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A protocol for prophylactic antibiotic use in managing mandibular fractures requiring open reduction and internal fixation: a prospective clinical trial

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A PROTOCOL FOR PROPHYLACTIC ANTIBIOTIC USE IN MANAGING MANDIBULAR FRACTURES REQUIRING OPEN REDUCTION AND INTERNAL FIXATION: A PROSPECTIVE CLINICAL TRIAL

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A Dissertation submitted to the Faculty of Science, University of the Witwatersrand, in fulfilment of the requirements for the degree of Master of Dentistry, Maxillofacial and Oral Surgery.

Johannesburg, 2020.

DECLARATION

I, Gontse Pauline Mohotlhoane, declare that this Research Report is my own work. It is being submitted for the degree of Masters of Dentistry at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



_____ (Signature of candidate)

On 2nd day of DECEMBER 2020 at Johannesburg

DEDICATION

This is dedicated to my amazing family for the prayers, support, and endless love throughout this journey. To my son, Awande, and my mother, Modiegi, for being pillars of strength and a source of inspiration!

In loving memory of my father

Joseph Mohotlhoane

(1959- 2019)

Rest in power Mokoena!

ABSTRACT

***Introduction*:** The use of antibiotic prophylaxis in managing mandibular fractures is a common practice amongst oral and maxillofacial surgeons. The practices are however varied and unclear.

***Purpose*:** The purpose of this study was to evaluate the benefits of long term prophylactic antibiotic regimen following treatment of fractured mandibles with open reduction and internal fixation.

***Material and methods*:** A prospective, randomized controlled trial was undertaken at Wits Oral Health Centre. Patients with mandibular fractures who were managed with open reduction and internal fixation using mini plates via intra-oral approach were randomized into two groups. Group 1, the control group, was composed of patients who received a 1-day IV antibiotic cover intra-operatively and further 24 hour doses post-operatively (3 doses), before being discharged. Group 2, the study group, was composed of patients who received similar doses as the control group but with an additional 5 days of oral antibiotics upon discharge. The patients were reviewed over a period of 1, 4 and 6 weeks and the presence or absence of infection was recorded each week and analyzed.

Results: A total of 77 patients were analyzed, with 41(53.2%) in the non-antibiotic group and 36 (46.8%) in the antibiotic group. Overall infection rate at 6 weeks was 6.5% with a total of 18 patients in the non-antibiotic group and 9 patients in the antibiotic group who presented with infections over the 6-week review period. There was no significant difference ($p=0.34$) in the presence of infection between the antibiotic and the non-antibiotic groups but there was a notable increase in post-operative infection in patients with comorbidities in the non-antibiotic group.

***Conclusions*:** The extended use of antibiotic prophylaxis when managing mandibular fractures with open reduction and internal fixation offers no additional benefit in reducing post-operative infection. However, patients with comorbidities might be at an increased risk of post-operative infection and might benefit from an extended course of oral antibiotics.

ACKNOWLEDGEMENTS

A great acknowledgement to my supervisor, Prof Ephraim Rikhotso. Thank you for teaching and guiding me with kindness!!!

"KINDNESS- Loaning someone your strength instead of reminding them of their weakness."
TheMindsJournal

Jacintha Johnson and the Selective Surgical team for assisting with some of the graphic images.

Mpumalanga Department of Health and Wits Oral Health for awarding me the opportunity to pursue my studies.

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CHAPTER 1

1.1 INTRODUCTION

The anatomy of the mandible is divided into the temporomandibular joint, condylar head and neck, the ascending ramus, and the horizontal ramus or body (Banks, 1991) (Fig 1.1). It is furthermore divided into a dento-alveolar and a basal segment (Heslop, 1963). The mandible is connected to the skull by paired temporomandibular joints and is the only movable bone of the skull. Two sets of foramina are associated with mandible. The mental foramen below the first molar on the anterolateral surface of body of mandible and the mandibular foramen found on the medial surface of the ramus (Van De Graaf, 1998). The mandibular foramen contains the inferior alveolar nerve, artery, and vein. The mandibular nerve supply is through the mandibular branch of the trigeminal nerve, which innervates the temporomandibular joint, muscles, skin, mucosa, the periosteum and all the mandibular teeth. The inferior alveolar artery provides the dominant blood supply to the mandible. Once the mandibular nerve ends at the mental foramen, the inferior alveolar nerve and artery become mental nerve and artery (Nguyen, 2019).

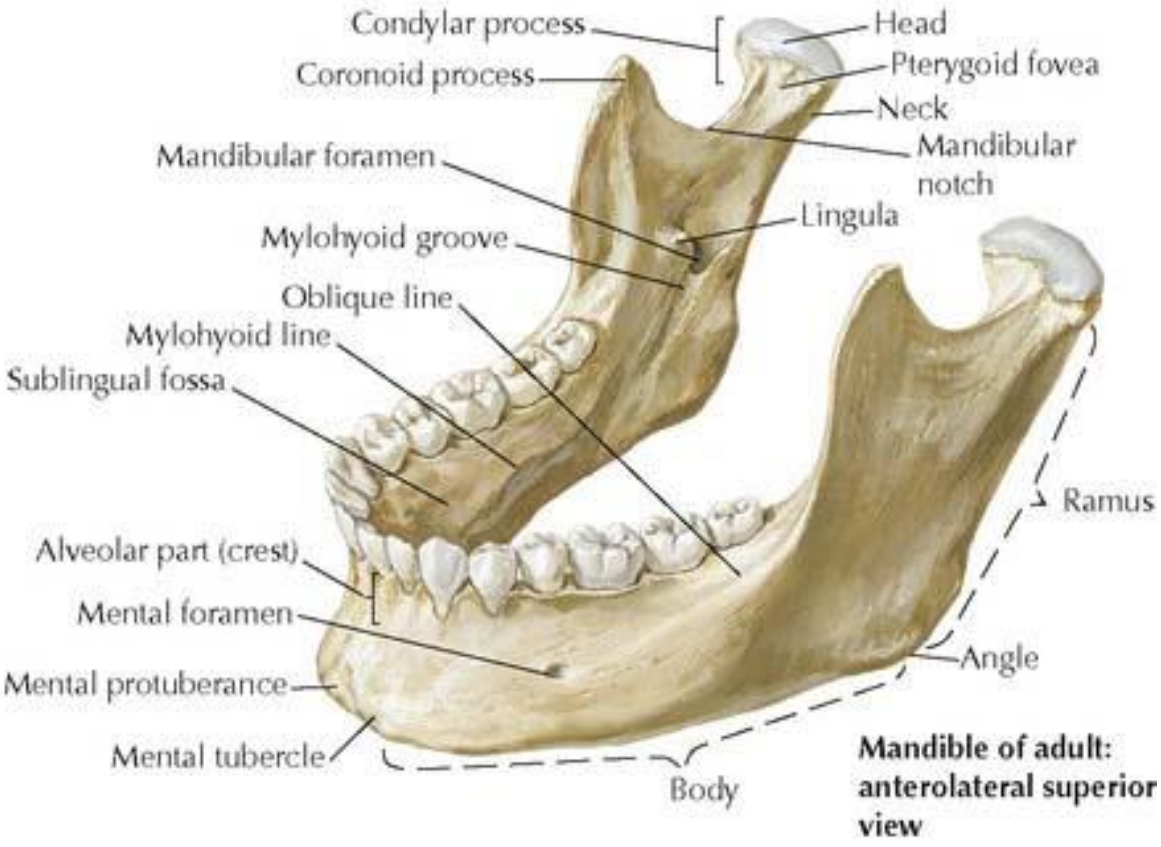


Figure1.1: Anatomy of the mandible (Netter, 2007)

Despite the fact that the mandible is the largest and strongest facial bone, it is the most commonly fractured bone in maxillofacial trauma due to its position on the face and its prominence (Upton, 1991). The fractures of the mandible can occur anywhere along the length of the jaw, depending on the direction and the force of the trauma, but certain areas are weaker and thus more prone to fractures. The mandible is stronger at the midline with progressively reducing strength towards the condyles (Anyanechi, 2011). The causes for the fractures of the mandible are varied and depend on demographics, economy, and geography. The causes range from trauma (motor vehicle accidents, assaults, sports injuries, etc.), iatrogenic, to pathological fractures. There are various factors that influence the type of injury sustained on the mandible such as the severity and anatomical site of impacting force, whether the mouth was open during the incidence and absence or presence of teeth (Anyanechi,2011).

On examining the patients, after they have been stabilized following the ATLS® protocol, a thorough head and neck assessment is important to identify or exclude any other injuries. Some of the most common signs and symptoms of mandibular fractures include (Fig 1.2):

- Pain, on palpation and function
- Swelling
- Trismus
- Altered nerve sensation
- Malocclusion
- Soft tissue lacerations, especially the gingiva
- Ecchymosis, floor of the mouth or the vestibule



Figure 1.2: A clinical picture showing a fracture of the mandible with associated gingival laceration between teeth 33 and 32.

Several radiographic investigations are required to confirm or support the clinical findings. The most cost-effective modalities are the plain films. When obtaining plain films, two views at right angles must be obtained to assess fracture displacement. A “mandible series” consists of the orthopantomogram (or it can be substituted with right and left lateral oblique views), posterior/anterior view, and reverse Towne’s view. (Fonseca, 2008) (Fig1.3). A CT scan, whenever available, can be used.

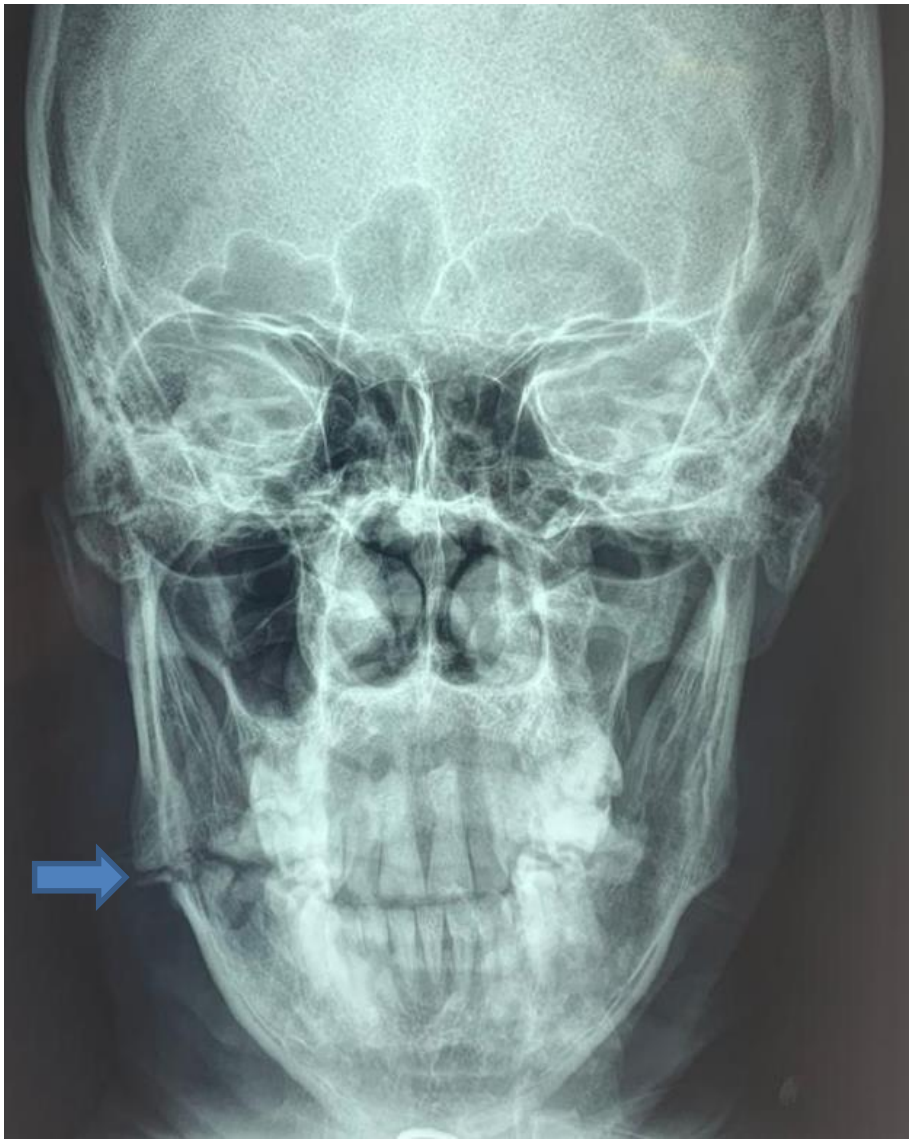


Figure1.3: A posterior/anterior view of a patient with a right-angle mandibular fracture (blue arrow)

