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The Evaluation of surgical antimicrobial prophylaxis prescribing patterns in Dr. George Mukhari Academic Hospital, Gauteng Province

A mini-dissertation submitted by

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DECLARATION

I declare that the mini-dissertation hereby submitted to the Sefako Makgatho Health Sciences University, for the degree of Master of Pharmacy, in the Faculty of Health Sciences, School of Pharmacy has not previously been submitted by me for a degree at this or any other university; that it is my work in design and execution, and that all material contained herein has been duly acknowledged.

Tshweu, J K (Ms) Date
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ABBREVIATIONS AND ACRONYMS

AMR: Antimicrobial Resistance

ASHP: American Society of Health-Systems Pharmacists

ATC: Anatomic Therapeutic Chemical Classification

CPGAS: Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery

DGMAH: Dr. George Mukhari Academic Hospital

ENT: Ear, Nose and Throat

HAI: Healthcare Associated Infection

ICD-10 Code: International Classification of Diseases

IDSA: Infectious Disease Society of America

INN: International Non-Proprietary Name

IPC: Infection Prevention Control

MEDUNSA: Medical University of South Africa

MDR: Multi-Drug Resistant

MRSA: Methicillin Resistant Staphylococcus Aureus

NDOH: National Department of Health (South Africa)

NICE: National Institute for Health and Care Excellence (England)

SAP: Surgical Antimicrobial Prophylaxis

SHEA: Society for Healthcare Epidemiology of America
SMU: Sefako Makgatho Health Sciences University
SMUREC: Sefako Makgatho University Research & Ethical Committee
SPSS: Statistical Package for Social Sciences
SSI: Surgical Site Infection
STG: Standard Treatment Guidelines
WHO: World Health Organisation
ABSTRACT

Introduction:

South African hospitals are challenged by the growing occurrence of resistant organisms. Approximately 49% of South African surgical patients receive surgical antimicrobial prophylaxis (SAP), however, 19% of these patients receive the inappropriate medicine. This highlights the significance of monitoring the consumption of antimicrobials in this group of patients to ensure the appropriate use thereof. The judicious use of antimicrobials supported by stewardship programs is regarded as one of the key components in preventing surgical site infections.

Objectives:

The objectives of the study were to describe the prescribing practices of SAP in surgical patients at a teaching hospital, including the choice of antimicrobial(s) for SAP; dosages used; timing of administration, the duration of SAP and also to evaluate prescriber compliance to standard treatment guidelines.

Method:

A retrospective review of adult patients who underwent a surgical procedure between January to May 2017 was conducted. Patient numbers were identified and systematically sampled from theatre registers; medical records were retrieved and data was manually collected. Prescribing patterns were compared to the South African National Department of Health’s standard treatment guidelines; reference was also made to the American’s Clinical Practice guidelines for antimicrobial prophylaxis in Surgery (CPGAS) 2013.

Results:

A total of 234 adult patients who underwent surgery were included in the study. Of these, the male population was 53% (124; n=234) and the mean age of patients was 37.99 years (SD=14.5). Gynaecological procedures were the most common at 27.4% (64; n=234), followed by general surgery at 18.4% (43; n=234).
Surgical antimicrobial prophylaxis was administered in 70% (164; n=234) of the population. Cefazolin was the most commonly used antimicrobial for this purpose in 64% (151; n=234) patients, followed by ceftriaxone in 3% (8; n=234) patients.

Choice of SAP was appropriate in 70% (163; n=234) of the population. The correct timing of SAP administration was observed in 69% (161; n=234). Prophylaxis was administered at correct dosages in 29% (68; n=234) cases and duration of SAP was administered in accordance with guidelines in 44% (103; n=234) of cases. None of the 14 surgical procedures (6%; n=234) that lasted more than four hours received a second dose SAP as per recommendations. When comparing compliance to guidelines between the studied sub-disciplines, significant differences do exist in all measures evaluated with regards to guideline compliance.

**Conclusion:**

Similar to this study, many studies conducted worldwide on institutions’ compliance to surgical antimicrobial prophylaxis still show that ideal practice of SAP is not achieved. Lack of specific institution guidelines and the inappropriate use of antimicrobials due to lack of awareness seem to be some of the contributing factors to this shortfall. Clinical pharmacists can play a major role in identifying challenges of SAP practices and implement interventional measures to ensure appropriate antimicrobial use.

**Recommendations:**

Development of hospital guidelines in partnership with the institution’s antimicrobial stewardship team and surgeons is recommended to achieve optimal results. Post interventional studies are also necessary to ensure efforts are yielding positive results.
CHAPTER 1: INTRODUCTION

CHAPTER 1

INTRODUCTION

1.1 INTRODUCTION

The World Health Organisation (WHO) enlists hand washing, appropriate and judicious use of antimicrobials, antiseptic skin preparation, good surgical technique, proper wound care and instrument decontamination and sterility as key to the prevention of surgical site infections (SSIs) (WHO, 2009). This chapter introduces the concept of surgical antimicrobial prophylaxis according to Standard Treatment Guidelines (STG) as a tool to combat the occurrence of SSI’s. It also discusses the background and the rationale for the study. The aim, objectives, research question and the importance of the study are also discussed.

1.2 BACKGROUND AND RATIONALE FOR THE STUDY

Antimicrobial resistance (AMR) has become a global health threat. Decades of inappropriate use of antimicrobials and poor infection prevention and control (IPC) have resulted in the rise of multi-drug resistant infections both internationally and in South Africa (Boyles, Whitelaw, Bamford, Moodley, Bonorchiis, Morris, Rawoot, Nicker, Lusakiewicz, Black, Stead, Lesosky, Raubenheimer, Dlamini & Mendelson, 2013). To address this problem, antimicrobial stewardship programmes are implemented to promote rational antimicrobial use. Surgical antimicrobial prophylaxis (SAP) guidelines form part of such initiatives (Saied, Hafez, Kandeel, El-Kholy, Ismail, Aboushady, Attia, Hassan, Abdel-Atty, Elfekky, Girgis, Ismail, Abdou, Okasha & Talaat. 2015).

Complications of surgical care have also become one of the major causes of death and disability worldwide. Patient morbidity can occur, including decline in functional status and quality of life. Surgical site infections are said to be the second leading cause of hospital-acquired infections with approximately 500 000 infections per year in the United States (Goede, Lovely, Thompson & Cima, 2013). Studies in
developing countries, including sub-Saharan Africa, reported a death rate of 5-10% associated with major surgery (WHO, 2009).

Surgical antimicrobial prophylaxis guidelines, based on current clinical evidence, are designed to give surgical teams a standardised approach to rational, safe and effective use of antimicrobials for the prevention of SSIs (Gouvea, Novaes, Pereira & Iglesias, 2015). They are aimed at decreasing the occurrence of SSIs by preventing the development of infections caused by organisms that colonise or contaminate the surgical site (Gouvea, Novaes, Pereira et al., 2015).

A study conducted in Kenya considering the evolving trends of SAP in surgery found that the practice continues to improve; but guidelines are yet to be adopted in low income countries (Ongom & Kijjambu, 2013). Current practices in an Ethiopian hospital were also found to be different from both their National and the American Society of Health-Systems Pharmacists (ASHP) guidelines, citing the use of broad-spectrum antimicrobials and prolonged use of SAP as the main deviations (Mohamoud, Yesuf & Sisay, 2016).

In South Africa, a study aimed at ensuring and monitoring correct SAP to all patients in a private hospital in Cape Town, found no improvement with the choice of antimicrobials and duration of prophylactic treatment post-surgery. Improvement was however seen with regards to correct prophylactic dose and administration timing prior to the incision (Griesel, Leadsom & Krishnaswamy, 2014).

Studies on compliance to SAP guidelines are extensively conducted and published. Results of such studies show that the inappropriate use of antimicrobials and non-adherence to recommended guidelines are still of great concern (Rafati, Shiva, Ahmadi & Habibi, 2014). Urgent attention should thus be directed to the correct use of SAP. The emergence of multidrug resistant (MDR) gram negative bacterial infections, increased incidence of resistant gram positive bacterial infections such as methicillin-resistant Staphylococcus aureus (MRSA) and an increase in the use of broad spectrum antimicrobials in South Africa has been observed (Boyles, Whitelaw, Bamford et al., 2013). This study will hence investigate the prescribing practices and use of antimicrobials for SAP in DGMAH, additionally aiming to
CHAPTER 1: INTRODUCTION

determine whether there is compliance to the identified local and international guidelines.

The South African Standard Treatment Guidelines and Essential Medicine List, Hospital level (NDOH, 2015), published by the Department of Health, will be the first point of reference to measure compliance for this study, as these are guidelines to which South African medical practitioners must adhere. The American Society of Health-Systems Pharmacists (ASHP) guidelines are generally used as benchmark in most SAP studies and are greatly accepted by the world of healthcare providers as primary evidence on SAP and will therefore also be used to measure compliance in this regard (Gautam, Kumar, Kosey & Sandhu, 2015). These guidelines were developed in collaboration by the American Society of Health-Systems Pharmacists, the Infectious Diseases of Society of America (IDSA), the Surgical Infection Society (SIS), and the Society of Healthcare Epidemiology of America (Bratzler, Dellinger, Olsen, Perl, Auwaerter, Bolon, Fish, Napolitano, Sawyer, Slain, Steinberg & Weinstein, 2013).

1.3 RESEARCH QUESTION

South African hospitals are challenged with the growing occurrence of resistant organisms. Approximately 49% of South African surgical patients receive SAP, however, only 19% of these patients receive an inappropriate drug (Mendelson, 2015). This highlights the significance of monitoring the consumption of antimicrobials in this group of patients to ensure their appropriate use (Meyer & Sibanda, 2016). This study intends to describe the prescribing practices of SAP in surgical patients and determine whether surgical antimicrobial prophylaxis practices in DGMAH are in line with standard treatment guidelines.

1.4 AIM OF THE STUDY

To determine the prescribing patterns of surgical antimicrobial prophylaxis in DGMAH and to evaluate compliance to South African and international standard treatment guidelines.
1.5 OBJECTIVES OF THE STUDY

The objectives of the study were as follows:

- To describe the prescribing practices of SAP in surgical patients at a teaching hospital.
  
The study on practice patterns will include a look at the types of surgery conducted; presence of pre-existing infection(s) in these patients; SAP indication; the choice of drug for SAP; dosages of SAP drug(s) used; timing of SAP administration and the duration of SAP.

- To determine if the SAP prescribed was according to South African or international surgical antimicrobial prophylaxis guidelines

1.6 IMPORTANCE OF THE STUDY

Effective antimicrobial drugs are prerequisites for both preventive and curative measures, protecting patients from potentially fatal diseases and ensuring that complex procedures, such as surgery, can be provided at low risk. Yet systematic misuse and overuse of these drugs have put every nation at risk (WHO, 2015). The world is heading towards a post-antibiotic era in which common infections could once again kill, hence the World Health Assembly adopted a global action plan on antimicrobial resistance (WHO, 2015). The objectives of this action plan included strengthening the knowledge and evidence base through surveillance and research and to optimise the use of antimicrobial medicines in human and animal health (WHO, 2015). In South Africa, a national AMR strategy document has been developed as a framework for managing antimicrobial resistance, to limit further increases in resistant microbial infections (NDOH, 2014). The aim is to develop and implement a national AMR strategy that complements international efforts towards containment of the growing threat of AMR in human and animal health (NDOH, 2016).

