การเปรียบเทียบการให้ยาปฏิชีวนะครั้งเดียวและหลายครั้งเพื่อป้องกันการติดเชื้อหลังการผ่าตัด
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COMPARISON OF SINGLE-DOSE AND MULTI-DOSE

ANTIBIOTIC PROPHYLAXIS IN ORTHOGNATHIC SURGERY:

A RETROSPECTIVE COHORT STUDY

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วัตถุประสงค์ของงานวิจัย: (1) เพื่อเปรียบเทียบผลการป้องกันการติดเชื้อภายหลังการผ่าตัดแก้ไขความ
ผิดปกติของขากรรไกรและการสบฟันระหว่างกลุ่มที่ได้รับยาปฏิชีวนะครั้งเดียวและหลายครั้ง และ (2) เพื่อระบุ
ปัจจัยที่เกี่ยวข้องกับการการติดเชื้อภายหลังการผ่าตัดแก้ไขความผิดปกติของขากรรไกรและการสบฟัน

ระเบียบวิธีวิจัย: ประวัติการรักษาของคนไข้ที่ได้รับการผ่าตัดแก้ไขความผิดปกติของขากรรไกรและการ
สบฟันในคณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ระหว่างปี 2557-2559 จะถูกนำมาคัดแยกข้อมูล
ประกอบไปด้วยข้อมูลประชากร ประวัติทางการแพทย์ที่ผ่านมาเพื่อประเมินความเสี่ยงในการผ่าตัดและให้ยาระงับ
ความรู้สึก การผ่าตัดแก้ไขความผิดปกติขากรรไกรที่ได้รับและอาการแทรกซ้อน รูปแบบของการให้ยาปฏิชีวนะ และ
การติดเชื้อบริเวณแผลผ่าตัด ข้อมูลจะถูกเก็บภายในระยะเวลา 30 วันเพื่อวินิจฉัยการติดเชื้อบริเวณแผลผ่าตัดตาม
เกณฑ์ของศูนย์ควบคุมและป้องกันโรคของสหรัฐอเมริกา

ผลการศึกษา: จาก 168 คน พบคนไข้ 3 คน มีอาการแสดงของการติดเชื้อ และคนไข้อีก 4 คน มีอาการ
แสดงของโพรงอากาศในขากรรไกรบนอักเสบ ในกลุ่มคนไข้ที่มีการติดเชื้อ เป็นคนไข้ที่ได้รับยาอะม็อกซีซิลลินร่วมกับ
กรดคลาวูลานิก 1.2 กรัม แบบฉีดครั้งเดียวในช่วงการนำสลบ 1 คน ได้รับยาเพนิซิลลิน 2 ล้านหน่วย แบบฉีดทุก 4
ชั่วโมง 2 คน โดย 1 ใน 2 คนได้รับยาอะม็อกซีซิลลิน แบบรับประทาน 1 กรัม วันละ 2 ครั้ง เป็นเวลา 1 สัปดาห์ ซึ่ง
ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างรูปแบบของการให้ยาปฏิชีวนะและการติดเชื้อบริเวณแผลผ่าตัด
(p = 0.472) และพบความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างระยะเวลาการผ่าตัดที่เพิ่มขึ้นและการติดเชื้อ
บริเวณแผลผ่าตัด (p = 0.030) ปัจจัยอื่นๆ ที่เกี่ยวข้อง เช่น อายุ เพศ ความเสี่ยงในการผ่าตัดและให้ยาระงับ
ความรู้สึก การสูบบุหรี่ ประเภทของการผ่าตัดขากรรไกร ปริมาณเลือดที่สูญเสียระหว่างผ่าตัด การถ่ายเลือดระหว่าง
ผ่าตัด การปลูกกระดูกและการแบ่งแยกกระดูกไม่ดี พบว่าไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติกับการติดเชื้อ
บริเวณแผลผ่าตัด นอกจากนี้ ไม่พบความสัมพันธ์ระหว่างปัจจัยต่างๆ ที่มีผลต่อการติดเชื้อบริเวณแผลผ่าตัดกับโพรง
อากาศในขากรรไกรบนอักเสบหลังการผ่าตัด

สรุปผลการศึกษา: การให้ยาปฏิชีวนะแบบครั้งเดียวเพียงพอต่อป้องกันการติดเชื้อภายหลังการผ่าตัด
และการผ่าตัดที่ใช้เวลานานมีแนวโน้มเกิดการติดเชื้อบริเวณแผลผ่าตัดมากขึ้น

ภาควิชา   ศัลยศาสตร์   ลายมือชื่อนิสิต ....