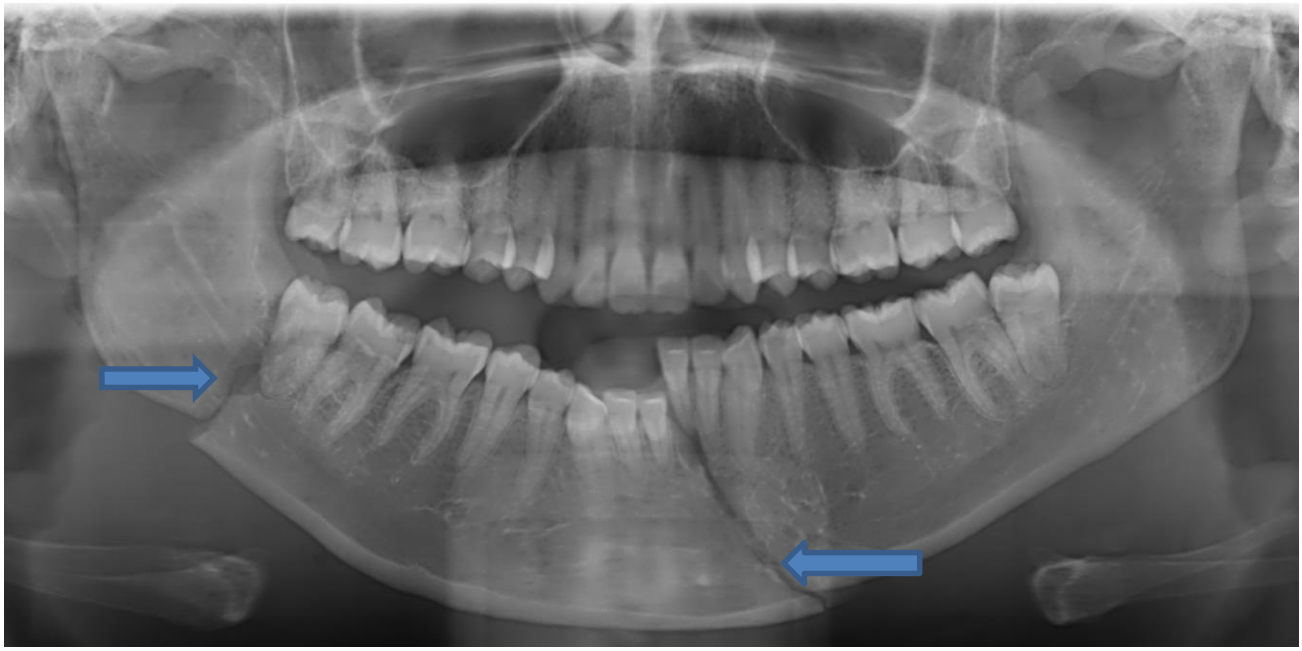


Figure1.4: An orthopantomogram indicating displaced bilateral mandibular fractures (Blue arrows)

Various classification systems were developed to facilitate communication and assist with the formulation of treatment plans for mandibular fractures:

a. Classification according to the location of the fracture: (Rowe & Kiley classification, 1968)

- Dentoalveolar segment
- Symphysis
- Parasymphysis
- Body
- Angle
- Ascending ramus
- Condylar process
- Coronoid process

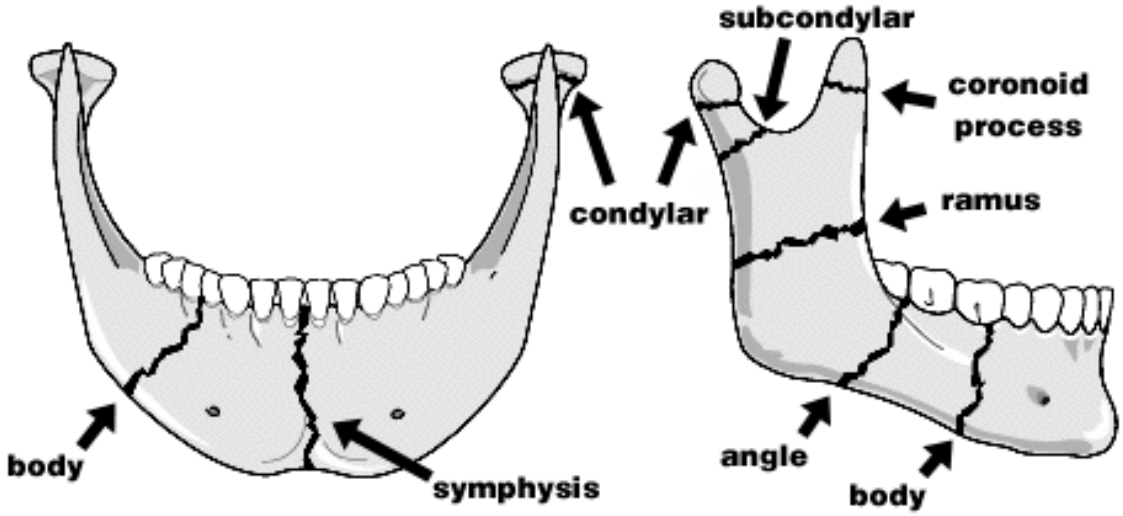


Figure 1.5: Various locations of mandibular fractures (Rowe and Killey, 1968)

b. Classification according to pattern of fracture (Kruger's general classification, 1986)

- Simple
- Compound
- Greenstick
- Comminuted
- Complex or complicated
- Telescoped or impacted
- Pathological
- Displaced

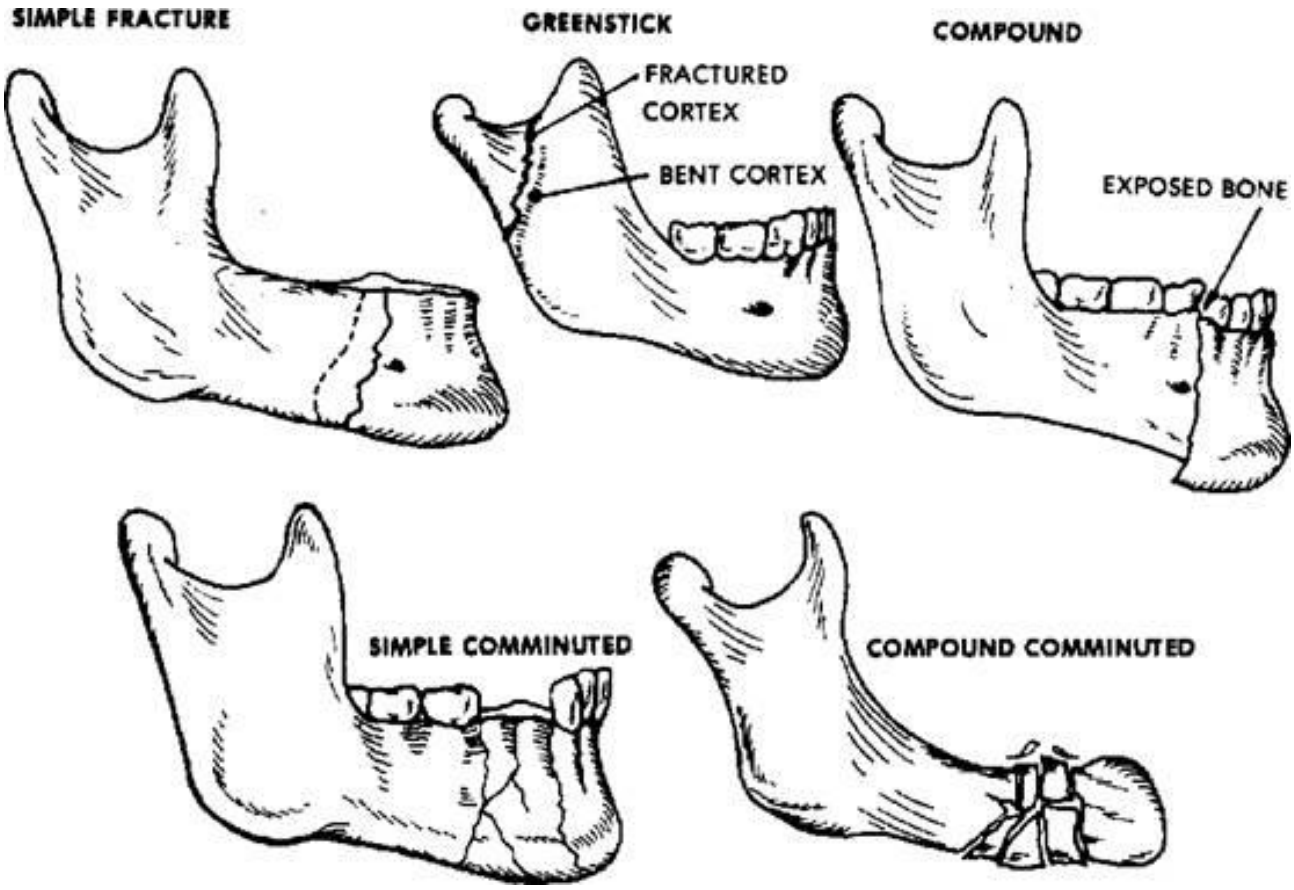


Figure1.6: schematic drawing showing different patterns of mandibular fractures (Kruger, 1986)

c. Classification according to the dentition (Kazanjian and Converse, 1974) (Fig1.7)

- Class I: Teeth are present on both side of the fracture
- Class II: Teeth are present only on one side of the fracture line
- Class III: Fracture in edentulous patients