Antimicrobial stewardship programmes in South Africa, as well as other countries, have shown to be successful in promoting rational antimicrobial use, improve patient
outcomes and reduce adverse consequences of antibiotic use, including antimicrobial resistance, toxicity and unnecessary costs (Meyer & Sibanda, 2016).

Studying SAP practices as part of antimicrobial stewardship efforts address both international and national aims in the fight against AMR. Surgical antimicrobial prophylaxis accounts for one of the most common reasons for prescribing antimicrobials, primarily to prevent hospital acquired SSIs (Jocum, 2018). In line with the global threat towards public health as a result of AMR, this study aimed to assess whether medical practitioners were adhering to the latest guidelines’ recommendations on SAP use.

Although the global burden remains unknown due to difficulty gathering reliable data, it is estimated that hundreds of millions of patients are affected by health associated infections (HAIs) each year, leading to significant mortality and financial losses for health systems (WHO, 2016).

Given the burden of SSIs in many countries and the numerous gaps in evidence-based guidance there is a need for guidelines based on strategies with proven effectiveness and a global approach. Comprehensive SSI prevention guidelines should include more innovative and recent approaches (WHO, 2016).

This study reports antimicrobial use in terms of SAP practices in a teaching hospital and suggests ways to utilise these findings to form a baseline from which interventions can be made towards effective SAP practice. Challenges and good practice areas were identified. Relevant stakeholders will be made aware of the findings in order to implement corrective measures to achieve better patient outcomes, reduction in antimicrobial resistance and cost.

1.7 OUTLINE OF THE DISSERTATION

This study will be discussed in five chapters as demonstrated in Figure 1.1. Chapter one discusses the background and rationale of the study. It also covers the research question, aim and the objectives of the study. Chapter two will look at literature about surgical antimicrobial prophylaxis; the headings covered in the literature
review include defining SAP, common surgical pathogens, choice of antimicrobials, surgical wound classifications and measure of compliance.

Chapter three will explain the methodology employed to conduct the study. This includes the study design, site, population and sample. The data collection procedure, and the collection instrument will be described. The methodology chapter also includes a discussion on the pilot study; data entry and analysis; reliability and validity and concludes with a discussion on the ethical consideration.

The results of the study and the discussion thereof in a form of a manuscript will be addressed in Chapter 4. The dissertation concludes with a chapter on the limitations, recommendations and conclusion of the study.

Figure 1.1: Layout of the dissertation

1.8 CONCLUSION

Inappropriate use of antimicrobials for both treatment and prophylaxis purposes has contributed to the ever increasing worldwide threat of AMR. Studying current practices and gathering baseline data is the first step in establishing where the challenges lie to provide guidance on what needs to be done to correct inappropriate use of SAP. Antimicrobial stewardship programmes aiming at implementing corrective measures where antimicrobial use is concerned can play a big role in reducing SSIs and ultimately AMR.
CHAPTER 2

LITERATURE REVIEW

2.1 INTRODUCTION

In this chapter, a literature review of studies on the evaluation of compliance to SAP guidelines are discussed. Topics covered include defining surgical antimicrobial prophylaxis, common surgical pathogens, the choice of antimicrobials, surgical wound classification and the measures of compliance to guidelines. A summary of the literature review concludes this chapter.

2.2 DEFINING SURGICAL ANTIMICROBIAL PROPHYLAXIS

Surgical antimicrobial prophylaxis is defined as the administration of a short pre-operative course of an antimicrobial to a patient to prevent SSIs (El Hassan, Elnour, Farah & Shebab, 2015). The goal thereof is to prevent infections from developing in high risk patients and procedures. Surgical Site Infections are the second most common type of adverse event occurring in hospitalised patients, accounting for 14-16% of all HAIs and 40% among all surgical patients (Rafati, Shiva, Ahmadi et al., 2014). A hospital associated infection is a new infection that develops after at least 48 hours of hospitalisation; there must be no evidence that the infection was present or incubating at the time of admission (NDOH, 2015). Surgical Site Infections are a type of HAI whereby a wound infection happens after an invasive (surgical) procedure (NICE, 2008). It is also defined as an infection that occurs within 30 days of surgery or within one year of surgery if an implantable device was introduced (Griesel, Leadsom & Krishnaswamy, 2014).

Surgical site infections can either be incisional or affect an organ/space. Incisional SSIs can further present as superficial or deep incisional. An organ/space SSI is a wound that involves a part of the anatomy that has been opened and operated on throughout the surgical procedure. Only one third of SSIs are said to be within the organ/space, however more than 90% of deaths occur due to them (Anderson & Sexton, 2016).
2.3 COMMON SURGICAL PATHOGENS AND THEIR SOURCES

The most common source of pathogens that cause SSIs are the endogenous flora of the patient’s skin, mucous membrane and hollow viscera. Approximately 80% of the bacteria in the SSI originates from the patient’s skin (WHO, 2009). *Staphylococcus aureus*, *coagulase-negative Staphylococci*, *Enterococci*, *Escherichia coli* and *Pseudomonas aeruginosa* are the pathogens most commonly isolated from surgical wounds (Kanji, 2011). In clean-contaminated procedures including of the abdominal, biliary tract, colorectal, gynaecological and urological systems the predominant organisms may include gram negative rods, anaerobes and enterococci in addition to normal skin flora (Bratzler, Dellinger, Olsen et al., 2013).

Over decades, the causative organisms associated with SSIs have changed in many hospitals worldwide; therefore institutions must consider local patterns of resistant organisms such as MRSA to inform the choice of antimicrobials used (Jocum, 2018).

2.4 SURGICAL WOUND CLASSIFICATIONS

The choice of SAP is primarily guided by the pre-operative wound classification. Wounds are classified as clean, clean-contaminated, and contaminated or dirty (Anderson & Sexton, 2016). Closed, uninfected wounds, without penetrating the viscera or the presence of pus, are termed clean wounds. In clean-contaminated wounds the viscera is entered under controlled conditions but without unusual contamination during the operation. A contaminated wound may be an open accidental wound with pus present during the surgical procedure, resulting from a major break in sterile technique or from an operation with gross viscous spillage (Anderson & Sexton, 2016). Dirty or infected wounds include old traumatic spillage with retained or devitalised tissue and those that involve existing clinical infection or perforated viscera (WHO, 2009).

Surgical wounds that are expected to be clean generally do not require SAP except where the consequences of SSIs could be severe; these include procedures in
which prosthetic material or implants are used (Jocum, 2018). Antimicrobial prophylaxis is indicated for procedures with clean-contaminated wounds; in conjunction with good pre and intra-operative infection control techniques (NDOH, 2015). Prophylaxis should be as short as possible to avoid resistance leading to infections that are difficult to treat (Kanji, 2011). A course of antimicrobial treatment, not prophylaxis, is required for procedures with contaminated and dirty wounds (WHO, 2009).

### 2.5 CHOICE OF ANTIMICROBIALS

The requirement of SAP depends on the type of surgical procedure, the most frequent pathogens seen in this procedure, safety and efficacy of the antimicrobial, current evidence-based literature and the cost (Kanji, 2011).

For most procedures, cefazolin, a first generation cephalosporin, is the drug of choice for prophylaxis, as it is most widely studied and with proven efficacy. It has a desirable duration of action, spectrum of activity for pathogens (especially gram-positive cocci such as *Staphylococcus aureus* and most *Streptococci*) commonly encountered in surgery, and due to its safety and low cost (Bratzler, Dellinger, Olsen et al., 2013).

The use of agents with gram negative and anaerobic cover is dependent on the surgical site (e.g. upper respiratory, gastrointestinal and genitourinary tract) and whether the surgery will cut across a hollow viscous and mucous membrane that may have resident flora (Kanji, 2011). American Society of Health-Systems Pharmacists advocates for the use of vancomycin for prophylaxis in procedures involving prosthetic device implantation in areas with high MRSA rates (Bratzler, Dellinger, Olsen et al., 2013).

### 2.6 MEASURE OF COMPLIANCE

To reduce the burden of SSIs, the Center for Disease Control and Prevention (CDC), in partnership with other health organisations, created a surgical care improvement project and developed six infection prevention measures targeted at reducing post-operative infections (Salkind & Rao, 2011). These measures, which
have been widely disseminated and include guidance on the choice of the correct antimicrobial; correct dose; administration of the antimicrobial within 60 minutes prior incision; and not continuing the antimicrobial after surgery (except for 24 hours for cardiac procedures) (NDOH, 2015). International guidelines such as the ASHP and the South African standard treatment guidelines have been developed based on these measures (Bratzler, Dellinger, Olsen et al., 2013 & NDOH, 2015).

### 2.6.1 CORRECT CHOICE OF ANTIMICROBIALS

The choice of an agent for SAP is reported as one of the most frequently encountered incorrect actions in SAP (Kaya, Aktas, Senbayrak, Tekin, Otzprak, Aksoy, Fırat, Yenice, Oncul, Gunduz, Solak, Kadanali, Carla S E, Caglayan D, Yılmaz A, Bozkurt I, Elmaslar T, Tartar A S, Aynioglu A, Kocyigit & Koksal, 2016). The medicine of choice for SAP has to have a broad spectrum of activity, it needs to be highly concentrated in the surgical wound tissue, and also be affordable (Kaya, Aktas, Senbayrak et al., 2016). The chosen antimicrobial should be active against the common pathogens causing SSIs in the specific procedure (Jocum, 2018). First generation cephalosporins, particularly Cefazolin has been extensively studied in this regard, it has proven efficacy as it’s spectrum is active against *Staphylococci*, some gram negative and many other bacteria that are likely to contaminate the surgical site (Jocum, 2018). Clindamycin serves as an alternative in patients with beta-lactam allergies. Metronidazole is added in some clean contaminated procedures in which anaerobic cover is essential (Kanji, 2011). The choice of antimicrobials for specific surgical procedures are listed as part of SAP guidelines in Appendix 1 (NDOH, 2015; Bratzler, Dellinger, Olsen et al., 2013).

### 2.6.2 DOSE SELECTION

When selecting a dose for prophylaxis, the antimicrobial agent’s pharmacokinetic and pharmacodynamics properties and patient’s factors should be taken into consideration to ensure adequate serum and tissue concentration (Bratzler, Dellinger, Olsen et al., 2013).

