health System Pharmacists Therapeutic Guidelines (2016). Clinical Practice guidelines for antimicrobial prophylaxis in surgery. www.ashp.org. Accessed 13/05/2016.

Apostolopoulou E, Dimitros Z and Aikaterini G (2016). The impact of irrational perioperative antimicrobial prophylaxis on the nursing workload. *Health Sci. J.* www.hsj.gr. Accessed 15/05/2016.

Bond CA and Raehl CL (2007). Clinical and economic outcomes of pharmacist-managed antimicrobial prophylaxis in surgical patients. *Am. J. Health Syst. Pharm*. **64**: 1935-1942.

Bozkurt F, Kaya S and Gulsun S (2013). Assessment of perioperative antimicrobial prophylaxis using ATC DDD Methods. *Int. J. Infect. Dis.* **17:**e1212-e1217.

Brook I (2015). Brain abscess treatment and management. *Medscape*. http://reference.medscape.com/article/212946-treatment. Accessed 26/05/2016.

Collins S (2013). SSI prevention: crossing environments of care, standardizing incision management. *Infect. Control Today*; www.infectioncontroltoday.com. Accessed 14/5/2016.

Daniel W.W. (2010). Biostatistics: Basic concepts and Methodology for the health sciences. 9th Edition, John Wiley and Sons, Inc. Wiley India (P), New Delhi, India.

European Medicines Agency (2015). Medication errors. www.ema.europa.eu. Accessed 6/6/2016.

Gouvea M, Novaes CO and Pereira D (2015). Adherence to guidelines for surgical antimicrobial prophylaxis: a review. *Braz. J. Infect. Dis.* **19**:517-524.

Ha J-S, Oh S-M and Kang J-H (2012). Efficacy of short term versus long term antimicrobial prophylaxis for preventing surgical site infections after clean neurosurgical operations. *Korean J. Neurotrauma.* **8**:104-109.

Hammad MA, Al-Akhali KM and Mohammed AT (2013). Evaluation of surgical antimicrobial prophylaxis in Aseer Area hospitals in the Kingdom of Saudi Arabia. *JPCS.* **6**:1-7.

Hawn MT, Richman JS and Vick CC (2013). Timing of surgical antimicrobial prophylaxis and the risk of surgical site infection. *JAMA Surg*. **148**: 649-657.

Jiang X, Jianjun MA and Hou F (2016). Neurosurgical site infection prevention: single institute prevention. *Turkish Neurosurg*. **26**: 234-239.

Junker T, Mugajic E and Hoffmann H (2012). Prevention and control of surgical site infections: review of the Basel Cohort Study. *Swiss Medical Weekly*. **142**: w13616.

Lorensia A, Wahjuninasih E and Wijokongko G (2012). Study of drug related problems in the use of antimicrobial prophylaxis for appendectomy in a hospital in Sidowjo. A Conference presentation at the Federation of Asian Pharmaceutical Association, Bali, Indonesia. www.researchgate.net. Accessed 14/05/2016.

Lundine KM, Nelson S and Duffy PJ (2010). Adherence to perioperative antimicrobial prophylaxis among orthopaedic trauma patients. *Can. J. Surg.* **53**:367-372.

Ozgun H, Ertugul BM and Soyder A (2010). Perioperative antimicrobial prophylaxis: adherence to guidelines and effects of educational intervention. *Int. J. Surg.* **8**:159-163.

Sharma MS, Suri A and Chandra SP (2012). Cost and usage patterns of antibiotics in a tertiary care neurosurgical unit. *Indian J. Neurosurg.* **1**:41-47.

Testa M, Stillo M and Giacomelli S (2015). Appropriate use of antimicrobial prophylaxis: an observational study in 21 surgical wards. *BMC Surg.* **15**:63.

Ulu- Kilic A, Alp E and Cevahir F (2015). Economic evaluation of appropriate duration of antimicrobial prophylaxis for prevention of neurosurgical infections in a middle income country. *Am. J. Infect. Control.* **43**: 44-47.

WHO Collaborating Centre for Drug Statistics and Methods (2016). ATC DDD Classification for Anti-infectives. WHOCC-ATC/DDD index. www.whocc.no/atc ddd index/?code. Accessed 8/6/2016.