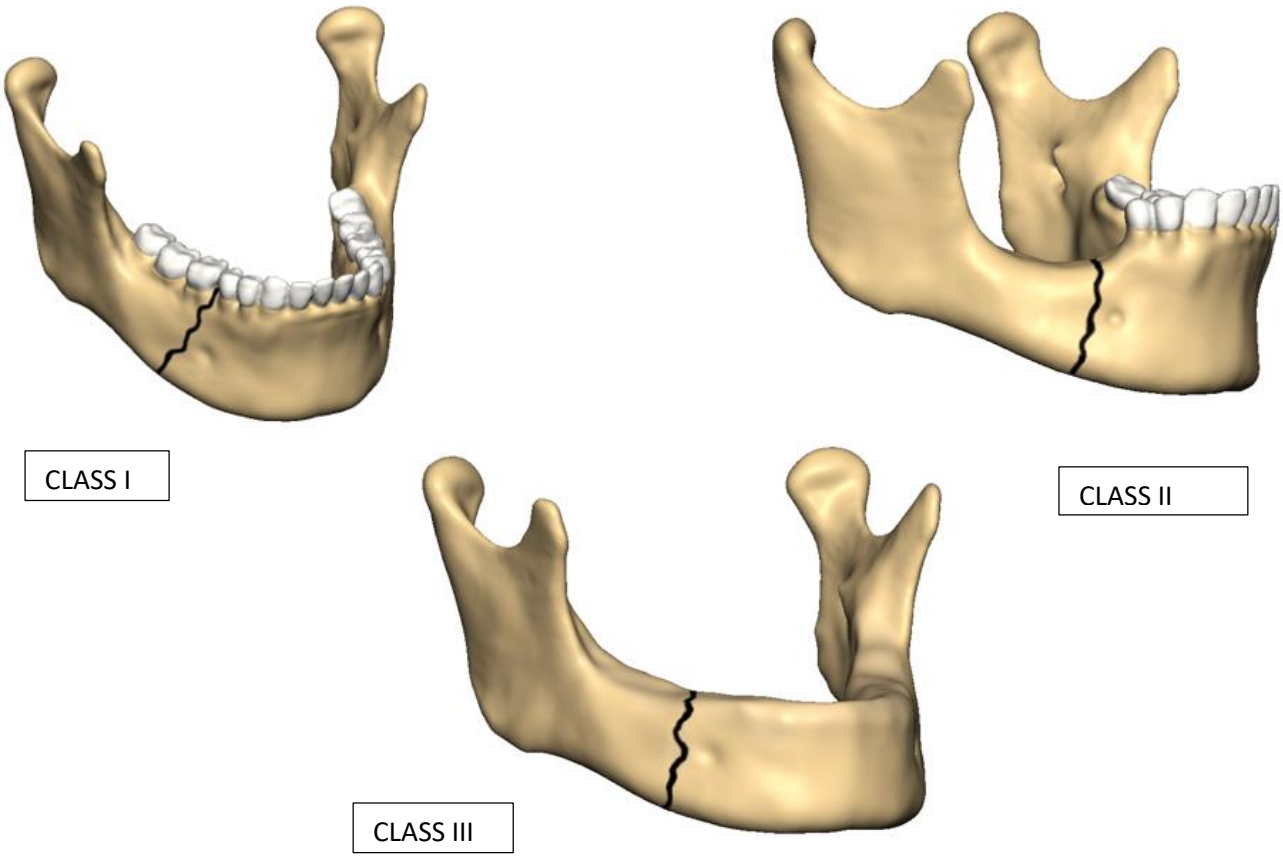


Fig1.7: Classification of mandibular fractures based on presence/ absence of teeth (courtesy of Selective Surgical)

Treatment of mandibular fractures

The goals of treatment of mandibular fractures are:

(1) to restore the patient to form and function, with return to preinjury occlusion and achieving anatomic reduction where possible
(2) to achieve osseous union predictably (Peterson, 2012).

Historically, management of mandibular fractures has always placed emphasis on the importance of reduction and immobilization (Fonseca, 2008). Techniques for closed reduction and stabilization were then developed. The concept of maxillomandibular fixation (MMF), which involved wiring the teeth together into a stable occlusion to stabilize the fractures, was introduced. Several methods of MMF have been described; these include the use of external bandages, Gunning's splints, and the use of external frame and pin fixation. Various forms of

interdental wiring methods, which are still in use to date include Erich arch bars and Ivy loops. The methods of close reduction were not without limitations and complications. Challenges such as limited patient function and inadequate fracture reduction were encountered. These led to the development of open reduction, with trans-osseous wiring being used to stabilize and reduce the fractures. The technique was termed "Thomas silver wire" technique. The trans-osseous wiring was later replaced with the use of plates and screws. The modern systems that are in use today for ORIF of mandibular fractures originate from orthopaedic surgery.

Several factors need to be taken into consideration when managing patients with mandibular fractures. The classification of the fractures plays an important role in the decision-making process concerning appropriate treatment. An understanding of biomechanics is also necessary for evaluating the effectiveness of fixation techniques. The muscle attachment and counteracting forces play an important role in determining pattern direction and degree of displacement. During normal function, the mandible will develop areas of tensile, compressive, and torsional forces. The forces are varied for different parts of the mandible.

- The angle and the body of the mandible experience tension forces and compression forces at the superior and lower borders respectively.
- The parasymphyseal and symphyseal fractures have torsional forces on the lingual surface and compression on the labial surface. Anterior to the mental foramen, there are torsional forces, hence the need for two plates when doing ORIF of the mandible.

The fractures can be managed conservatively, with intermaxillary fixation (IMF) or with open reduction, with or without internal fixation. Although there are varying opinions regarding which one is better between ORIF and IMF, certain injuries can only be managed by ORIF. The decision with regards to management is dependent on factors such as patient factors (age, general health, associated injuries, etc.), the type and location of the fractures, displacement of the fracture, resources, skilled clinicians and time lapsed from injury to treatment (Nasser, 2013).

Open reduction without internal fixation is a treatment option where the fractures are reduced under direct vision, however no fixation device is used. This option requires the patient to be placed in MMF for a period of 5-6 weeks to allow bony union.

ORIF in definition is when direct fixation is used, the fracture site is opened, visualized, and reduced; and then stabilization is applied across the fracture site (Miloro, 2014). Internal

fixation implies the placement of wires, screws, plates, rods, pins and other hardware directly to the bone to stabilize the fracture. A large number of mandibular fractures are treated with ORIF because it is seen to be giving superior stabilization, better healing and earlier return to function (Schaller, 2013). When doing an ORIF of the mandibular fractures, either an intraoral or extraoral approach can be used, or a combination of both. Based on the location, age of the fracture and the pattern; a fixation (rigid or non-rigid) system is then decided.

The use of trans-osseous wiring is a form of non-rigid fixation. This wire provide stability only by preventing mobility of the gap but cannot neutralize torsion and/or shear forces (Petersons, 2012). Because of the limited stability obtained from the wire, MMF is applied for at least 5 weeks in adults. In a study by Dulabh and Rikhotso (2017), they compared three treatment options when managing angle fractures of the mandible and found less infection rate with the use of the upper border wire (8%) , as opposed to use of mini plates(16%). Although this treatment is less invasive with least associated infections, relatively easy and cost effective, it exposes patients to long periods of immobilization. For this reason, miniplates have largely replaced trans-osseous wiring during ORIF for craniofacial fractures.

The most common post-operative complications associated with ORIF of mandibular fractures are infections, non-union, mal-union and malocclusion, neurosensory disturbances, tooth loss or vitality loss, etc. (Nasser, 2013). Numerous risk factors are associated with the infections encountered in ORIF of the mandible. Factors such as non-compliance by the patient post-operatively, a significant delay in treatment, maintaining teeth in the fracture line and patient's immune status may contribute to infections following ORIF of mandibular fractures.

1.2 BACKGROUND LITERATURE

In an effort to reduce infection post-mandibular fractures, prophylactic antibiotics are often prescribed, especially for cases requiring open reduction and internal fixation. The term prophylaxis is defined as the use of antibiotics in an absence of clinical signs of infection at the time of treatment. The risk of infection is related to the type of wound: clean, clean-contaminated, contaminated, or dirty. The more contamination in the wound, the higher the risk of postsurgical infection (Escobar, 2006). Fractures of the mandible in the dentate segments are due to seepage of oral flora through the periodontal ligament or a mucosal tears, considered to be contaminated with an increased risk of infections (Dogra, 2015).

The knowledge of common oral pathogens and resistance status can guide the clinician towards appropriate selection of prophylactic and empirical antibiotics. The infections are primarily caused by normal oral bacterial flora, which consists of both anaerobic and aerobic gram-positive cocci and anaerobic gram-negative rods. When these bacteria gain access to deeper underlying tissues, as through a necrotic dental pulp or through a deep periodontal pocket or mucosal laceration, they may cause infections. Oral disease arises because of a change in the proportion of certain species with greater pathogenic potential within the indigenous flora. The change in the commensal microbiota is followed by the disruption of the host immune homeostasis and development of inflammatory response (Sultan, 2018). It is important to understand that micro-organisms in the oral cavity are generally not pathogenic and are part of the host's normal commensals. They are opportunistic pathogens that cause disease only when there is some breach in the host defense mechanism (such as a compound fracture of the jaws). The aetiology of odontogenic infections is usually attributed to the endogenous flora of the mouth, and not to the introduction of non-resident bacteria.

Instead of being mainly aerobic in nature, the typical odontogenic infections are considered to be polymicrobial, consisting of both anaerobes and aerobes, with anaerobes generally outnumbering aerobes four-fold at least. The concept of a mixed aerobic-anaerobic infection is an important one relative to cervico-facial sepsis of odontogenic origin. In general, the individual species isolated from exudates in experimental animals are non-infective in pure culture and independently are often incapable of producing infection when transferred to healthy animals. However, they contribute to the infectious milieu through bacterial synergism.

This implies that an odontogenic infection is due to the interdependent and synergistic metabolism of a variety of micro-organisms. Individual members of the group produce metabolites that are essential for the growth of the micro-organisms in the group. They produce substances that create favourable pH in the environment or they consume oxygen and facilitate anaerobic growth. This concept of mixed infection exhibiting bacterial synergism and interdependency has important implications for prevention and treatment of cervicofacial sepsis of odontogenic origin (Rikhotso and Ferretti, 2002).

Studies have been carried out to determine the need, timing, duration, route, and dosages of prophylactic antibiotics to reduce the risk of post-operative infection when managing mandibular fractures. No clear data has however been produced in establishing guidelines when using the antibiotics (Miles, 2006). The practices vary from using antibiotics pre-, intra- and post-operatively or in combination (Schaller, 2013). The choice of antibiotics can be affected by several factors such as patient's reported allergies and medical conditions, the surgical approach to procedure, drug availability, etc. (Spaey, 2015).

In the study carried out by Schaller et al., (2013), 59 patients who were treated with ORIF of the mandible were analyzed after being randomized into two groups. This was a prospective, randomized, double blind, placebo-controlled clinical trial; designed to evaluate the role of post-operative prophylactic antibiotics in the treatment of facial fractures. Patients in the two groups received antibiotics intravenously every 8 hours from admission until 24 hour post-operatively. Upon discharge, the patients in group 1 received Amoxicillin/clavulanic acid 625 mg orally 8 hourly for another 4 days and oral placebo was given to group 2 patients at the same interval. The patients were followed up from 1 week post-operatively up until six months. The conclusion drawn from the study was that there is no need for an extended antibiotic regimen when managing mandibular fractures with ORIF.