The South African and the ASHP guidelines differ slightly in this measure. The South African guideline recommends a dose of 1g Cefazolin in adult patients
weighing less than 80kg and 2g in patients weighing above 80kg (NDOH, 2015). The ASHP guidelines recommend the dose of Cefazolin at 2g for adult patients weighing less than 120kg and 3g for patients above 120kg (Bratzler, Dellinger, Olsen et al., 2013). Appendix 2 addresses dose recommendations for SAP agents from both guidelines.

2.6.3 ROUTE OF ADMINISTRATION

The favoured route of administration for a majority of surgical procedures is intravenous, as it produces fast, reliable and predictable plasma and tissue concentrations and compliance is also good in this measure, due to its convenience (Ongom & Kijjambu, 2013). Antimicrobials for prophylaxis should all be administered intravenously since serum levels after oral administration depend on the rate of absorption from the gastrointestinal tract that varies between individuals, therefore being unreliable (Jocum, 2018). Topical administration is the primary route in ophthalmic procedures and in patients undergoing colorectal procedures, oral antimicrobials may be used for prophylaxis in conjunction with mechanical bowel preparation (Ongom & Kijjambu, 2013).

2.6.4 TIMING OF THE PROPHYLACTIC DOSE

Adequate prophylaxis needs the delivery of the antimicrobial to the incision site before contamination occurs (Ongom & Kijjambu, 2013). This requires timeous administration of the antimicrobial to ensure serum and tissue concentrations exceeding the minimum inhibitory concentration (MIC) at incision time (Kanji, 2011). Prophylaxis with Cefazolin should be given within 60 minutes before incision, usually at induction (NDOH, 2015). Fluoroquinolones and Vancomycin should be given within 120 minutes before incision due to prolonged administration time required for these agents (Bratzler, Dellinger, Olsen et al., 2013).

2.6.5 REDOSING OF PROPHYLAXIS

Re-administration of the prophylactic dose intra-operatively is necessary in cases where the procedure exceeds four hours and when considerable blood loss (more
than 1500ml) occurs. The antimicrobial should be re-administered at one to two times the half-life of the drug (Salkind & Rao, 2011).

### 2.6.6 DURATION OF PROPHYLAXIS AND OR NUMBER OF DOSES

The ASHP recommends a shortened post-operative course of antimicrobials involving a single dose or a continuation for less than 24 hours. However, in cardiac surgical procedures, administration of cefazolin for 24 hours is recommended (Bratzler, Dellinger, Olsen et al., 2013). Length of intravenous antimicrobial use for treatment and prophylaxis is a concern in many studies and is documented as one of the major causes of antimicrobial resistance (Kaya, Aktas, Senbayrak et al., 2016). A systematic review of literature conducted by the WHO on prophylaxis prolongation identified five studies which reported an increase in adverse reactions when prophylaxis was extended beyond the duration of surgery (Jocum, 2018).

### 2.7 CHALLENGES IN UTILISATION OF SURGICAL ANTIMICROBIAL PROPHYLAXIS

Efforts are continuously being undertaken to establish and update guidelines for the appropriate use of antimicrobials for prophylaxis but the implementation thereof is still a challenge. Factors that may contribute to this lack of compliance include failure of professionals to update their knowledge, dependence on old clinical practice rather than updated evidence-based guidelines, lack of policies drafted by institutions and or failure to implement these guidelines (Gouvea, Novaes, Pereira et al., 2015).

Inappropriate practices in SAP is linked to a deviation in the choice of antimicrobial, dose, timing and length of administration. In a study including 16 centres where 166 surgical procedures were analysed, it was found that the choice of antimicrobial was inappropriate in 40% of cases with duration of use being inappropriate in 29% of cases (Kaya, Aktas, Senbayrak et al., 2016). Another study, in which 765 surgical procedures were reviewed, reported that appropriate actions regarding antimicrobial selection, duration and timing were made in only 8% of cases (Kaya, Aktas, Senbayrak et al., 2016).
2.8 ANTIMICROBIAL STEWARDSHIP AND THE ROLE OF THE PHARMACIST IN SAP PRACTICES

Antimicrobial stewardship programmes which focuses on education, auditing and feedback have proven to yield positive results in optimising SAP guidelines (Shing Ng & Chong, 2012). Antimicrobial resistance is a result of many wrong chains of events that include irrational prescriptions, inappropriate monitoring and irrational dispensing (Gautam, Kumar, Kosey et al., 2015). Pharmacists at every level are essential for implementing rationality in medication use; pharmacists with specialist skills must facilitate implementation of evidence-based antimicrobial prescribing (Gautam, Kumar, Kosey et al., 2015).

Assessment of current antimicrobial prescribing patterns is an important step towards promoting appropriate use of antimicrobial agents (Nagdeo, Sonarkar, Thombare, Akhtar & Dasgupta, 2015). An improvement in SAP prescribing habits were observed in a study by Nagdeo et al where educational interventions by clinical pharmacists were implemented.

Clinical pharmacists hold a key role in overall acceptance and implementation of these evidence-based antimicrobial use guidelines, ultimately improving health related outcomes in patients and a reduction in post-operative SSI development (Gautam, Kumar, Kosey et al., 2015). As an important partner to practitioners, the clinical pharmacist plays a very important role in building a bridge between practitioners’ decisions and health outcomes of patients (Gautam, Kumar, Kosey et al., 2015).

Post intervention studies are also necessary to measure if the institutions are on the right track and to determine if continuing education may still be necessary (Nagdeo, Sonarkar, Thombare et al., 2015). Clinical pharmacists can play an important role in ensuring compliance to SAP; which will curtail the overuse of antimicrobials and reduce the emergence of resistance.
2.9 CONCLUSION

Literature shows that there are numerous studies addressing SAP guidelines and even more evaluating the adherence of surgical teams to these guidelines. However, evidence still indicate that misuse of prophylactic antimicrobials is extensive and a wide disparity of overall compliance to SAP is seen (Shing Ng & Chong, 2012).

The ASHP Therapeutic Guidelines (2013) define SAP as a method of preventing an infection by decreasing the load of organisms at the surgical site and thereby aiming to furthermore decrease associated morbidity and mortality, length of stay and the accompanied cost (Bratzler, Dellinger, Olsen et al., 2013).

The efficacy of SAP depends on several factors including the selection of appropriate antimicrobial, timing of administration, dosage, duration of prophylaxis and route of administration (Shing Ng & Chong 2012).

Implementation of SAP guidelines in practice is a huge responsibility. Including a clinical pharmacist in this area holds the key to successful implementation of these guidelines and applying them to patient level (Gautam, Kumar, Kosey et al., 2015).

2.10 SUMMARY

The literature review chapter covers all aspects addressed by this study. The importance of SAP prophylaxis was highlighted, with a focus on the use in South Africa. The principles, recommendations and regimens of SAP use in South Africa and internationally were outlined. The next chapter will give a systematic description of the methodology applied in conducting this study.
CHAPTER 3: METHODOLOGY

CHAPTER 3

METHODOLOGY

3.1 INTRODUCTION

This chapter presents the methodology followed to conduct the study, starting with a discussion of the study design, site, population and sample selection. The data collection process, pilot study, data entry, followed by the data analysis are explained in detail. The chapter concludes with methods used to ensure the reliability and validity of the data collected and the ethical considerations of the study.

3.2 STUDY DESIGN

The study followed a cross-sectional quantitative design. A retrospective review was conducted by studying the prescribing patterns in selected files for patients who underwent surgery at DGMAH. A retrospective study looks backwards and examines exposures to suspected risk or protection factors in relation to an outcome that is established at the start of the study (www.statsdirect.com).

Cross-sectional study design is a type of observational study design. The participants in a cross-sectional study are selected based on the inclusion and exclusion criteria set for a study (Setia, 2016). Once the participants have been selected for the study, the investigator follows the study to assess the exposure and the outcomes. The investigator can study the association between these variables and may also estimate the prevalence of the outcome in those surveyed (Setia, 2016). The strength of a cross sectional study include that it is usually conducted relatively faster, inexpensive and can be conducted before planning a cohort study or a baseline in a cohort study. These study designs may be useful for public health planning, monitoring, and evaluation (Setia, 2016).

This study was also conducted within a quantitative paradigm. Quantitative research is a structured way of collecting and analysing data obtained from different sources. Quantitative research involves the use of computational, statistical, and mathematical tools to derive results (www.sisinternational.com). It is conclusive in its purpose as it
tries to quantify the problem and understand how prevalent it is by looking for projectable results to a larger population. It has a wide scope and is typically used to explore the causes of potential problems that may exist (www.sisinternational.com).

3.3 STUDY SITE

The study took place at Dr. George Mukhari Academic hospital (DGMAH). The hospital, formerly known as Ga-Rankuwa Hospital, was first established in 1972 and is located in Ga-Rankuwa township, on the North-Western part of the Tshwane Region of Gauteng Province (DGMAH, 2017).

DGMAH was initially a regional hospital, tertiary services were added after the establishment of Medical University of South Africa (MEDUNSA) in 1974, to which DGMAH serves as the health sciences teaching component. DGMAH gained academic status in 2011, which was followed by the establishment of the new Sefako Makgatho Health Sciences University (SMU). DGMAH is also a teaching platform for the Ga-Rankuwa Nursing College (DGMAH, 2017). The mission of the hospital include to provide quality health care service to North Western part of the Tshwane district, Limpopo and Northwest Province; to train health professionals in undergraduate and postgraduate and to provide a conducive platform for relevant health research and development.

DGMAH has a capacity of 1650 approved beds and provides healthcare services to a population of about 1 200 000. The hospital has 16 surgical wards with an overall bed capacity of 640. The main theatre complex consists of 14 operating rooms and there are 3 satellite theatres (DGMAH, 2017). Surgical procedures performed include thoracic, gynaecological, orthopedic, general, ENT (Eye Nose and Throat), ophthalmology, urology, neurosurgery, plastic and cardiology. An average of 700 elective and 600 emergency surgical procedures are conducted every month as per theatre statistics (DGMAH, 2017).

3.4 STUDY POPULATION AND SAMPLE

Based on the average number of surgical procedures conducted in DGMAH per month (700 elective and 600 emergency surgical procedures), the calculated sample
estimate to achieve statistical significance is 385. The conservative proportion was used to estimate the sample size with a 5% margin of error and a 95% confidence interval. Data will be collected from patients’ files that have undergone a surgical procedure during the period of January 2017 to May 2017. The data for this period reflects the status quo, since no intervention has taken place. Systematic sampling with every fourth patient file from the theatre register was used.

3.5 DATA COLLECTION

3.5.1 DATA COLLECTION PROCEDURE

The patients who underwent surgical procedures during the study period was identified from the main theatre registers. Medical records or files of these patients were then requested from the hospital filing room. Patients’ demographics, nature of the operation, induction and finishing time was retrieved from the intra-operative form and safety checklist inside the file. Information needed to address the objectives of the study was also retrieved from the patient medical history, which included: the date the patient has undergone a surgical procedure; data of administration of the SAP agent including the name of the medication, time and route of administration. This was done to also see if the SAP agent was administered within one hour of incision for Cefazolin or 120 minutes for Vancomycin, Fluoroquinolones or Gentamycin; to determine if the correct antimicrobial was given at the correct dose for the specific surgical procedure; from the length of the procedure to determine if re-dosing was necessary and if it was performed; and to determine if SAP was discontinued within 24 hours of the surgical procedure.
3.5.2 DATA COLLECTION INSTRUMENT

The data collection instrument (Appendix 3) used in the study was developed and compiled by the researcher to address the aim and objectives of the study. This sheet was adapted from a similar study done on SAP by Kaya, Aktas, Senbayrak et al., in 2016.

A study number was assigned to all participants. All identifying information such as patient names and file number were disregarded to maintain confidentiality. Patient demographics included the age; weight; height and gender of the patients.

The primary diagnosis referring to the patient’s reason(s) for admission was identified; the ICD-10 code thereof were also recorded on the sheet. ICD-10 is the abbreviation for the International Classification of Diseases and Related Health Problems (10th revision). It is a coding system developed by the WHO, that translates the written description of medical and health information into standard codes (WHO, 2016).

The clinical information needed to address the objectives of the study included the name and date of the surgical procedure(s) undergone, the induction and end time, name(s) and dosage form(s) of antimicrobial drugs administered prior and post...
procedure(s), timing and duration of administration. Presence of an infection prior to a surgical procedure(s) was also recorded.

3.6 PILOT STUDY

After the Sefako Makgatho University’s Research and Ethical Committee (SMUREC) granted approval, a pilot study was conducted with 10 patients who underwent a surgical procedure in December 2016 to test the adequacy of the data collection form to retrieve the required data.

The purpose of this was to ensure that the data collection sheet was sufficient and covered all objectives that the study aimed to address. All shortcomings, mistakes, unnecessary or insufficient aspects were identified and the data collection sheet was updated accordingly.

The pilot study is an integral part of conducting a study. It is necessary for developing and testing adequacy of the research instrument(s), assessing whether the research protocol is realistic and workable and can identify logistical problems which might occur using proposed methods (Van Teijlingen & Hundley, 2001).

3.7 DATA ENTRY AND ANALYSIS

Information from the data collection sheet was captured on a Microsoft Excel™ spreadsheet. The chi-square test and correlations were used to determine association between practice and guidelines, using SPSS version 24 statistical package. All data was proof-read by a second independent researcher for preciseness and correctness. Data was cleaned and checked prior to analysis.

The assessment of compliance to guidelines (Appendix 1) regarding SAP in this study were based on the South African Department of Health STGs (NDOH, 2015). Further reference were also made to the Clinical Practice guidelines for antimicrobial prophylaxis in Surgery (CPGAS) 2013; which were developed by the American Society of Health-system Pharmacists (ASHP), the Infectious Disease Society of America (IDSA), and the Surgical Infection Society for Healthcare Epidemiology of America (SHEA) (Bratzler, Dellinger, Olsen et al., 2013).
The measures used to determine if practice for individual participants met the requirements of the guidelines as extensively addressed under literature review were as follows:

- Appropriate SAP agent selection, based on the surgical procedure performed (Appendix 1).
- Appropriate dose of the selected SAP agent (Appendix 2).
- Timing of administration of the SAP needs to be within 60 minutes prior to incision for Cefazolin, 120 minutes prior incision for Fluoroquinolones and Vancomycin.
- Redosing of the SAP agent should be administered in procedures lasting for more than four hours.
- Discontinuation of SAP should be implemented within 24 hours.

3.8 RELIABILITY AND VALIDITY

Reliability is defined as the ability of a research tool to consistently produce the same results (Heale & Twycross, 2015).

The reliability and validity of data were tested in a pilot study to establish the effectiveness and ensuring that the data collection sheet was sufficient and contained every aspect that the researcher wanted to address in the study. The pilot study was conducted after the protocol received ethical clearance.

To ensure precision, only data obtained from the data collection form was used and all information double checked. A statistician was consulted to accurately define the statistical significance of collected data.

Validity is the extent to which a concept is measured in a quantitative study (Heale & Twycross, 2015) and also describes the extent to which a measure accurately represents the concept it claims to measure (Roberts, Priest & Traynor, 2006). There are two broad measures of validity, namely external and internal.

External validity addresses the ability to apply with confidence the findings of the study to other people and other situations and ensures that the conditions under which the study is carried out are representative of the situations and time to which the results
are to apply (Roberts, Priest & Traynor, 2006). The sample of participants drawn from the population of interest must be representative of the population of patients that have undergone a surgical procedure at the time of the study. Most disciplines of surgeries conducted in the hospital were included in the study and the sample size was statistically calculated based on the number of procedures conducted.

Internal validity addresses the reasons for the outcomes of the study and assists to reduce other, often unanticipated, reasons for these outcomes (Roberts, Priest & Traynor, 2006). Reliability and validity are ways of demonstrating and communicating the consistency of research processes and the trustworthiness of the research findings. In order to enhance validity for this study, a pilot study was done which enabled the researcher to determine if the information provided by the data collection tool is sufficient for the objectives of this study and that the same results can be reproduced with the same data.

3.9 ETHICAL CONSIDERATION

Ethical approval for the study was obtained from the SMUREC prior to the commencement of the study (Appendix 3). Written permission to conduct the study at DGMAH was also obtained from the office of the director of clinical services in the hospital.

A retrospective review of data obtained from files of patients who underwent surgery was done, thus no patient consent was required. Patient information was kept confidential, a patient identification number were assigned to each patient and only the study number was used during data analysis.

3.10 SUMMARY

This chapter detailed a stepwise approach on how this study was conducted. It explained the design that the study followed, how the sample size was calculated, the data collection procedure, instruments used and how all data was analysed. A pilot study was conducted, testing whether the collection sheet was able to meet the objectives of the study. This chapter ended with a definition and explanation of reliability, validity and bias, as well as the necessary ethical considerations.
implemented throughout the study period. In the following chapter the results of the study will be reported on in the form of a manuscript and then discussed.
CHAPTER 4
MANUSCRIPT

4.1 INTRODUCTION

The results of the study are presented in a manuscript format, using the South African Journal of Infectious Diseases journal guidelines as attached in Appendix 5.

4.2 MANUSCRIPT FOR PUBLICATION

Surgical antimicrobial prophylaxis among adult patients in a teaching hospital in South Africa.

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Abstract

Introduction:

South African hospitals are challenged with the growing occurrence of resistant organisms. Approximately 49% of South African surgical patients receive surgical antimicrobial prophylaxis (SAP), however 19% of these patients receive the inappropriate medicine. This highlights the significance of monitoring the consumption of antimicrobials in this group of patients to ensure their appropriate use. The judicious use of antimicrobials supported by stewardship programs is regarded as one of the key components in preventing surgical site infections.
Objectives:

The objectives of the study were to describe the prescribing practices of SAP in surgical patients in a teaching hospital including the choice of antimicrobial(s) for SAP; dosages used; timing of administration and the duration of SAP and also to evaluate prescriber compliance to standard treatment guidelines.

Method:

A retrospective review of adult patients who underwent a surgical procedure between January to May 2017 was conducted. Patient numbers were identified and systematically sampled from theatre registers, medical records were then retrieved and data was manually collected. Prescribing patterns were compared to the South African National Department of Health’s standard treatment guidelines and reference was also made to the American’s Clinical Practice guidelines for antimicrobial prophylaxis in Surgery (CPGAS) 2013.

Results:

A total of 234 adult patients who underwent surgery were included in the study. The male population was 53% (124; n=234) and the mean age of patients was 37.99 years (SD=14.5). Gynaecological procedures were the most common at 27.4% (64; n=234) followed by general surgery at 18.4% (43; n=234).

Surgical antimicrobial prophylaxis was administered in 70% (164; n=234) of the population. Cefazolin was the most commonly used antimicrobial for this purpose in 64% (151; n=234) patients, followed by ceftriaxone in 3% (8; n=234) patients.

Choice of SAP was appropriate in 70% (163; n=234) of the population. The correct timing of SAP administration was observed in 69% (161; n=234). Prophylaxis was administered at correct dosages in 29% (68; n=234) cases and duration of SAP was administered in accordance with guidelines in 44% (103; n=234) cases. None of the 14 surgical procedures (6%; n=234) that lasted more than four hours received a second dose SAP as per guidelines. When comparing compliance to guidelines...
between the studied sub-disciplines, significant differences do exist in all measures
evaluated with regards to guideline compliance.

**Conclusion:**

Similar to this study, many studies conducted worldwide on institution’s compliance
to surgical antimicrobial prophylaxis still show that ideal practice of SAP is not
achieved. Lack of specific institution guidelines and the inappropriate use of
antimicrobials due to lack of awareness seem to be some of the contributing factors
to this shortfall. Clinical pharmacist can play a major role in identifying challenges
of SAP practices and implement interventional measures to ensure appropriate
antimicrobial use.

**Recommendations:**

Development of hospital guidelines in partnership with the institution’s antimicrobial
stewardship team and surgeons is recommended to achieve optimal results. Post
interventional studies are also necessary to ensure efforts are yielding positive
results.

**Keywords:**

Surgical antimicrobial prophylaxis, guidelines, compliance and prescribing patterns.

The authors declare that there is no conflict of interest to declare.

The paper has not been published nor presented at any meeting or conference.
INTRODUCTION

Decades of injudicious antimicrobial consumption is a major driver of the emergence of multi-drug bacterial resistance. There is a global need to improve the utilisation of antimicrobials since the current situation is a direct threat to patient safety (Boyles, Whitelaw, Bamford et al., 2013). Antimicrobial stewardship programmes including the assessment of current surgical SAP patterns are encouraged globally to ensure rational antimicrobial usage (Nagdeo, Sonarkar, Thombare et al., 2015).

The goal of SAP is to reduce the incidence of surgical site infections (SSI) by preventing the development of infection caused by pathogens that may contaminate the surgical site (Gouvea, Novaes, Pereira et al., 2015). Surgical site infections is a type of hospital-acquired infection (HAI) whereby a wound shows infection after an invasive (surgical) procedure or within 30 days of surgery (NICE, 2008; Griesel, Leadsom & Krishnaswamy, 2014).

Surgical site infections make up 14% to 16% of all HAIs and are a common complication. Among surgical patients, SSIs account to 40% of all infections (Rafati, Shiva, Ahmadi et al., 2014). Patients with SSIs are five times more likely to be readmitted to hospital, twice as likely to die and are hospitalised seven days longer on average than patients in whom SSIs did not develop (Rafati, Shiva, Ahmadi et al., 2014).

The appropriate use of SAP is one of the measures recommended, in addition to good surgical technique, to reduce the risk of SSIs (WHO, 2009). Surgical antimicrobial prophylaxis is standard practice for patients undergoing some clean and clean-contaminated surgical procedures (Ongom & Kijjambu, 2013). Recommendations common to SAP guidelines include appropriate selection of the antimicrobial agent according to the type of surgery, appropriate dose according to patient weight, administration within 60 minutes prior surgical incision for Cefazolin and 120 minutes prior incision for Vancomycin and Fluoroquinolones and discontinuation of SAP within 24 hours of surgery (Ongom & Kijjambu, 2013).