Kyzas et al., (2011) carried out randomized and non-randomized trials evaluating a possible impact of the prophylactic use of antibiotics in patients with mandibular fractures and concluded that the overall evidence to support the use of prophylactic antibiotics is of poor quality and larger randomized control trials are needed to guide clinical practice. In an assessment to analyze clinical practices in the literature, Kyzas et al., (2011) reported penicillin to be the most commonly used antibiotic. However, the exact number of days of antibiotic use is not reported and in most of the studies, the dosages are not specified (Panayiotis et al., 2011).

In a retrospective study by Lovato et al., (2009), 150 patients who were treated with both open reduction and internal fixation, and closed reduction over a period of 7 years were analyzed. The patients were analyzed in 2 groups: group 1 were managed with antibiotics only intra-operatively and group 2 were given both the intra-operative dose plus the post-operative dose which consisted of no more than 24 hours antibiotics in the post-operative period. Patients were followed up using a standardized form at 1, 2, 4 and 6 weeks. In group 1, 8 of 75 patients (10.67%) developed infections and in group 2, 10 of 75 patients (13.33%) developed infections. No statistically significant difference was observed between the two groups (p-value=0.8). It is unclear how patients were allocated between the two groups, a major disadvantage of retrospective and non-randomized studies. Furthermore, they did not elaborate on the type of antibiotics given. Despite these weaknesses, this study provided valuable information in an attempt to resolve the controversy related to use of antibiotics following treatment of MFs. A randomized, prospective study with a bigger sample size and longer follow-up would have enhanced the value of the outcome of this study

Abubaker et al., (2001) carried out a prospective randomized double-blinded study using a placebo control. A sample size of 30 patients, who were managed with either closed reduction or with ORIF of the mandibular fractures, was divided into two groups and analyzed. Both the control and the study group received a similar antibiotic regimen pre-, intra, and 12 hours postoperatively. Each group received penicillin G, 2 million units intravenously, every 4 hours through the preoperative period, intraoperative period, and for 12 hours postoperatively. Group 1 then received penicillin VK, 500 mg every 6 hours for 5 days. Group 2 received oral placebo using the same schedule for the same duration as group 1. No statistically significant differences (p=0.01) were noted between the groups. Their conclusion was that the use of postoperative antibiotics in uncomplicated fractures of the mandible had no benefit in reducing the incidence of post-operative infection. In this study, the sample size of 30 patients was small and a larger size could have improved the credibility of the study. This study also focused on patients managed with ORIF and those that were managed with closed reduction for mandibular fractures. There was also no explanation of what constituted an uncomplicated fracture.

In a study by Miles et al., (2006), patients with MFs received pre-operative antibiotics which were not standardized but maintained until the time of surgery. The patients received pre-operative dose of antibiotics either orally or intravenously. Antibiotic included penicillin G with or without metronidazole, a cephalosporin or clindamycin. Patients were then randomized

at the time of surgery into 2 groups whereby both groups received intra-operative antibiotics, which consisted of Cephazolin 2g, and Penicillin G Benzathine. The 1 group was discharged with 5-7 days course of penicillin and the other group did not receive any further antibiotics postoperatively. Although they reported in their study that there was no significant statistical difference in the 2 groups (p=0.399), the limitations to the study were that the pre-operative use of antibiotics was not controlled by the study protocol and the randomization process regarding intraoral and extraoral approaches was not clarified.

Dogra et al., (2014) carried out a double blind, randomized, placebo-controlled trial to analyze the infection rates in patients with uncomplicated mandibular fractures. Two groups of patients with 20 patients per group were analyzed, with both groups receiving an intravenous dose of Amoxicillin + clavulanic acid (30mg/kg/day). The dose was continued intraoperatively and 24 hours post-operatively. Patients with penicillin allergy were excluded in the study. Group 1 patients received placebo and group 2 received amoxicillin + clavulanic acid in two divided doses for the next four days. The infection rates in group 1 was 18.2% and group 2 was 15.7%. It was concluded in the study that the incidence of infection between the two groups was not statistically significant (p=0.58). They found that the distribution of infection according to anterior and posterior location of the fractures was significant, with all the infected fractures being located posteriorly and no infections noted with anterior fractures. The sample size in this study is small in our opinion.

With a rise in the need for antibiotic stewardship and the global concern of emergence of bacterial multidrug resistance and the cost of antibiotics, there is a need for evidence-based guidelines in using antibiotics when managing fractures of the mandible and other maxillofacial conditions. There is a further need to curb the excessive use of antibiotics, which is one of the major reasons for abuse of prophylactic antibiotics (Condon, 1991).

To date, in our unit, there is no existing protocol about the timing and duration of antibiotic administration when managing mandibular fractures with ORIF. The practices are currently at the discretion of the operating surgeon, which often leads to subjective and haphazard application of treatment a schedule.

Against this background, we have conceived this study to assess whether extended post-operative antibiotics offer better prevention of postoperative infections than perioperative antibiotics in patients with mandibular fractures.

1.3 AIM

This study aimed to determine the necessity and effectiveness of perioperative and post-operative antibiotic administration in patients with mandibular fractures treated by ORIF.

1.3.1 OBJECTIVES

1.3.1.1 to analyze incidence of infection in mandibular fractures managed with ORIF

1.3.1.2 to compare the rate of infection in patients who receive 1-day intravenous (IV) antibiotics and those that receive the 1day IV antibiotic cover plus an additional 5 day oral antibiotics post-operatively.

1.3.2 SIGNIFICANCE OF THE STUDY

This study will add valuable data to the ongoing debate on the need and duration for antibiotics in the management of MFs. It is hoped that viable recommendations from this study will enable the Department of Maxillofacial and Oral Surgery at the University of Witwatersrand to develop evidence based standard protocols for the use of antibiotics in patients with MFs.

1.3.3 HYPOTHESIS

The research hypothesis was that there is no difference in outcomes between use of antibiotics intra-operatively only, and intra-operative dose of antibiotics combined with post-operative antibiotic administration.

1.4 MATERIALS AND METHODS

The prospective, randomized controlled trial was undertaken at Wits Oral Health Centre Patients with mandibular fractures were treated with open reduction and internal fixation using miniplates were analyzed in this study.

The patients were categorized into two groups. The first group, the control group, was composed of patients who received a 1-day IV antibiotic cover intra-operatively and further 24 hours doses post-operatively (3 doses), before being discharged. The second group, the study group, was composed of patients who received similar doses as the control group but with an additional 5 days of oral antibiotics upon discharge. All patients had intermaxillary fixation for two weeks post ORIF of the mandible. The antibiotics for the purpose of the study given were follows:

- Augmentin 1.2g IV intra-operatively and 3 doses post operatively
- Amoxil 500 mg capsules orally 8 hourly for 5 days after being discharged from hospital

Patients allergic to penicillin received Clindamycin 600g IV intra-operatively and the 3 doses post-operatively, and Clindamycin 300mg orally 6 hourly for 5 days.

The patients were randomly selected once they had agreed to participate in the study. Lots drawn from closed envelopes were used to randomize the patients. Each patient that participated in the study was requested to sign a consent form that was discussed with the patient at the time of admission. Whenever necessary, the consent form was explained to the patients in their preferred language. An information sheet was issued to the patient, which explained the basis of the study. The sheet also included the researcher's and the ethics committee's contact details.

Surgical procedure

All patients were managed under general anesthesia with nasotracheal intubation. Sterile protocols were observed. A prophylactic dose of Augmentin® 1.2g stat was administered intravenously, and patients allergic to penicillin were given Clindamycin® 600mg stat. Local anesthetic was administered, followed by placement of eyelet wires or an Erich arch bar.

A full thickness mucoperiosteal flap was raised to expose the fracture site/s. Fractures were mobilized and debrided under direct vision. Once the patient was placed in intermaxillary fixation, 2 mm mini plates were used at the fracture site to reduce and stabilize the fracture/s.

The mini plates were secured with monocortical titanium screws, with at least two screws on either side of the fracture.

MMF was released, closure of the incision with a resorbable suture was done. Patients were placed into MMF after the throat pack was removed, prior to extubation.

Patients were discharged within 24 hours after the operation and were reviewed in 1, 4, and 6 weeks intervals from date of discharge, or as needed. All patients who participated in the study were placed into intermaxillary fixation for 2 weeks as a way of standardizing the treatment. On evaluation, a surgeon who was blinded to the antibiotic schedule administered to the patient reviewed them. Postoperative data collected included oral hygiene status and evaluation for the presence of infection.

<u>The following criteria for infection was used:</u>

- Pus drainage at surgical site
- Increasing facial swelling a week beyond date of operation
- Fistula formation at surgical site

<u>Inclusion criteria</u>

- Isolated mandibular fractures
- Patients 18 years and older
- Treatment with ORIF via intra-oral approach

<u>Exclusion criteria</u>

- Patients who present with an infection at the time of treatment
- Patients who were not managed with open reduction and internal fixation of the mandibular fractures.
- Patients below the age of 18
- Patients who presented with complications more than six weeks post-surgery
- Non-compliant patients who did not present for follow up over the six-week period
- Patients already on antibiotic therapy at the time of presentation
- Gunshot wounds
- Patients with associated facial fractures such as zygomatic and maxillary fractures
- Fractures older than 14 days

- Fractures managed with extra-oral approaches
- Pathological fractures
- Medically compromised patients such as AIDS patients, uncontrolled diabetes, malnourished patients, etc.

1.4.1 ETHICS

An ethical clearance was obtained from the university's Human Research Ethics Committee; clearance number M181035. Permission to utilize the clinical records was obtained from the Wits Oral Health Centre's Chief Executive Officer and Head of School prior to commencing with the study. Patient confidentiality was maintained throughout the period of the study. All patients who participated in the study were issued an information sheet that contained the contact details of the Human research ethics office to answer any question related to the study.

1.4.2 DATA ANALYSIS

Descriptive statistics of median and interquartile range was used to summarize the continuous variables (age, date of injury – presentation and date of injury-operation) and percentage and frequency was used to report the categorical variables (gender, site of fracture, comorbidity, HIV status, presence of pus and groups). The significant difference between the continuous variables was measured by using the Mann Whitney U test for non-parametric test and the measure of association between the categorical variables was measured by using the two-tailed Fischer's exact test. The measure of change over the timeline was measured using the McNemar's test. For all the inferential statistics, level of significance was set at p-value less than 0.05.

Test for normality

Shapiro-Wilk test was used to determine the normal distribution of the continuous variables (age, date of injury – presentation and date of injury-operation). The results show that the variables are not normally distributed (p-value <0.05) (Table 1), therefore non-parametric descriptive statistics of median and interquartile range was used to present the data.