A study by Gouvea, Novaes, Pareira, et al (2015), reviewed adherence to SAP guidelines from nine countries and found adherence to appropriate choice of
antimicrobials ranging from 22% to 95%, administration at the correct time ranging from 12% to 100% and appropriate discontinuation of antimicrobials in 5.8% to 91% of cases (Gouveia, Novaes, Pereira et al, 2015). Significant variations are observed demonstrating a need for better adherence to SAP guidelines.

Furthermore, current practices in an Ethiopian hospital were found to be different from both the national and American Society of Health-Systems Pharmacists (ASHP) guidelines, citing the use of broad-spectrum antimicrobials and prolonged use of SAP as the main deviations (Mohamoud & Aklilu, 2016).

In South Africa, a study aimed at monitoring and ensuring all patients receive the correct SAP in a private hospital, found no improvement with the choice of antimicrobials and duration of prophylactic treatment post-surgery. Improvement was however seen with regards to correct prophylactic dose and timing prior to incision (Griesel, Leadsom & Krishnaswamy, 2014).

Although principles of SAP are clearly established and several guidelines have been published, the application of these guidelines are still a challenge (Tourmousoglou, Yiannakopoulou, Kalapothaki et al., 2008).

Limited research and guidelines have been conducted and developed on SAP use in South Africa (FIDSSA Congress, 2013), stressing the importance of this study to address this gap. The aim of this paper is to describe the prescribing patterns of SAP in a teaching hospital and the current compliance to SAP guidelines for adult patients. This study’s findings also form a baseline from which interventions can be made towards effective SAP practice.

METHODOLOGY

Study design, setting and population

A cross-sectional quantitative design was followed. A retrospective chart review was conducted, studying SAP prescribing patterns in selected medical records for patients who underwent surgery at a teaching hospital situated in Gauteng.
The teaching hospital has a capacity of 1650 beds, which includes 16 surgical wards, as well as the main theatre complex consisting of 14 operating rooms. This is the second largest hospital in South Africa, providing services to approximately 1.7 million people from the surrounding area. Surgical procedures performed at this institution include thoracic, gynaecological, orthopaedic, general, eye nose and throat (ENT), ophthalmology, urology, neurosurgery, plastic and cardiology.

**Study sampling and period**

Medical records or files of patients identified from the theatre register were manually retrieved from the filing room. Systematic sampling was used to select every fourth file number from the theatre register of patients who have undergone any surgical procedure over a period of five months. Of the 365 patient-files requested, only 234 were retrieved and included in the study. Ophthalmic procedures and patients below the age of 18 were excluded.

**Measure of Compliance to the Guidelines**

To reduce the burden of SSIs, the Center for Disease Control and Prevention (CDC), in partnership with other health organisations, created a surgical care improvement project and developed six infection prevention measures targeted at reducing post-operative infections (Salkind & Rao, 2011). These measures which were adopted worldwide and used to develop guidelines include recommendations on the choice of antimicrobial, dose, timing of SAP administration and not continuing the antimicrobial after surgery.

The assessment of compliance to SAP guidelines for this study were based on the South African National Department of Health Standard Treatment Guidelines (STG) (NDOH, 2015). Further reference was also made to the Clinical Practice guidelines for antimicrobial prophylaxis in Surgery (CPGAS) 2013, which were developed by the American Society of Health-system Pharmacists (ASHP), the infectious Disease Society of America (IDSA) and the Surgical Infection Society for Healthcare Epidemiology of America (SHEA) (Bratzler, Dellinger, Olsen et al., 2013).
SAP appropriateness was evaluated to measure compliance with regards to the following (NDOH, 2015; Bratzler, Dellinger, Olsen et al., 2013):

- SAP agent selection, based on the surgical procedure performed
- SAP dose selection
- Timing of SAP administration
- Re-dosing of the SAP in procedures lasting for more than four hours
- Duration of SAP

**Data collection and instrumentation**

Patients’ files were manually reviewed and data recorded on the data collection instrument. This instrument was developed based on previously published studies on adherence to SAP with a few changes to meet the study objectives (Nagdeo, Sonarkar, Thombare et al., 2015).

Key information included patient demographics, the primary diagnosis and ICD-10 code, the name of surgical procedure(s) undertaken and the surgery sub-discipline (e.g. urology) to which the procedure belonged. Furthermore, where SAP was administered, data collected included information on the presence of pre-existing infection in the patient, the induction and end time of procedure, name and dose of antimicrobial drugs administered prior and post procedure as well as timing of antimicrobial administration prior incision and duration of administration.

**Data analysis**

All statistical analysis was performed using the Statistical Package for the social sciences (SPSS) version 24 package. Data was analysed descriptively using percentages, the chi-square test and correlations for comparisons to determine the association between current practice and guideline recommendations. These were conducted at the 95% confidence interval; all tests were considered significant when p <0.05.
Ethical consideration

Ethical approval was obtained from the Sefako Makgatho University Research and Ethics Committee prior to the commencement of the study (Reference SMUREC/P/227/2017: PG). Permission to conduct the study was also obtained from the director of clinical services and the surgical directorate of the hospital. The confidentiality and anonymity of the population was maintained by assigning study numbers to the patients selected.

RESULTS

Patient demographics

During the five months, a total of 234 patients who underwent surgery were included in this study. The male population was 53% (124; n=234), the mean age of patients was 37.99 years (SD=14.5) and the mean weight was 70.63kg (SD=17.8). Table 1 lists the primary diagnoses. Patients admitted for elective caesarean section (15; 6.4%), ectopic pregnancy (12; 5.1%) and multi fibroids uterus (10; 4.2%) were the most common identified diagnoses.

Table 1: Primary Diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N=234</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective Caesarean Section</td>
<td>15</td>
<td>6.4</td>
</tr>
<tr>
<td>Ectopic Pregnancy</td>
<td>12</td>
<td>5.1</td>
</tr>
<tr>
<td>Multi Fibroids Uterus</td>
<td>10</td>
<td>4.2</td>
</tr>
<tr>
<td>Acute Appendicitis</td>
<td>9</td>
<td>3.8</td>
</tr>
<tr>
<td>Femur Fracture</td>
<td>8</td>
<td>3.4</td>
</tr>
<tr>
<td>Diabetes Foot Sepsis</td>
<td>6</td>
<td>2.6</td>
</tr>
<tr>
<td>Emergency Caesarean Section</td>
<td>6</td>
<td>2.6</td>
</tr>
<tr>
<td>Urethral Stricture</td>
<td>6</td>
<td>2.6</td>
</tr>
<tr>
<td>Abdomen Stab Wound(s)</td>
<td>5</td>
<td>2.1</td>
</tr>
<tr>
<td>Empyema Thoracis</td>
<td>5</td>
<td>2.1</td>
</tr>
<tr>
<td>Other</td>
<td>152</td>
<td>64.9</td>
</tr>
</tbody>
</table>

There were 66 patients (28%; n=234) included in the study with confirmed pre-existing infections before undergoing surgical procedures; this group of patients
would not require SAP as they were already on antimicrobial therapy at the time of surgery.

Figure 1 demonstrates that gynaecological (64; n=234) 27.4%, general (43; n=234) 18.4% and orthopeadic procedures (38; n=234) 16.2% accounted for most surgeries performed within the study.

![Types of surgeries by disciplines](image)

**Figure 1:** Type of Surgery per Discipline

The majority of surgeries had a duration of between 0.5 and 2 hours. Surgeries lasting longer than 4 hours was only present in 6% (14; n=234) of patients but these are important as they require a re-dosing of SAP for Cefazolin.
SURGICAL ANTIMICROBIAL PROPHYLAXIS UTILISATION

Antimicrobials used for SAP

Cefazolin was the most commonly used antimicrobial for prophylaxis in 64% (151; n=234) of cases, followed by Ceftriaxone in 3% (8; n=234) of cases, as seen in Table 2. Antimicrobial drugs were not administered pre-operatively in 30% (70; n=234) of patients; these included cases where SAP was not indicated, where prophylaxis was incorrectly withheld and in cases where SAP was only administered post-operatively.
Table 2: Antimicrobial drugs administered pre-operatively for SAP

<table>
<thead>
<tr>
<th>Antimicrobial International Non-Proprietary Name (INN)</th>
<th>ATC code</th>
<th>Number of Prescriptions (n=234) - antibiotics not received (70)</th>
<th>% = 164</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin</td>
<td>J01DB04</td>
<td>151</td>
<td>64</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>J01DD04</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>G01AF01</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>Amoxycillin/Clavulanic acid</td>
<td>J01CR02</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>J01FA10</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>J01GB03</td>
<td>1</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Measure of Compliance

Figure 3 shows that in 69.7% (163; ) of cases, practice in terms of SAP indication was correct. The appropriate indication for SAP also include cases where prophylaxis was correctly withheld. SAP is indicated for procedures with clean-contaminated wounds; defined as entering the respiratory, alimentary, genital or uninfected urinary tracts under controlled conditions (NDOH, 2015). Wounds that are expected to be clean generally do not require antimicrobial prophylaxis, except where consequences of surgical site infection could be severe, for instance joint replacements (NDOH, 2015).
SAP Dosage

Prophylaxis was administered at correct dosages in 41% (68; n=164) of patients that actually received SAP pre-operatively. However, overall compliance to this measure was 29% (68; n=234), which is influenced by the percentage of patients that did not receive SAP. In 23% (54; n=234) of cases, patients’ weight were not recorded, therefore correct dosing could not be confirmed. Incorrect doses were administered in 27% (63; n=234) of cases that received SAP.

Dosages were deemed correct if they were prescribed according to either the South African STG or the ASHP guideline.

SAP Timing

All patients that received SAP pre-operatively did so at anaesthetic induction time and none of these patients received a second dose of prophylaxis peri-operatively. This included the 6% (14; n=234) of cases where surgical procedures lasted for more than four hours.
Duration of SAP

In 188 patients (80%, n=234), SAP did not continue beyond the surgical procedure. This include cases where patients did not receive prophylaxis at all, as well as cases where it was not indicated. Compliance to guidelines was however evident in only 44% (103; n=234) of cases. In 8.5% (20; n=234) of cases SAP continued for 24 hours. Administration of prophylaxis continued up to 48 hours in 4% (9; n= 234) of cases.

Table 3 shows the level of adherence of different sub disciplines included in the study, as well as the overall compliance of each sub discipline. SAP appropriateness was evaluated with regards to correct choice of SAP agent, administration time, dose, re-dosing and duration of SAP.

Table 3: Measure of Compliance to SAP by Discipline

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cardiothoracic</th>
<th>ENT</th>
<th>General</th>
<th>Gynaecology</th>
<th>Neurosurgery</th>
<th>Orthopaedic</th>
<th>Urology</th>
<th>Vascular</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=234 (number) %</td>
<td>(24) 10</td>
<td>(16) 7</td>
<td>(43) 18</td>
<td>(64) 27</td>
<td>(16) 7</td>
<td>(38) 16</td>
<td>(30) 13</td>
<td>(3) 1</td>
<td>234</td>
</tr>
<tr>
<td>Correct Choice of SAP (number) %a</td>
<td>(20) 83</td>
<td>(11) 69</td>
<td>(26) 60</td>
<td>(47) 73</td>
<td>(10) 62.5</td>
<td>(31) 81.5</td>
<td>(15) 50</td>
<td>(3) 100</td>
<td>(163) 70</td>
</tr>
<tr>
<td>Correct Administration Time (number) %</td>
<td>(16) 66</td>
<td>(7) 43.7</td>
<td>(31) 72</td>
<td>(49) 76.5</td>
<td>(12) 75</td>
<td>(28) 73.6</td>
<td>(15) 50</td>
<td>(3) 100</td>
<td>(161) 69</td>
</tr>
<tr>
<td>Correct Dose (number) %</td>
<td>(14) 58</td>
<td>(2) 12.5</td>
<td>(12) 28</td>
<td>(15) 23.4</td>
<td>(3) 18.7</td>
<td>(13) 34</td>
<td>(7) 23</td>
<td>(2) 67</td>
<td>(68) 29</td>
</tr>
</tbody>
</table>
Discussion

The results of the study reflects current practice as far SAP in adult patients are concerned for this institution. Five measures of appropriateness to SAP were reviewed including the choice of SAP agent, timing of the first dose, SAP dosage, re-dosing and duration of SAP. Most of the surgical sub-disciplines in the hospital were represented in the study. At the time of the study the hospital did not have a written standard operating procedure for surgical antimicrobial prophylaxis.

Gynaecological procedures were the most common at 27% (64; n=234), followed by general surgery procedures at 18% (43; n=234) and orthopeadic procedures at 16%(38; n=234). General procedures at 41.6% and orthopeadic procedures at 10% were also identified as most common in a review of 250 patients in a tertiary hospital (El Hassan, Elnour, Farah et al., 2015). In another study from 80 patients who had undergone surgery, general procedures were also the most common (Nagdeo, Sonarkar, Thombare et al., 2015).
In this study 70% of the population (164; n=234) received SAP. Indication for SAP was found to be appropriate in 69.7% (163; n=234) as per guidelines; this includes cases where SAP was appropriately withheld. This was higher than what was found in a study in paediatric patients of the same institution whereby SAP was only received in 32.3% of the population. However, practice was found to be comparable in that 77.3% of cases wherein SAP was indicated, it was administered (Van der Sandt, Shellack, Mabope et al., 2018).

Cefazolin was the antimicrobial most commonly administered pre-operatively for SAP in 64% (151; n=234) of patients, followed by Ceftriaxone at 3% (8; n=234); this is similar to findings from a study by Rafati, Shiva, Ahmadi et al (2014) where Cefazolin was the most widely used antimicrobial agent in 91.7% of cases. Cefazolin is an ideal antimicrobial to be used for surgical prophylaxis; it is extensively studied for this purpose as it is effective against commonly encountered organisms in surgical wounds, has minimal side effects, highly concentrated in the surgical wound and is inexpensive (Nagdeo, Sonarkar, Thombare et al., 2015).

Of all the patients that received SAP pre-operatively, 70% of the population (164; n=234) received it at the same time as anaesthetic induction, which is well within 60 minutes before a surgical incision. This performance is better than that found in a multicenter study involving 745 patients, whereby only 37.6% of patients received antimicrobial prophylaxis within 60 minutes prior incision in the pre-interventional period and 41.6% in a post interventional period; a statistically non-significant change (Saied, Hafez, Kandeel et al., 2015). The South African SAP guidelines states that prophylaxis must be given within 60 minutes before incision, usually at anaesthetic induction (NDOH, 2015), while the ASHP guidelines also recommend administration within 60 minutes before surgical incision, but prefers a more specific time frame than just at induction of anaesthesia (Bratzler, Dellinger, Olsen et al., 2013).

The most inappropriate SAP prescribing practices for this study were observed with the dosing of SAP and re-dosing in procedures that lasted more than four hours. Only 29% (68; n=234) of the population received the correct dose. This finding is lower than what was observed in a study by El Hassan, Elnour, Farah et al (2015),
where a percentage of compliance to dosing at 40.3% were reported from 250 patients in a tertiary institution. Another study by Muller, Leroy, Henon et al (2015), found antimicrobial doses complied with recommended guidelines in 84.6%; however patients whose body mass index were missing were not evaluated for this measure. Antimicrobial agents need to be administered in doses that will attain sufficient blood and tissue concentrations for the duration of the procedure to be effective (Jocum, 2018).

Re-administration of the prophylactic dose intra-operatively is necessary in cases where the procedure exceeds four hours (NDOH, 2015). The antimicrobial should be re-administered at one to two times the half-life of the drug (Bratzler, Dellinger, Olsen et al, 2013). In this study there were 14 surgical procedures (6%; n=234) that endured for more than four hours. None of these patients received a second dose of SAP as per guidelines. Poor adherence to re-dosing guidelines was also observed in a multicentre study of 1 019 patients; surgery lasted more than four hours in 1.7% of patients and only 23.5% of these patients received the second dose of SAP intra-operatively (Chandrananth, Rabinovich, Karahalios et al., 2016). Good adherence to redosing was observed in a study including 4 078 patients from the United States; failure to re-dose eligible patients was seen in only 0.5% of cases. In this study, a computerised intra-operative decision support system was implemented to acquire almost real-time information of the procedure to give guidance alerts in the operating room (Kasatpibal, Whitney, Dellinger et al., 2017).

This study found an overall compliance of 44% (103; n=234) regarding the duration of SAP as per guidelines. These results are similar to that of a study done in a tertiary hospital in Abu Dhabi, where it was found that out of 250 procedures only 40% of patients received the appropriate number of doses (1-3), while 59.7% received more than three doses. In this study, orthopedic and neurosurgery sub-disciplines were the least compliant (El Hassan, Elnour, Farah et al., 2015). The ASHP guidelines recommend a shortened post-operative course of antimicrobials involving a single dose or a continuation for less than 24 hours. However, administration of Cefazolin for 24 hours is recommended in cardiac surgical procedures (Bratzler, Dellinger, Olsen et al., 2013). Prolonged prophylaxis have
shown no benefit and may be harmful due to the development of drug toxicity and super-infections (Rafati, Shiva, Ahmadi et al., 2014).

When comparing compliance to guidelines between the included surgery sub-disciplines, noteworthy differences do exist in all measures evaluated and this confirms the need for better adherence to SAP guidelines. In this study, the choice of SAP was found to be most appropriate in procedures of vascular and orthopedic nature at 100% (3; n=3) and 81.5% (31; n=38) respectively. It should be noted that only three procedures were included for vascular discipline. Choice of SAP was most inappropriate in urology and general procedures at 50% (15; n=30) and 60% (26; n=43). Vascular procedures at 100% (3; n=3) and gynaecological procedures at 76.5% (49; n=64), were more compliant to SAP administration time as opposed to ENT at 43.7% (7; n=16) and urology at 50% (15; n=30). Vascular and cardiology procedures also had the highest compliance for both correct dosing and duration of SAP; both disciplines were the overall most compliant for all five measures of compliance, at 73.4% and 54% respectively. A significant variation in practice was also identified in a review that looked at different studies measuring the appropriateness of SAP use. This review reported a difference of between 70.3% to 95% with regards to compliance to the appropriate indication measure; 12.7% to 98% to appropriate timing and 5.8% to 91.4% to appropriate duration. Overall compliance ranged from 0.3% to 84.5% (Gouvea, Novaes, Masterson et al, 2015).

Limitations

The collection of data depended on the availability of manually stored patient files. This proved a major challenge for the study as only 60% of requested files could be retrieved. Since the study was conducted retrospectively, the availability of information also depended on personnel documenting it; some data was found missing in the patient records. This study did not investigate the cause and relationship of the results. The inclusion criteria of patients that underwent surgery, but did not received SAP resulted in a certain percentage of population in which some measures of compliance could not be assessed. Further studies taking these limitations into consideration is needed.
CHAPTER 4: MANUSCRIPT

Conclusion

The study shows that prescribing patterns of SAP in this teaching hospital deviated from guidelines. Overall compliance to the five measures studied was low. Cases of inappropriate choice of SAP agent and prolonged use were identified. This practice is also evident in literature. Even though Cefazolin is administered as an agent of choice for SAP in most cases there are still instances where inappropriate antimicrobials are used for this purpose. Inappropriate antimicrobial use may lead to various adverse effects such as development of SSIs, selection for AMR and increased costs. Practice is commendable when it comes to timing of the pre-operative dose of SAP. Non-compliance was mostly seen with the inappropriate dosing and the absence of re-administration of SAP in eligible procedures. There is some variances in terms of compliance between sub-disciplines with regards to the choice of SAP agent, timing, dosing and duration of SAP. This could be attributed to a lack of hospital guidelines or standard operating procedure for SAP. Successful prescribing patterns of SAP can be achieved with close monitoring, education and increased compliance to guidelines.
References


Publish Ahead of Print

CHAPTER 5: LIMITATIONS, RECOMMENDATIONS AND CONCLUSIONS

CHAPTER 5

LIMITATIONS, RECOMMENDATIONS AND CONCLUSIONS

5.1 INTRODUCTION

The study being the first of its kind for adult surgical patients in this institution aimed to review patient files from most of the surgical sub-disciplines. This chapter addresses the limitations encountered when conducting the study. Recommendations are also discussed, followed by a conclusion. A summary for the study ends this chapter.

5.2 LIMITATIONS

The study was retrospective in nature, therefore data was obtained from archived files in a manually operated filing room. Only 60% of the requested files could be retrieved. Due to a small sample size results should be generalised with caution for SAP practices across South Africa. Hospital charts were used for data collection, thus accuracy depended on the accuracy of the hospital files. Some information was found missing from the files; weight for example was not recorded in 23% of the population, therefore appropriate dosing could not be confirmed in these patients. There was no dedicated space on the intra-operative sheet for SAP administration time but was rather listed by the anesthetists with medicines used for induction. It was therefore presumed that the SAP agent was also administered at anesthetic induction time. This study did not investigate the cause and relationship of the results. Furthermore, the surgery sub-disciplines had various operation forms in addition to the main intra-operative sheet, therefore many forms contained the same information for the same patient. The study did not evaluate the surgical teams knowledge or attitude towards the implementation of SAP.
5.3 RECOMMENDATIONS

The results found in this study can motivate reasons for more education and training on SAP and AMR, in order to promote behavioural change in prescribing patterns. It further identified the need for institution-specific SAP guidelines, as well as revision of the hospital intra-operative sheet(s) to include all SAP measures of compliance, comprising space for the name of antimicrobial agents, dose, time of administration and duration of prophylaxis. The need for targeted interventions on education and the relevance of these forms were also identified. Additional qualitative research would allow for a more comprehensive understanding of knowledge and perceptions of antimicrobial prescribing.