Table 1.1: Test for normality

	Shapiro-Wilk		
	Statistic	**df**	**Sig.**
Injury-Presentation	0.939	75	0.001
Injury-Operation	0.662	75	0.000
Surgery time	0.927	75	0.000
Age	0.950	75	0.005

CHAPTER 2

2.0 RESULTS

2.1 Participants' biographical and clinical characteristics

A total of 77 patients with mandibular fractures were included in the study; the median age of the patients was 32(26-38) years and the majority (92.2%) of the participants were males. Table 2.1 shows the clinical and biographical data of the study patients. The aetiology of the fracture was alleged assault in 57 patients (74%), motor vehicle accidents in 11 (14.3%) and pedestrian vehicle accident in 5 (6.5%). The most common site of fracture was the angle (35.1%), followed by angle and body (26%) and parasymphysis and angle (10.4%) fractures. Comorbidities were present in 17 (22.1%) participants (Figure 2.2), and 12 (71%) of these patients were living with HIV (Table 2.1, Figure 2.1,)

Table 2.1: Clinical and biographical data of the patients (N=77)

Variables	Patient numbers (N=77)
Gender	
Male	71(92.2%)
Female	6(7.8%)
Age in years	32(26-38)
Injury-Presentation (days)	4(2-6)
Injury-Operation (days)	9(6-12)
Comorbidities	
Yes	17(22.1%)
No	60(77.9%)
HIV status	
Yes	12(15.6%)
No	65(84.4%)
Site of fracture	
Angle	27 (35.1%)

Body	4 (5.2%)
Angle and body	20 (26%)
Parasymphysis and angle	6 (7.8%)
Body and symphysis and angle	1 (1.3%)
Parasymphysis	2 (2.6%)
Symphysis	3 (3.9%)
Symphysis/angle	5 (6.5%)
Symphysis/condyle	7 (9.1%)
Parasymphysis and condyle	2(2.6)
Cause of fracture	
Assault	57(74%)
Epileptic fall	2(2.6%)
Fall from height	2(2.6%)
Motor vehicle accident (MVA)	11(14.3%)
Pedestrian vehicle accident (PVA)	5(6.5%)

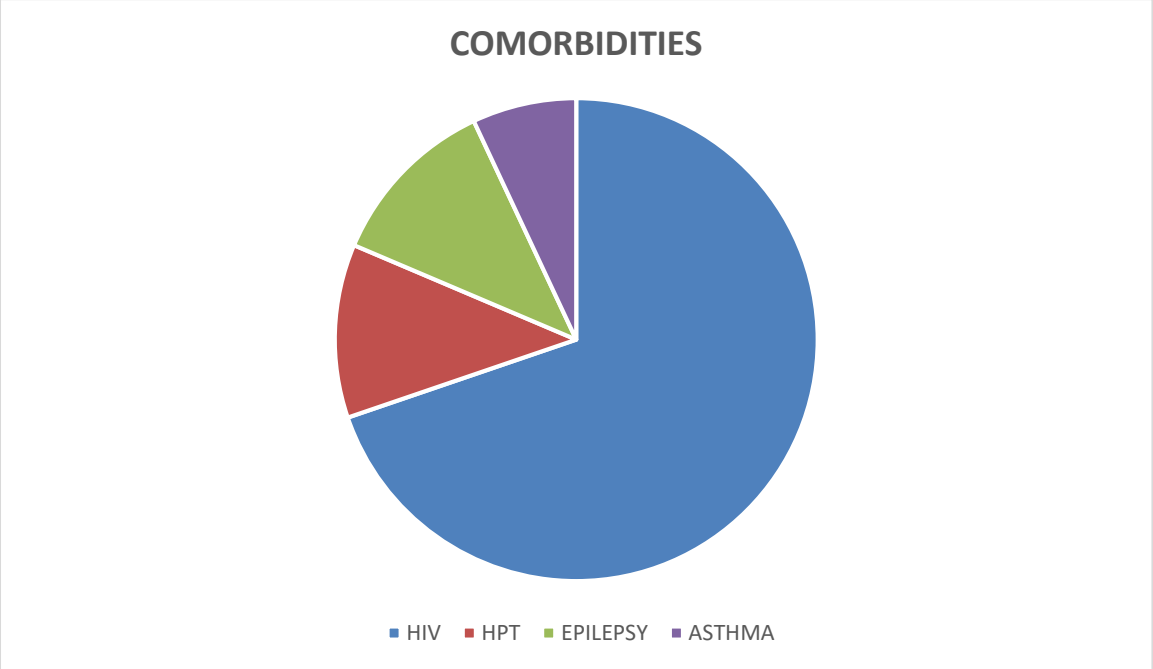


FIGURE 2.1: An indication of the number of patients who presented with comorbidities. HIV (12), HPT (Hypertension) (2), Epilepsy (2), Asthma (1).

2.2 Comparison of the two groups at baseline

Of the 77 patients, 41(53.2%) were randomized into the non-antibiotic group and 36 (46.8%) into the antibiotic group. Figure 2.2 shows the percentage distribution between the two groups, antibiotic (ANB) and non-antibiotic (Non-ANB) groups.

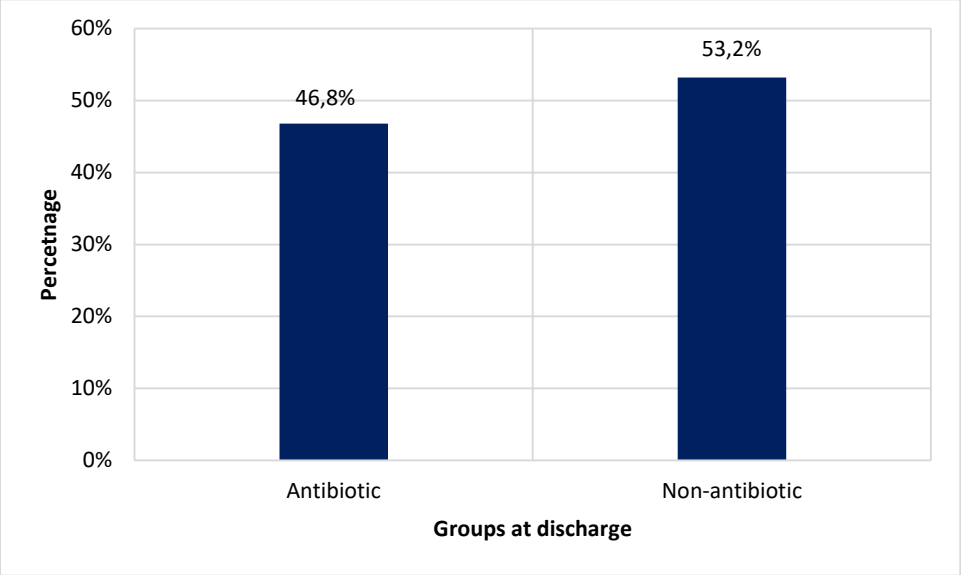


Figure 2.2: Antibiotic vs Non-antibiotic group (N=77)

Table 2.2 below shows the difference between the antibiotic and non-antibiotic groups at baseline. As shown in the Table, there was no significant difference or association between the groups at baseline in all the variables except for the days between injury and presentation and the surgery time. Patients in the antibiotic group had a significantly higher number of days before presentation compared to the patients in the non-antibiotic group (p=0.04). The mean surgical time was 70 min (range 55-90 min) and 82 min (range 65-124 min) in the antibiotic and non-antibiotic groups respectively (p=0.04).

Table 2.2: Presentation of descriptive data between the groups at baseline

Variables	**Antibiotics (n=36)**	**Non-antibiotic (n=41)**	**p-value**
Gender			
Male	32(88.9%)	39(95.1%)	0.41
Female	4(11.1%)	2(4.9%)	
Age (years)	32(26-38)	29.5(26-38.75)	0.74

Date of Injury to Presentation (days)	5(3-7)	3(2-5)	0.04*
Date of Injury to Operation	10(8-13)	9(6-11)	0.09
Surgery time (minutes)	70(55-90)	82(65-124)	0.04*
Comorbidities			
Yes	9(25%)	8(19.5%)	0.59
No	27(75%)	33(80.5%)	
HIV status			
Yes	6(16.7%)	6(14.6%)	1.00
No	30(83.3%)	35(85.4%)	
Site of fracture			
Angle	14(38.9%)	13(31.7%)	0.83
Body	2(5.6%)	2(4.9%)	
Angle and body	8(22.2%)	12(29.3%)	
Parasymphysis and angle	3(8.3%)	5(12.2%)	
Body and symphysis and angle	0	1(2.4%)	
Parasymphysis	1(2.8%)	1(2.4%)	
Symphysis	1(2.8%)	2(4.9%)	
Symphysis and angle	4(11.1%)	1(2.4%)	
Symphysis and condyle	3(8.3%)	4(9.8%)	
Cause of fracture			
Assault	24(66.7%)	33(80.5%)	0.58
Epileptic fall	2(5.6%)	-	
Fall from height	1(2.8%)	1(2.4%)	
MVA	6(16.7%)	5(12.2%)	
PVA	3(8.3%)	2(4.9%)	

Post-operatively, eight patients (10.39%) presented with infections at the surgical sites at the one-week review. This was increased to 14 patients (18.18%) at four weeks and then reduced to 5 patients (6.5 %) at six weeks postoperatively (Figure 2.3)

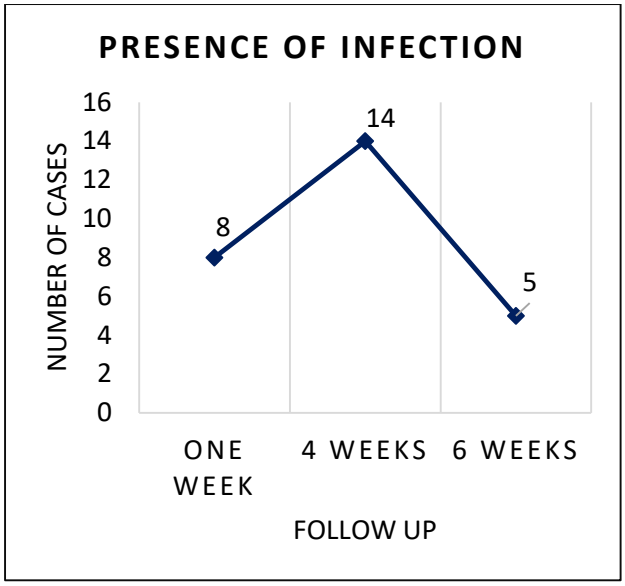


Figure 2.3: Presence of infection at surgical sites from week one to week six

2.3 Comparison of presence of infection between the antibiotic and non-antibiotic group

As illustrated in Figure 2.4, there was an equal number of patients with infection at week one in both groups. In the Non-antibiotic group, the number of patients with infection increased to 10 (24.39%) by week four, whilst the number of patients with infection in the antibiotic group remained at four. At six weeks, the number of patients with infection in the Non-antibiotic group and the antibiotic group had reduced to four (9.76%) and one (2.78%) respectively.