5.4 CONCLUSION

SAP practices in this teaching hospital in South Africa diverge from current guidelines. Full compliance to the five criteria was not met by any of the surgery sub-disciplines and inappropriate over-use, as well as under-use of SAP occurs. The lowest adherence was seen with re-dosing of the SAP agent in eligible procedures. This study’s findings were consistent with existing literature, which described variation in SAP use. The importance of the proper use of SAP cannot be over-emphasised, as it contributes to AMR and is associated with a significant decreases in SSI-associated morbidity and mortality. Reasons for concern have been identified and therefore, continued surveillance and quality improvement interventions are required. Local standardised SAP guidelines in South Africa are also needed and clinical pharmacists can play a vital role in ensuring compliance to these guidelines.

5.5 SUMMARY

The aim of this retrospective cross-sectional study was to determine the prescribing patterns of surgical antimicrobial prophylaxis in a teaching hospital and to evaluate compliance to South African and international standard treatment guidelines. The review looked at 234 adult patients who underwent a surgical procedure between January and May 2017. Surgical sub-disciplines studied included gynaecological,
general, ENT, orthopedic, vascular, neurosurgery, urology and cardiothoracic procedures.

Compliance to all five measures was not achieved by any of the surgical sub-disciplines and significant variations in compliance amongst them was also identified. It can therefore be concluded that prescribing patterns of SAP in a teaching hospital deviated from guidelines. Antimicrobial stewardship and education programs need to be implemented to improve compliance to guidelines.


REFERENCES


REFERENCES


APPENDICES

APPENDIX 1: SURGICAL ANTIMICROBIAL PROPHYLAXIS GUIDELINES

Recommendations for selection of Antimicrobial agents for specific surgical procedures and alternative agents as adapted from the latest South African Standard treatment (SATG) and ASHP guidelines for Surgical Antimicrobial Prophylaxis (NDOH, 2015; Bratzler, Dellinger, Olsen et al., 2013).

<table>
<thead>
<tr>
<th>TYPE OF SURGERY</th>
<th>ANTIMICROBIAL RECOMMENDED SATG</th>
<th>ANTIMICROBIAL RECOMMENDED SATG</th>
<th>ASHP RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CEFAZOLIN IV</td>
<td>CEFAZOLIN IV AND METRONIDAZOLE IV</td>
<td>SAME</td>
</tr>
<tr>
<td>ORTHOPAEDIC SURGERY</td>
<td>Primary total hip or total knee replacement; internal fixation of hip; spinal procedures; open reduction and internal fixation of fractures; insertion of prostheses, screws, plates etc.</td>
<td>Lower limb amputation.</td>
<td>SAME</td>
</tr>
<tr>
<td>GASTROINTESTINAL SURGERY</td>
<td>Gastric/duodenal/oesophageal hernia repair.</td>
<td>Billiary, colorectal, manipulation of viscera, appendicectomy, divisions of adhesions, exploratory laparactomy.</td>
<td>SAME</td>
</tr>
<tr>
<td>THORACIC SURGERY</td>
<td>Non-cardiac procedures including: Pneumonectomy, lobectomy, lung resection and thoracotomy</td>
<td>Cefazolin IV alone as drug of choice.</td>
<td>SAME</td>
</tr>
<tr>
<td>CARDIAC SURGERY</td>
<td>Coronary artery bypass surgery/routine cardiac valve surgery (continue cefazolin IV 8 hourly for 24 hours), cardiac device insertion (pacemaker implantation).</td>
<td></td>
<td>SAME</td>
</tr>
<tr>
<td>VASCULAR SURGERY (Prophylaxis in NOT recommended for other clean procedures)</td>
<td>Vascular reconstruction: abdominal aorta, groin incision (continue 8 hourly for 24 hours), AV fistula and ligation of varicose veins.</td>
<td>Lower limb amputation.</td>
<td>SAME</td>
</tr>
</tbody>
</table>
### APPENDICES

<table>
<thead>
<tr>
<th>UROLOGY</th>
<th>Clean procedures with AND without entry into urinary tract.</th>
<th>Clean contaminated procedures.</th>
<th>SAME. Fluoroquinolone IV is a drug of choice for lower instrumentation with risk factors for infection.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLASTIC AND RECONSTRUCTIVE SURGERY (Prophylaxis is NOT recommended for clean bone and soft tissue surgery).</td>
<td>Craniotomy procedures. Other clean contaminated procedures.</td>
<td></td>
<td>SAME</td>
</tr>
<tr>
<td>HEAD AND NECK SURGERY (Prophylaxis is NOT recommended for other procedures such as tonsillectomy, sinus procedures, etc.).</td>
<td>Clean contaminated with no incision through the oropharyngeal mucosa. Clean with placement of prosthesis. With incision through the oropharyngeal mucosa. Clean contaminated cancer surgery.</td>
<td></td>
<td>SAME</td>
</tr>
<tr>
<td>OBSTETRICS/GYNAECOLOGY (Prophylaxis is NOT recommended for clean bone and soft tissue surgery).</td>
<td>Caesarean section Hysterectomy, laparotomy procedures, vaginal repairs.</td>
<td></td>
<td>SAME. Cefazolin IV alone as drug of choice for Hysterectomy(vaginal and abdominal)</td>
</tr>
<tr>
<td>NEUROSURGERY (Prophylaxis is NOT recommended for other minor clean procedures).</td>
<td>Craniotomy, CSF shunt/drain, laminectomy.</td>
<td></td>
<td>SAME</td>
</tr>
<tr>
<td>ENDOSCOPIC GASTROINTESTINAL PROCEDURE (Prophylaxis is NOT recommended for all other procedures, with or without biopsy).</td>
<td>Percutaneous endoscopic gastronomy insertion/ revision.</td>
<td></td>
<td>SAME</td>
</tr>
<tr>
<td>GENERAL SURGERY (Prophylaxis is NOT recommended for uncomplicated clean procedures e.g. wound revision, excision of scar tissue, etc.).</td>
<td>Clean contaminated procedures (mastectomy, node biopsy, etc.), splenectomy.</td>
<td></td>
<td>Not addressed in ASHP recommendations</td>
</tr>
</tbody>
</table>

Note: Clindamycin 600mg IV is used in patients with Beta-Lactam allergies. Addition of metronidazole is unnecessary in these cases since clindamycin has good coverage against gram positive and anaerobic organisms. ASHP recommends the use of vancomycin as an alternative to clindamycin in surgical procedures involving prosthetic devices implantation in areas where MRSA risk is high. Gentamicin is added to clindamycin in gastrointestinal, clean-contaminated urology and obstetric/gynaecological (e.g. hysterectomy, laparotomy procedures and vaginal repair) surgeries.
APPENDICES

APPENDIX 2: DOSAGE RECOMMENDATIONS

Dosage recommendations for Antimicrobial agents as adapted from the latest South African Standard treatment and ASHP guidelines for Surgical Antimicrobial Prophylaxis (NDOH, 2015; Bratzler, Dellinger, Olsen et al., 2013).

<table>
<thead>
<tr>
<th>ANTIMICROBIAL NAME</th>
<th>SATG ADULT DOSE RECOMMENDATION</th>
<th>ASHP ADULT DOSE RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin IV</td>
<td>If &lt; 80kg: 1g</td>
<td>If &lt; 120kg: 2g</td>
</tr>
<tr>
<td></td>
<td>If &gt; 80kg: 2g</td>
<td>If &gt; 120kg: 3g</td>
</tr>
<tr>
<td>Metronidazole IV</td>
<td>500mg</td>
<td>500mg</td>
</tr>
<tr>
<td>Gentamycin IV</td>
<td>6mg/kg/single dose</td>
<td>5mg/kg/single dose</td>
</tr>
<tr>
<td>Clindamycin IV</td>
<td>600mg</td>
<td>900mg</td>
</tr>
<tr>
<td>Ceftriaxone IV</td>
<td>Not addressed</td>
<td>2g</td>
</tr>
<tr>
<td>Vancomycin IV</td>
<td>Not addressed</td>
<td>15mg/kg</td>
</tr>
</tbody>
</table>
### APPENDIX 3: DATA COLLECTION SHEET

<table>
<thead>
<tr>
<th>Patient demographics</th>
<th>Primary diagnosis</th>
<th>ICD-10 code</th>
<th>Surgical Procedure name</th>
<th>Pre-existing infection(s)- If Yes Indicate treatment</th>
<th>Date of the Procedure</th>
<th>Length of Procedure</th>
<th>Surgical Antimicrobial Prophylaxis</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Drug Name(s) And Dosage form</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Time of admin. prior Surgical Procedure</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Duration of Prophylaxis</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Dosing intervals</td>
<td></td>
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<tr>
<th>Study nr:</th>
<th>Age:</th>
<th>GN/GP no:</th>
<th>Weight:</th>
<th>Height:</th>
<th>Gender:</th>
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<tr>
<td>1</td>
<td></td>
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<tr>
<th>Study Nr:</th>
<th>Age:</th>
<th>GN/GP no:</th>
<th>Weight:</th>
<th>Height:</th>
<th>Gender:</th>
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</table>
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APPENDIX 4: SMUREC CLEARANCE CERTIFICATE

Sefako Makgatho Health Sciences University
Research & Postgraduate Studies Directorate
Sefako Makgatho University Research Ethics Committee
(SMUREC)

Molotlegi Street, Ga-Rankuwa 0208
Tel: (012) 521 5517/3698 | fax: (012) 521 3749
Email: lorato.phiri@smu.ac.za
P.O. Box 163 Medunsa 0204

APPROVAL NOTICE - NEW APPLICATION

07 September 2017

Miss JK Tshiveu
Department of Pharmacy
P.O.Box 219
Medunsa, 0204

MEETING: 07/2017

SMUREC Ethics Reference Number: SMUREC/P/227/2017: PG

The New Application received on 21 August 2017, was reviewed by members of Sefako Makgatho University Research Ethics Committee 07 September 2017 and was approved on 07 September 2017.

Title: Evaluation of surgical antimicrobial prophylaxis prescribing patterns in Dr George Mukhari Academic Hospital, Gauteng Province

Researcher: Miss JK Tshiveu
Supervisor: Ms L Molele
Co-supervisor: Ma E Bronkhorst
Department: Pharmacy
School: Pharmacy
Degree: M Pharm

Please note the following information about your approved research protocol:

Approval Period: 07 September 2017 – 07 September 2018

Please remember to use your protocol number (SMUREC/P/227/2017: PG) on any documents or correspondence with the REC concerning your research protocol.

Please note that the REC has the prerogative and authority to ask further questions, seek additional information, require further modification, or monitor the conduct of your research and the consent process.

After Ethical Review: Please note a template of the progress report is obtainable in the Research Office and should be submitted to the Committee before the year has expired. The Committee will then consider the continuation of the project for a further year if necessary. Annually a number of projects may be selected randomly for an external audit. Translation of the consent document in the language applicable to the study participants should be submitted.

International Organisation (COR0205885), Institutional Review Board (IRB000010595) Expiry date: 09 December 2018,
Federal Wide Assurance (FWA000029440) Expiry date: 03 March 2021 and NHREC No: REC 200408-003

Sincerely,

PROF C BAKER
DEPUTY CHAIRPERSON SMUREC

Date: 01/09/2017
APPENDICES

APPENDIX 5: AUTHOR’S GUIDELINES FOR SUBMISSION TO THE SOUTH AFRICAN JOURNAL INFECTIOUS DISEASES

Manuscripts submitted to the SAJID must be in the form of Research Articles, Brief Reports, Clinical Case Studies, Correspondence, Reviews, State-of-the-Art Articles, Commentaries and Opinion Papers, Editorials or Supplement Articles. The Journal welcomes the publication of Guidelines, Conference Proceedings Newsletters or Press Releases, and Book Reviews. Articles, Brief reports and Reviews are peer reviewed; other categories are reviewed by the Editors. Commentaries and Editorials are generally invited contributions, indicating the authors’ identity, while manuscripts in the form of Reviews, and State-of-the-Art Articles may also be requested by the Editors.

All manuscripts must have conflict of interest and funding statements. When authors submit a manuscript, whether an article or a letter, they are responsible for disclosing all financial and personal relationships that might bias their work. To prevent ambiguity, authors must state explicitly whether potential conflicts do or do not exist. Authors should do so in the manuscript on a conflict-of-interest notification page that follows the title page.

Manuscripts describing research in human subjects or animals must indicate ethics clearance from appropriate research review committees. When reporting experiments on human subjects, authors should indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.

Articles describe original investigations at an acceptable degree of completion, constituting an advance in the field. Articles must not exceed 3500 words of text, without counting the abstract, references or legends, and illustrations and tables must be limited to the minimum necessary for clear and concise presentation. The abstract
must either be structured, using Background, Methods, Results, and Conclusions as headings and comprising no more than 250 words, or unstructured with a 200 word limit. Articles are limited to a maximum of 7 insets (tables and figures combined) and 50 references.

Brief Reports present complete studies that are narrower in scope than those described in Articles or that present new developments. Manuscripts that are descriptive or primarily methodological in nature, or that describe in vitro chemotherapeutic studies should, in general, be submitted as Brief Reports. Brief Reports include an abstract (no more than 100 words) and are limited to a total of no more than 2000 words of text, a total of 2 inserts (tables or figures), and 15 references.

Correspondence (letters) must be submitted in reference to a previous publication in SAJID (within the previous 12 months), or relate to a topical matter in line with the interests of FIDSSA, PHASA or their affiliated societies. Please prepare the letter in manuscript format, including a title page. The letter must not exceed 750 words of text, 1 insert (table or figure) and 10 references.

Commentaries and Editorials are generally invited by the Editor and are overviews of articles in SAJID, or of other research in epidemiology or infectious diseases, or matters relating to public health and other issues of special interest to FIDSSA, PHASA or their associated societies. Unsolicited commentaries are also considered.

Reviews and State-of-the-Art Articles that are research oriented or fall within the fields of interests of FIDSSA, PHASA or any of their affiliated societies will be considered for publication by SAJID. Prospective authors of such manuscripts are advised to communicate with the Editor in advance to ensure that a specific contribution is deemed appropriate and timely. Manuscripts of Reviews and State-of-the-Art Articles will be peer-reviewed.
APPENDICES

Reviewers

The Journal would encourage authors to supply the names of at least 2 potential reviewers for their manuscript, as well as to indicate any reviewers they would feel may have a potential conflict of interest with regard to their submission.

Supplements

Requirements for supplement manuscripts generally follow those for SAJID manuscripts, including conflict of interest and funding statements. Inquiries relating to suitability of topic, programme organisation, production and costs should be made to the Editor.

Evaluation of manuscripts

Review procedure. The Editor-in-Chief and Emeritus Editor screen all unsolicited manuscript submissions and some of these are rejected without further review. All other manuscripts are sent to a minimum of two outside experts for review. After receipt of the reviewers’ reports, the Editor-in-Chief and the Emeritus Editor with administrative assistance of the Journal Secretary discuss the merits of the manuscripts and the Editor-in-Chief makes the final decision to accept, reject, or request revision of the manuscript. A request for revision does not guarantee ultimate acceptance of the revised manuscript.

Related manuscripts. If there appears to be significant overlap between a manuscript submitted to SAJID and another submitted manuscript by the same authors to SAJID or another journal, the editors will take the matter up with the corresponding author, and based on the response, take appropriate action (ask for modification, or reject with detailed explanation). Further action may include informing the appropriate authority in the authors’ resident institution and if overlapping is discovered after publication in SAJID, publishing an appropriate announcement to that effect in the journal.
APPENDICES

DOCUMENT REQUIREMENTS

Checklist

The following are required for your manuscript to be processed:

- Covering letter
- Word count limits
- Conflict of interest statement
- Funding statement
- List of potential reviewers

Covering Letter

All manuscripts submitted to SAJID must be accompanied by a letter declaring that the manuscript has not been submitted or accepted for publication elsewhere. This letter must confirm and declare that all authors have seen and approved the content and have contributed significantly to the work. Authors should suggest potential unbiased reviewers who are qualified to review their manuscript. A covering letter must also accompany a revised submission and must address issues raised in the review process.

Manuscript Preparation

The SAJID complies with the Uniform Requirements for Manuscripts Submitted to Biomedical Journal Journals (Ann Intern Med 2000; 133:229-231 [editorial]; http://www.icmje.org , full text). Text, tables, references, and legends must be double-spaced. Italics should be used for genus and species names and for genes but not for in vivo, in vitro, in situ, et al., or other Latin-derived expressions. For layout of manuscript and appropriate style see a recent issue of SAJID.
Title page

On the title page, please supply a running head of not more than 40 characters and spaces, a title of not more than 160 characters and spaces, the names and affiliations of all the authors, and word counts of the abstract and text. Each author’s first name, subsequent initials and surname must be used.

Footnote page

Footnotes must include:

- Statement that authors either have or have not a commercial or other association that might pose a conflict of interest (e.g. pharmaceutical stock ownership, consultancy, advisory board membership, relevant patents, or research funding)
- Statement naming sources of financial support (including grant numbers)
- Name, date (month and year), and location (city, and country if not South Africa) of a meeting at which all or part of the information has been presented (include an abstract number, if available)
- Name and e-mail address of the person to whom correspondence should be addressed
- Current affiliations for authors whose affiliations have changed since completion of the study

Abstract.

The abstract for an Article may be structured with the headings Background, Methods, Results, and Conclusions (250-word limit) or unstructured (200-word limit). Abstracts of Brief Reports should be no more than 100 words. Whether structured or unstructured, the abstract must state the purpose of the research, the methods used, the results, and the conclusions. Do not cite references in the abstract. Include up to
10 key words, separate from the abstract. Please remember that the abstract is particularly useful for literature retrieval purposes.

Text

The text of Articles must be no longer than 3500 words, and that of Brief Reports no longer than 2000 words. The Methods section must include a statement that informed consent was obtained from patients or their parents or guardians, and human experimentation guidelines of the National Department of Health (http://www.doh.gov.za) or the South African Medical Research Council (MRC; http://www.sahealthinfo.org/ethics/index.htm) and/or those of the authors’ institution(s) were followed in the conduct of clinical research or that animal experimentation guidelines (see MRC website above) were followed in animal studies.

References

Articles are generally limited to 50 references, Brief Reports to 15 references. Only works that have been published or accepted for publication can be included in the reference list. Unpublished observations by the authors (authors’ unpublished data) personal communications (SP Stanley, personal communication), and manuscripts submitted for publication (J Odendaal, S Coovadia and J Radebe, submitted) should be mentioned parenthetically in the text Please number references in order of appearance; those cited only or first in tables or figures are numbered according to the order in which the table or figure is cited in the text. Example: If table 3 is cited in the text after reference 20, a new reference cited in table 3 will be reference 21.

References must follow the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (http://www.icmje.org, full text). Provide all authors’ (or editors’) names when there are fewer than 7; for 7 or more, list the first 3 and add “et al.” Titles of journals not listed in Index Medicus should be spelt out in full. Reference to a doctoral thesis or Master’s dissertation should include the author, title, institution, location, year and publication information, if published. For online resources, include a URL and date accessed. Accuracy of references is the responsibility of the authors.
Examples of the proper format are as follows:


Acknowledgment(s)

The page preceding the references may include a statement thanking those who assisted substantially with work relevant to the study.

Statistical analysis

The statistical analyses used should be identified both in the text and in all tables and figures where the results of statistical comparison are shown.
Units of measure

All Data should be expressed in metric units; use of SI units is encouraged. Use °C for temperature.

Tables and figures

Articles are limited to a maximum of seven inserts (tables and figures combined), Brief Reports to a maximum of two inserts. Data should not be repeated in both a table and a figure. Abbreviations and acronyms used in tables and figures must be explained in the table footnotes and figure legends, even if already defined in the text.

Tables should be numbered in the order of mention in the text. Tables should be typed double-spaced throughout, with no vertical or internal rules. Footnotes and accompanying explanatory material should be kept to a minimum. Footnotes should be placed below the table and designated by superscript lowercase letters (listed in order of location when the table is read horizontally). Each column must have an appropriate heading describing the data in the column below, and units of measure must be clearly indicated. For further instructions on the preparation of tables in Word, consult the Special Instructions for Tables.

Figures should be also numbered in the order of mention in the text and should appear at the end of the manuscript and references. Your figures should be prepared in accordance with the Guidelines for Submission of Artwork. Letters, numbers, and symbols should be clear and of sufficient size to be legible when the figures are reduced. Photomicrographs should have internal scale markers. Figures reproduced from other publications must be accompanied by permission from the copyright holder. If the manuscript is accepted, the author will be required to send one complete set of glossy, hard-copy figures.

Figure legends should be double-spaced and appear on a separate page preceding the figures. Any abbreviations or symbols used but not defined in the figure itself must be defined in the legend.
Style


For commercially obtained products mentioned in the text, list the full names of manufacturers. Generic names of drugs and other chemical compounds should be used.

Nomenclature

SAJID recommends the latest widely accepted nomenclature, as set out in documents prepared by recognised international agencies e.g. the International Journal of Systematic and Evolutionary Microbiology, *Bergey’s Manual of Determinative Bacteriology* (9th ed., revised, Williams & Wilkins, 1993), *Virus Taxonomy – The Classification and Nomenclature of Viruses: Sixth Report of the International Committee on Taxonomy of Viruses* (Springer-Verlag, 1995). The latter document also supplies standard abbreviations for virus species.