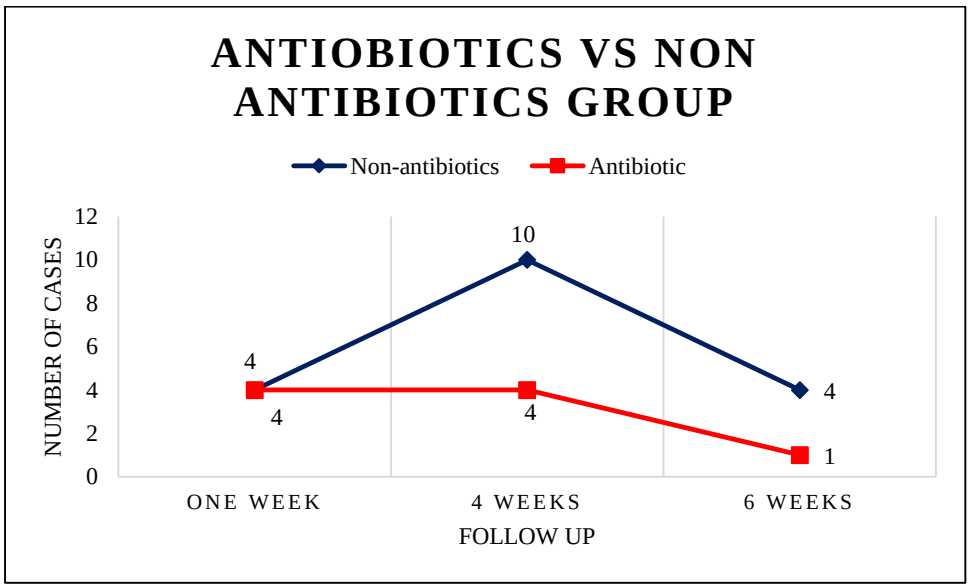


Figure 2.4. Association between the presence of infection between the groups

As shown in Table 2.3, using Fischer's exact test, there was no significant association between the presence of infection and the group ($p>0.05$). Although in the Non-antibiotic group there was an initial increase of the number of patients with infection in the 4th week, at six weeks the number of patients with infection was the same as in the first week.

Table 2.3: Association between presence of infection and the groups

	Antibiotic	**Non-antibiotic**	**p-value**
Week one			
Clear	32(88.9%)	37(90.2%)	1.00
Infection	4(11.1%)	4(9.8%)	
Week four			
Clear	32(88.9%)	31(75.6%)	0.15
Infection	4(11.1%)	10(24.4%)	
Week six			
Clear	35(97.2%)	37(90.2%)	0.36
Infection	1(2.8%)	4(9.8%)	

2.3.1 Measure of change across the weeks

McNemar's test was used to determine the significant change at various timelines. The results showed that there was no significant change in the number of patients that moved from presence of infection to absence in the total population at week four (p=0.109) and week six (p=0.581) as shown in Table 2. 4. Although there was as significant difference in the number of patients that moved from presence of infection to absence from the 4th week to the 6th week (p-value=0.049).

Table 2.4: McNemar's Test for significant difference over the weeks

	Week 1	**Week 4**	**p-value**	**Week 4**	**Week 6**	**p-value**	**Week 1**	**Week 6**	**p-value**
Clear	69	63	0.109	63	72	0.049	69	72	0.581
Infection	8	14		14	5		8	5	

The significant change was also measured in the various groups. In the Non-Antibiotic group, there was also no significant change in the number of patients that moved from presence of infection to absence in the total population at week four (p=0.07) and week six (p=1.00) as shown in Table 2.5.

Table 2.5: McNemar's Test for significant difference over the weeks for the non-antibiotic group

Non antibiotic	**Week 1**	**Week 4**	**p-value**	**Week 4**	**Week 6**	**p-value**	**Week 1**	**Week 6**	**p-value**
Clear	37	31	0.07	31	37	0.146	37	37	1
Infection	4	10		10	4		4	4	

In the antibiotic group, there was also no significant change in the number of patients that moved from presence of infection to absence in the total population at week four (p=1.00) and week six (p=0.375) as shown in Table 2.6.

Table 2.6: McNemar's Test for significant difference over the weeks for the antibiotics

Antibiotic									
	Week 1	Week 4	p-value	Week 4	Week 6	p-value	Week 1	Week 6	p-value
Clear	32	32	1	32	35	0.375	32	35	0.375
Infection	4	4		4	1		4	1	

2.3.2 Association between presence of infection and gender

Table 2.7: Association between presence of infection and gender

		Non antibiotic			**Antibiotic**		
Presence of infection	**Gender**	**Week 1**	**Week 4**	**Week 6**	**Week 1**	**Week 4**	**Week 6**
Clear	Male	35(94.6)	30(96.8)	35(94.6)	29(90.6)	29(90.6)	31(88.6)
	Female	2(5.4)	1(3.2)	2(5.4)	3(9.4)	3(9.4)	4(11.4)
Infection	Male	4(100)	0	0	3(75)	3(75)	1(100)
	Female	0	0	0	1(25)	1(25)	0
p-value		**1**	**0.43**	**1**	**0.39**	**0.39**	**1**

Table 2.7 shows the association between gender and the presence of infection. There was no significant association between gender and the presence or absence of infection in both groups ($p>0.05$).

2.3.3 Association between presence of infection and age

Table 2.8: Association between presence of infection and age

	Non-antibiotic group			**Antibiotic group**		
Age (years)	**Week 1**	**Week 4**	**Week 6**	**Week 1**	**Week 4**	**Week 6**
Clear	32.84(9.7)	33.1(10.00)	32.49(9.26)	32.75(7.87)	33.16(7.80)	32.54(7.0)
Infection	30(5.29)	30.9(7.33)	33.25(11.98)	31.25(6.19)	28(4.69)	34
p-value	0.57	0.53	0.88	0.72	0.11	0.85

Table 2.8 shows the association between the presence of infection and age. There was no significant difference in the age of the participants that had infection in both groups ($p>0.05$).

2.3.4 Association between delay in treatment and presence of infection

Table 2.9: Association between presence of infection and delay in treatment

	Non-antibiotic group			Antibiotic group		
Injury-Operation (Days)	**Week 1**	**Week 4**	**Week 6**	**Week 1**	**Week 4**	**Week 6**
Clear	6.03(6.18)	6.06(6.60)	5.73(6.16)	5.06(3.45)	5.09(3.42)	4.91(3.45)
Infection	4.5(3.00)	5.3(3.27)	7.25(3.40)	3.75(3.10)	3.5(3.32)	5
p-value	0.63	0.73	0.63	0.48	0.39	0.98

The mean delay in treatment was 10 days (range 8-13) and 9 days (range 6-11 days) for the antibiotic and the non-antibiotic groups respectively. Table 2.9 shows the association between the presence of infection and delay in treatment. There was no significant difference between delay in treatment and presence of infection ($p>0.05$) during the 6-weeks review period.

2.3.5 Association between presence of infection and site of fracture

Table 2.10: Association between presence of infection and site of fracture

		Non antibiotic			Antibiotic		
Site of fracture		Week 1	Week 4	Week 6	Week 1	Week 4	Week 6
Clear	Angle	13(35.1)	10(32.3)	13(35.1)	13(40.6)	13(40.6)	14(40)
	Body	2(5.4)	1(3.2)	2(5.4)	2(6.3)	2(6.3)	1(2.9)
	Angle and body	10(27)	10(32.3)	10(27)	7(21.9)	7(21.9)	8(22.9)
	Parasymphysis and angle	4(10.8)	4(12.9)	3(8.1)	1(3.1)	2(6.3)	2(5.6)
	Body, symphysis and angle	1(2.7)	1(3.2)	0	0	0	0
	Parasymphysis	0	0	1(2.7)	1(3.1)	1(3.1)	1(2.9)
	Symphysis	1(2.7)	1(3.2)	1(2.7)	1(3.1)	1(3.1)	1(2.9)
	Symphysis and angle	1(2.7)		1(2.7)	4(12.5)	3(9.4)	4(11.4)
	Symphysis and condyle	4(10.8)	4(12.9)	4(10.8)	2(6.3)	2(6.3)	3(8.6)
	Parasymphysis and condyle	1(2.7)	0	1(2.7)	1(3.1)	1(3.1)	1(2.9)
Infection	Angle	0	3(30)	0	1(25)	1(25)	0
	Body	0	1(10)	0	0	0	1(100)
	Angle and body	2(50)	2(20)	2(50)	1(25)	1(25)	0
	Parasymphysis and angle	0	1(10)	1(25)	1(25)	0	0
	Body and symphysis and angle	0	0	1(25)	0	0	0
	Parasymphysis	1(25)	1(10)	0	0	0	0
	Symphysis	1(25)	1(10)	0	0	0	0

	Symphysis and angle	0	1(10)	0	0	1(25)	0
	Symphysis and condyle	0	0	0	1(25)	1(25)	0
	Parasymphysis and condyle	0	0	0		0	0
	p-value	**0.1**	**0.26**	**0.22**	**0.55**	**0.71**	**0.11**

An assessment was done to investigate the association between presence of infection and site of the fracture. As shown in Table 2.10, there was no significant association between the site of fracture and the presence of infection (p>0.05).

Table 2.11: Association between presence of infection and HIV status

		Non antibiotic			**Antibiotic**		
	HIV status	**Week 1**	**Week 4**	**Week 6**	**Week 1**	**Week 4**	**Week 6**
Clear	Negative	31(83.8)	26(83.9)	33(89.2)	28(87.5)	27(84.4)	29(82.9)
	Positive	6(16.2)	5(16.1)	4(10.8)	4(12.5)	5(15.6)	6(17.1)
Infection	Negative	4(100)	9(90)	2(50)	2(50)	3(75)	1(100)
	Positive	0	1(10)	2(50)	2(50)	1(25)	0
p-value		1	1	0.1	0.12	0.54	1

2.3.6 Association between presence of infection and other comorbidities

Table 2.12: Association between the presence of infection and comorbidities

		Non antibiotic			**Antibiotic**		
	Comorbidity	**Week 1**	**Week 4**	**Week 6**	**Week 1**	**Week 4**	**Week 6**
Clear	No	29(78.4)	24(77.4)	32(86.5)	25(78.1)	24(75)	26(74.3)
	Yes	8(21.6)	7(22.6)	5(13.5)	7(21.9)	8(25)	9(25.7)
Infection	No	4(100)	9(90)	1(25)	2(50)	3(75)	1(100)
	Yes	0	1(10)	3(75)	2(50)	1(25)	0
p-value		**0.57**	**0.65**	**0.02***	**0.26**	**1**	**1**

Of the 17 patients with comorbidities, 7 (41.1%) had postoperative infections. There was a significant association between the presence of comorbidity and the presence of infection at the surgical site in the non-antibiotic group at week 6 (p-value=0.02). Further analysis using binary logistic regression showed that the odds of presenting with infection is 19.2 times higher in patients with comorbidities than in patients without comorbidities. This was however not

significant [(p-value=0.02), (95% CI=1.65-222.85)], the lower bound of the confidence interval crosses 1.

Six of the 7 patients who developed infections were HIV positive patients. Further analysis however revealed that there was no significant association between HIV status and the presence infection in both groups (p>0.05) (Table 2.11)

2.3.7 Association between presence of infection and cause of fracture

Table 2.13: Association between presence of infection and cause of fracture

		Non-antibiotic group			**Antibiotic group**		
		Week 1	**Week 4**	**Week 6**	**Week 1**	**Week 4**	**Week 6**
Clear	Assault	31(83.8)	24(77.4)	30(81.1)	22(68.8)	22(68.8)	23(65.7)
	Epileptic fall	0	0	0	1(3.1)	1(3.1)	2(5.7)
	Fall from height	0	0	1(2.7)	1(3.1)	1(3.1)	1(2.9)
	MVA	4(10.8)	5(16.1)	5(13.5)	5(15.6)	5(15.6)	6(17.1)
	PVA	2(5.4)	2(6.5)	1(2.7)	3(9.4)	3(9.4)	3(8.6)
Infection	Assault	2(50)	9(90)	3(75)	2(50)	2(50)	1(100)
	Epileptic fall	0	0	0	1(25)	1(25)	0
	Fall from height	1(25)	1(10)	0	0	0	0
	MVA	1(25)	0	0	1(25)	1(25)	0
	PVA	0	0	1(25)	0	0	0
	p-value	0.06	0.18	0.33	0.29	0.29	1

Relationship between the presence of infection and etiology of the fracture was assessed. There was no significant association between cause of fracture and the presence of infection in both groups (p>0.05) (Table 2.13)

2.3.8 Association between presence of infection and surgery time

Table 2.14: Association between presence of infection and surgery time

	Non-antibiotic group			**Antibiotic group**		
Surgery time	**Week 1**	**Week 4**	**Week 6**	**Week 1**	**Week 4**	**Week 6**
Clear	82(65-124)	85(65-125)	82(65-124)	72.5(55-93.75)	70(55-93.75)	70(55-90)
Infection	98(75-124)	80(72.5-122)	82(65-123)	72.5(55-92.5)	67.5(55-92.5)	-
p-value	0.77	0.94	0.90	0.43	0.69	1.00

The mean surgery time for the 14 patients who developed post-operative infections in the non-antibiotic group was 97 minutes. For the antibiotic group, the mean surgery time for the five patients who developed infections was 64 minutes. The results of the association between presence of infection and length of the surgical procedure are shown in Table 2.14. These indicate that there was no significant difference between surgery times and the presence of infection in both groups ($p>0.05$).

CHAPTER 3

3.1 DISCUSSION

Even though the mandible is the largest and strongest facial bone, it is the most fractured bone in maxillofacial trauma due to its position on the face and its prominence (Upton, 1991). Various causative factors result in mandibular fractures, and although there are global variations, interpersonal violence features prominently (Gaal, 2016; Wan, 2012), followed by RTAs and falls. Ellis et al., *(*1985) and Silvennoinen et al., (1992) reported in their studies that violence and assaults are the most common causes of mandibular fractures. This is similar to our findings in that 74% of the fractures were caused by violence and assaults, followed by motor vehicle accidents and PVA (14.3% and 6.5% respectively). The percentage (74%) of mandibular fractures caused by blunt trauma due to interpersonal violence in the present study is, however, much higher than that reported by Ellis *et al.*, (1985) *at* 54.7% and Silvennoinen *et al.*, (1992) at 44%. This draws attention to the unfortunately high prevalence of blunt trauma due to interpersonal violence in this country. Previous studies in our unit have repeatedly demonstrated a very high prevalence of assault in patients with craniofacial fractures (Desai et al., 2010; Mogajane et al., 2018; Rikhotso and Ferretti, 2008).

Gender and age distribution of patients with mandibular fractures in the present study were similar to those reported in previous studies (Gaal et al., 2016; Miles et al., 2006; Abubaker and Rollert, 2001). Of the 77 patients in the present study, 71 (92.2%) were males and six (7.8%) were females, with a median age of 32 (range 26-38 years).

Although infection rates associated with ORIF mandible have significantly decreased with the use of antibiotics, it is still a major complication and a common cause of non-union and malunion of repaired mandibular fractures (Lovato, 2009). The use of prophylactic antibiotics in the management of mandibular fractures is a common practice; however, there are no clear guidelines (Schaller, 2013). The practices range from pre-operative, intra-operative to post-operative or a combination. This lack of clear guidelines on the duration of prophylactic use of antibiotics often leads to haphazard, injudicious, and indiscriminate application of treatment schedules, which in turn predispose to the emergence and widespread prevalence of antibiotic resistance.

The present study was informed by the need to evaluate the benefit of extended postoperative antibiotic regimen following ORIF of the mandible when compared to perioperative antibiotic

regimen. The latter, the control group, composed of patients who received 4 doses of IV antibiotics (a single intraoperative dose of IV antibiotic cover and further 3 doses of IV antibiotics 24 hours post-operatively), before being discharged. The second group, the study group, composed of patients who received similar doses as the control group but with additional 5 days of oral antibiotics upon discharge. We hypothesized that there is no significant difference between patients receiving short-term antibiotics and those that received an extended antibiotic regimen.

In this study it was found that the number of patients who presented with post-operative infections at the one week, 4 weeks and 6 weeks review was 8 (10.39%), 14 (18.18%) and 5 (6.5%) respectively. At six weeks, the number of patients with infection in the Non-antibiotic group and the antibiotic group had reduced to four (9.76%) and one (2.78%) respectively. There was no significant difference ($p=0.36$) between the presence of infection and the group (Antibiotic versus the Non-antibiotic groups), thus confirming our hypothesis of no clinically significant difference in terms of surgical site infections between short and extended usage of antibiotics. This finding corroborates previously reported studies that the overall evidence supporting prolonged use of prophylactic antibiotics for mandibular fractures is poor and that their extended use is probably not warranted (Miles etc.).

A prospective randomized trial by Miles et al., (2006) reported an overall 12.1% infection rate in their study designed to evaluate the efficacy of post-operative regimen in the open treatment of mandibular fractures. The distribution of the infection was 9.8% in the antibiotic group and 1.8% in the non-antibiotic group. Similar to our result, no statistically significant difference ($p=0.399$) between the antibiotic and non-antibiotic group was reported during the 5-8 weeks follow-up. The limitation to the study was that patients received unknown pre-operative antibiotics (not mandated by the study protocol) until the day of surgery. This however is a common problem in that most patients with mandibular fractures are placed on antibiotics for prophylactic reasons at the initial consultation. These antibiotics are prescribed by the referring doctors whose comprehension of odontogenic infections and the prophylaxis thereof is often limited. Gaal et al., (2016) have shown that there is no increase in surgical site infections secondary to lack of preoperative antibiotics from consultation to surgery. Unless there is an infection noted, pre-operative antibiotic prophylaxis is not deemed necessary (Escobar, 2004).

In addition, in a study by Miles et al., (2006), some patients received intraoperative antibiotics (penicillins/cephalosporins or clindamycin if allergic to penicillin) with metronidazole. It is

unclear why there was a need to add metronidazole for some patients. The widespread and often unindicated use of metronidazole may be the single biggest contributor to the rising level of resistance to metronidazole, and must be curbed (Yuvaraj., 2012; Poeschl et al., 2010). We agree with the use of penicillin (s) as it remains the first line drug therapy for prophylaxis and therapy of odontogenic infections. Despite these weaknesses, this study provided valuable insight to the controversy related to the benefit or lack thereof extended use of antibiotics following treatment of mandibular fractures.

Studies by Abubaker and Rollert (2001), Lovato et al., (2009); Schaller et al., (2013), Kyzas et al., (2011) and Dogra et al., (2014) have also concluded that the use of extended postoperative oral antibiotics in mandibular fractures has no benefit in reducing postoperative surgical site infections.

A similar study design by Dogra et al., (2014) which analyzed 39 patients with mandibular fractures undergoing ORIF, concluded that there was no significant difference between the antibiotic and non-antibiotic groups ($p=0.58$). The study however was more focused on the surgical site infection and assessing microbial load, which was analyzed over 3 days and 7 days reviews. There was no record of further follow up on the patients.

The findings in the present study corroborates previous reports that patients with comorbid conditions, especially those with immunocompromised medical conditions such as diabetes and HIV/AIDS, are at a higher risk of developing postoperative infections (Christensen et al., 2017; Schmidt et al., 1995; Miles et al.,2006). Of the 77 patients who participated in our study, 17 (22.1%) had comorbidities and 12 of these 17 were HIV patients on HAART. In each group, 3 patients presented with infective complications over the 6-week period. Interestingly, there was no statistically significant difference regarding postoperative infection between the ANB and Non-ANB groups in HIV patients. It appears like as long as these patients are compliant in taking their mediation (ARVs), have optimum CD 4 count and undetectable viral load, extended antibiotic use does not offer them any additional benefit. Although the number of patients who presented with infections post-operatively were significant (6 out of 12 HIV positive patients), the overall number of the patients in this study is too small to draw conclusions as to which HIV patients can be safely treated without extended use of postoperative antibiotics. For this reason, based on the present study, we are unable to recommend withholding extended use of antibiotics for 5 days postoperatively in HIV patients,

as their underlying immunosuppression renders them vulnerable to developing surgical site infections.

Miles et al., (2006) also reported a statistically significant (p=0.021) increase in the risk of postoperative infections in patients who abused tobacco and alcohol simultaneously, citing local and systemic effects of alcohol and tobacco on soft tissue/bone healing, poor nutrition and poor compliance with postoperative instructions. Our study did not investigate the relationship between combined use of alcohol/smoking and the infection rate.

Early treatment of mandibular fractures is reported to be associated with a decreased risk of post-operative infections (Abdelfadil, 2013). Both Champy et al., (1978) and Cawood., (1985) recommended that ORIF must be performed within 12-24 hours after the injury to minimize the risk of postoperative infection. Many of our patients however did not present for treatment until days after the injury. Given the trauma overload in our unit, excessive waiting lists, staff shortages and lack of readily available theatres; even if the patients had presented early, it would not have been possible to perform immediate surgery. In the non-antibiotic and the antibiotic groups, the mean delay from injury to treatment was 9 days and 10 days respectively (p= 0.54). We could however not detect any difference in postoperative infective complication rate for those fractures that were treated early or late. Similar to the findings by Gaal et al., (2004), and Dillon et al., (2012), delay in treatment was not significantly associated with increased risk of infection between the ANB and Non-ANB groups. This finding seems to suggest that the time to definitive surgical treatment does not influence the rate of infections at the surgical site, provided perioperative antibiotics are administered at the eventual surgery period. The rich blood supply in the head and neck region and the tolerance of the oral cavity to the oral microorganisms in which it is bathed are offered as possible reasons for this (Gaal et al., 2004). Another possible explanation for this observation in our study is that fractures older than two weeks were excluded from the study. Fractures older than two weeks often require increased anaesthetic and surgical time, which together with eburnation and increased mobility of the fragments may render them susceptible to infection, especially when no intermaxillary fixation is applied postoperatively.

In patients who presented with post-operative infections, the mean surgical time was 64 minutes and 97 minutes in the antibiotic (5 patients) and non-antibiotic groups (14 patients) respectively. The results showed no significant association between the surgical times and the infection rate. This is comparable to the study by Miles et al., (2006) who reported 119.5

minutes in the antibiotic group and 166.6 minutes in the non-antibiotic group, with no significant statistical difference between the antibiotic and non-antibiotic groups. Contrary to our finding, Shigeishi et al., (2015) reported an association between increased surgical time and risk of post-operative infections in patients who underwent head and neck surgeries. They however stated that this is dependent on the severity of the procedure and the surgeon's skills.

Studies have demonstrated that mandibular angle fractures, left angle in particular, result in greater complication rate than fractures in other locations in the mandible (Christensen et al., 2017; Gordon et al., 2011; Shetty et al., 2017). Possible explanations for this include a more severe mechanism of injury from right hand-dominant assailant ('right hook concept") and predominantly right-handed surgical registrars who may struggle to work on the left side of the patient early in their career. Dogra et al., (2014) also found that posterior location of the fracture in the mandible was a risk factor for development of infection. Contrary to these studies, our study was unable to show any relationship between site of fracture and presence of infection. Although there were more angle fractures in both groups, the rate of infection in the angle fractures was not significantly different from non-angle fractures. Also, we did not find that multiple or bilateral mandibular fractures result in an increase in infection rate.

Furthermore, the present study was unable to show any significant association between cause of fracture and the presence of infection in both groups ($p>0.05$).

The choice of the antibiotic in our study was based on the bacteria most likely to cause the infection, with penicillin being the first line of therapy (Escobar, 2004). Perioperative antibiotic regimen (which includes antibiotic given before surgical incision is made) is an accepted method of preventing postoperative infections in patients with compound mandibular fractures. This is informed by the classification of wounds based on the risk of infections (Paradisi, 1992; Peterson, 1990; Topazian 2002). In this regard, mandibular fractures involving the tooth-bearing region are classified as Class III contaminated wounds. Presence of infection or delay in their treatment renders them as Class IV wounds. Class III and Class IV wounds have a risk of infections ranging from 22-50%. Prophylactic antibiotics reduces this risk to as low as 10% (Abubaker and Rholert, 2001; Peterson, 1990; Paradisi, Chole and Yee, 1987). The principle of prophylactic use of antibiotics was elucidated by Burke, and includes amongst others, the use of antibiotics for a brief period, primarily intraoperatively (Uluap and Condon, 1992; Condon and Wittmann, 1991). Despite these well-established principles, there has been a proliferation of antibiotic resistance, predominantly arising from reckless and inordinate usage

of prophylactic antibiotics. This has continued despite the warning by *Fleming in 1945, **"The thoughtless person playing with penicillin treatment is morally responsible for the death of the man who finally succumbs to infection with the penicillin resistance organism. Hope the evil can be averted"***

Responsible use of antibiotics and establishment of best practices amongst clinicians will not only avert this catastrophe, but will also ease the financial burden countries spend annually managing adverse antibiotic effects, which include antibiotic associated colitis (e.g. *Clostridium difficile colitis*), antibiotic-related allergic reactions and drug-to-drug interactions (Centres for Disease Control and Prevention, 2013; World Health Organization, 2014; Li X, 2016)

3.2 CONCLUSION AND RECOMMENDATIONS

Whilst postoperative infection following treatment of mandibular fractures has been significantly reduced by the advent of antibiotics, it remains one of the major complications of mandibular fractures. Majority of the infections associated with mandibular fractures do not result in significant morbidities but they have the potential to develop into more significant sequelae, leading to extended hospitalisation with an increased financial burden. Despite evidence showing the value of prophylactic use of antibiotics in reducing the risks of postoperative infections, there is paucity of studies that give unambiguous evidence-based guidelines regarding the duration of their use in particular. This study was designed to investigate the effect of an extended course of oral antibiotics on the prevention of postoperative infections of mandibular fractures in addition to the perioperative intravenous antibiotics. Of the 77 patients, the overall infection rate at 6 weeks was 6.5%. There was no significant difference (p=0.36) in the incidence of infection between the groups (antibiotic and the non-antibiotic groups). The use of perioperative intravenous antibiotics only (up to 24 hours post-operatively) was not significantly associated with an increased risk of surgical site

infection. Patients with comorbidities however appear to have an increased risk of surgical site infections in the non-antibiotic group and would thus benefit from extended course of oral antibiotics.

Based on the outcome of the present study, we recommend the following protocol to reduce the risk of infection when treating isolated mandibular fractures by ORIF:

1. Prescribe mouth wash, and not antibiotics, at initial consultation, unless there is evidence of infection
2. Plan for early surgical intervention (if immediate surgery is not possible, plan for surgery at least within two weeks post-injury)
3. Treatment of the fractures in an asceptic environment
4. Use of IV perioperative Penicillin IV antibiotics (Clindamycin if allergic to penicillin) for up to 24 hours postoperatively
5. Removal of mobile, erupted teeth in the line of fracture line, especially those with exposed roots and fractures that presented late.
6. Thorough debridement of the fracture sites, with meticulous and atraumatic handling of the soft tissues
7. Avoidance of excessive stripping of the tissues when raising a flap, which may compromise vascular supply to the fractured segments
8. Use of oral antibiotics for 5 days only in patients with comorbidities

3.3 LIMITATIONS

The validity of the findings of this study is limited by the small sample size and lack of follow-up beyond the 6-week period. Notwithstanding its limitation, this study has added invaluable data to the growing evidence that extended use of oral antibiotics offers no additional benefit in reducing postoperative infections of mandibular fractures. Future prospective randomised-controlled studies, with larger sample size and longer follow-up, providing data such as the effect of smoking and alcohol, CD 4 count and the treatment approach (transoral or transbuccal) are recommended to validate the findings in this study.

CHAPTER 4

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CHAPTER 5

5. APPENDICES

5.1 Patient information sheet

Appendix1

INFORMATION SHEET (annexure 1)

Study title: A protocol for prophylactic antibiotic usage in managing mandibular fractures requiring open reduction and internal fixation: a prospective clinical trial

Good day!

My name is Dr Gontse Mohotlhoane and I am a Registrar at the Department of Maxillofacial and Oral Surgery at Charlotte Maxeke Johannesburg Academic Hospital. As part of my training, I need to do a research project. As you know your jaw is broken and you will need an operation in managing the broken jaw.

I am doing a study to analyze whether there is any need for antibiotics after an operation, when treating broken jaws. I am seeking your permission to use the details of your treatment to undertake this research. I only wish to have access to the records of your treatment; my involvement would thus be invisible to you and involve nothing that you would not experience in the normal course of your hospital treatment. You will either receive antibiotics only in the operation, or you will receive more doses after the operation. My study seeks to compare the incidence of post-operative infection as between the two groups. I will have no involvement in deciding which patient is allocated to either group.

Since we are unsure of the outcomes of the study, I cannot say at the outset that one group is at greater risk of infection than the other, nor can I say that there is greater benefit in being allocated to one group or the other.

Whether you choose to be part of the research or not, this will not compromise your overall treatment. Furthermore, you are free to withdraw from the study if you wish to, also without any compromise to your treatment, or having to give any reason.

There is neither payment nor cost to you, should you agree to be involved in the study.

Your personal information will not be published in this study, or made known to anyone except your attending physician, myself and my supervisor, Dr Ephraim Rikhotso. As with all patients with broken jaws, you will be requested to come for follow up appointments for 1 week, 4 weeks and 6 weeks, or as necessary, after surgery and I would like your permission to see the records of those visits too. There will be no additional treatment or testing as a result of my study. If you are interested in the results of the study, I will be pleased to send you a summary report on request.

If you have questions at any time, you may contact me, or my supervisor, as follows:

Principal Investigator:
Dr Gontse Mohotlhoane
Tel No. 073 410 6676
E-mail: gontsemoh@yahoo.com

Supervisor:
Dr Ephraim Rikhotso
Tel No 011 717 2130
E-mail: Risimati.Rikhotso@wits.ac.za

This study has been approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg ("Committee"). A principal function of this Committee is to safeguard the rights and dignity of all human subjects who agree to participate in a research project and the integrity of the research.
If you have any concern over the way the study is being conducted, please contact the Chairperson of this Committee who is Professor Clement Penny, who may be contacted on telephone number 011 717 2301, or by e-mail on Clement.Penny@wits.ac.za. The telephone numbers for the Committee secretariat are 011 717 2700/1234 and the e-mail addresses are Zanele.Ndlovu@wits.ac.za and Rhulani.Mukansi@wits.ac.za

Thank you for reading this Information Sheet.

Dr Gontse Mohotlhoane
January 2019

5.2 Consent form

Appendix 2

CONSENT FORM

Title of research project: A protocol for antibiotic use in managing mandibular fractures requiring open reduction and internal fixation: a prospective clinical trial

1. **I have been given a Study Information Sheet which explains the nature and processes involved in this study, which is attached hereto.**
2. **I was given time to read it, or had it read to me, in the language I best understand.**
3. **I was given time to ask any questions I wanted to and found any answers given to me to be reasonable and satisfactory.**
4. **I believe I fully understand why the study is being conducted and what the intended outcomes will be.**
5. **I understand that there will be no immediate benefit to me, should I agree to participate, nor will I receive any payment; conversely, participation will not cost me anything.**
6. **I understand that, even if I initially consent to take part in the study, I may subsequently withdraw at any time and would not be required to give any reasons; if that happened, any data collected about me for the purposes of the study would immediately be destroyed, unless I give consent for it to be retained**
7. **I have been given a range of contact details, listed below. If I require further information or become concerned about any aspect of this study, I am free to speak to any of these contacts.**

Contact details:

Dr Gontse Mohotlhoane, Principal Investigator
Tel No. 073 410 6676
E-mail: gontsemoh@yahoo.com

Dr Ephraim Rikhotso, Supervisor
Tel No 011 717 2130
E-mail: Risimati.Rikhotso@wits.ac.za

Dr CB Penny, Chairperson of the Human Research Ethics Committee (Medical) at the University of Witwatersrand, on telephone no. 011 717 2301, or by e-mail at Clement.Penny@wits.ac.za.
Ms. Z Ndlovu or Mr Rhulani Mkansi, Committee Secretariat, telephone nos.: 011 717 2700 or 1234, or by e-mail at: Zanele.Ndlovu@wits.ac.za or Rhulani.Mkansi@wits.ac.za

Name of Participant: _____
Date: _____
Place: _____
Signature or mark _____

Witnessed by:

Name of Witness: _____
Signature: _____
Date: _____

5.3 Data collection sheet

Appendix 3

DR MOHOTLHOANE RESEARCH PROJECT

STUDY NUMBER: AGE: GENDER : M / F MEDICAL HISTORY: DATE OF INJURY: *dd/mm/yr* DATE OF PRESENTATION: *dd/mm/yr* DATE OF OPERATION: *dd/mm/yr*

FRACTURE SITE:



*Please indicate location

ANTIBIOTIC THERAPY

INTRA-OPERATIVELY	
POST-OPERATIVELY	
TTO	

*Document details of the antibiotic given. If **no** post-operative antibiotics are given, leave area blank.

*Oral antibiotic to commence in ward Day1 post-operatively

GUIDELINE`

*IV mediation Augmentin 1.2g intra-operatively

* Discharge with Amoxil 500mg orally 8hourly 4days

*Clindamycin in Penicillin allergy: IVI 600mg and oral 300mg 6hourly for 4days

REVIEWS- PLEASE DOCUMENT IF ANY COMPLICATION

REVIEW 1 Date:*dd/mm/yr*	
REVIEW 2 Date:*dd/mm/yr*	
REVIEW 3 Date:*dd/mm/yr*	

For any queries, contact Dr Mohotlhoane on 0734106676 or #6748(CMJAH)

1

5.4 Ethics clearance

Appendix 4

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Dr GP Mohotlhoane
School of Oral Health Sciences
Department of Oral and Maxillofacial Surgery
Medical School
University

E-mail: gontsemoh@gmail.com

CC: Supervisor: Dr E Rikhotso <Risimati.Rikhotso@wits.ac.za>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 21/12/2018

REF: *R14/49*

PROTOCOL NO: **M181035** *(This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)*

PROJECT TITLE: *A protocol for prophylactic antibiotic usage in managing mandibular fractures requiring open reduction and internal fixation: a prospective clinical trial*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.

MSWorks2000/Iain0007/Clearscan.wps

TURN-IT-IN REPORT



ORIGINALITY REPORT

9%	5%	10%	6%
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