สาขาวิชา   ศัลยศาสตร์ช่องปากและแม็กซิลโลเฟเชียล   ลายมือชื่อ อ.ที่ปรึกษาหลัก ....

ปีการศึกษา 2560

5975818732 : MAJOR ORAL AND MAXILLOFACIAL SURGERY

KEYWORDS: ANTIBIOTIC PROPHYLAXIS / ORTHOGNATHIC SURGERY / SURGICAL SITE INFECTION

TEERAPHAT POCHANA: COMPARISON OF SINGLE-DOSE AND MULTI-DOSE ANTIBIOTIC PROPHYLAXIS IN ORTHOGNATHIC SURGERY: A RETROSPECTIVE COHORT STUDY. ADVISOR: ASSOC. PROF.SOMCHAI SESSIRISOMBAT, D.D.S., M.D., 93 pp.

Objective: (1) to compare the prophylactic effect of a single versus a multiple dose antibiotic regimens and (2) to determine factors related to surgical site infection in orthognathic surgery

Materials and methods: Medical records of patients underwent orthognathic surgery in the Faculty of Dentistry, Chulalongkorn University between 2014 and 2016 were extracted for medical data including demographic data, American Society of Anesthesiologists (ASA)-classified past medical history, orthognathic surgical procedures and complications, prophylactic antibiotic regimen, and surgical site infection. The records also contained 30-day follow-up information, according to the Centers for Disease Control and Prevention (CDC) diagnostic criteria for surgical site infection.

Results: Of 168 patients, three developed signs of infection and four presented maxillary sinusitis. In the infected group, one received 1.2g single-dose intravenous amoxicillin-clavulanate at induction while the remaining two patients were administered with 2 million units intravenous penicillin G every 4 hours perioperatively and one out of two received 1g oral amoxicillin twice a day for a week postoperatively. No significant association was found between types of antibiotic prophylaxis and surgical site infection (p = 0.472). Prolonged operation time significantly increased the risk of infection (p = 0.030). There was no significant difference in infection among other factors including age, gender, ASA score, smoking behavior, orthognathic surgical operations, blood loss, blood transfusion, bone grafting and bad split. Moreover, there was no significant association between contributing factors related to surgical site infection and postoperative maxillary sinusitis.

Conclusion: The results suggest that the single-dose antibiotic prophylaxis can be sufficient in prevention of surgical site infection. Prolonged operation time increases the risk of infection.

Department: Oral and Maxillofacial Surgery   Student's Signature ------------------------------

Field of Study: Oral and Maxillofacial Surgery   Advisor's Signature ------------------------------

Academic Year: 2017

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LIST OF ABBREVIATIONS

ASA	American Society of Anesthesiologists
BSSRO	Bilateral sagittal split ramus osteotomy
CDC	Centers for Disease Control and Prevention
IPD	In-patient departure
mg	Milligram
MIC_{90}	Minimum inhibitory concentration with 90 percent reduction of bacterial pathogen
NNIS	National Nosocomial Infections Surveillance
OPD	Out-patient departure
SSI	Surgical site infection
SAP	Surgical antimicrobial prophylaxis, or Surgical antibiotic prophylaxis

PART I

INTRODUCTION

1.1 Background

1.1.1 Orthognathic surgery

Orthognathic surgery is a surgical correction of dentofacial deformities which are multifactorial problems including inherited tendencies, antenatal problems, systemic conditions during growth, trauma, and environment (1). These problems present as jaw discrepancies and skeletal malocclusion. As a consequence, these patients have a poor quality of life in both oral health and general well-being (2).

1.1.1.1 Management of dentofacial deformities

The primary concerns for patients to seek treatment are esthetic appearance, function, and psychosocial condition (3). The multidisciplinary approach between orthodontic treatment and orthognathic surgery is essential in moderate-to-severe degree of deformities which growth modification or camouflage alignment cannot correct. The operation may involve single (either maxilla or mandible) or dual jaws. (4-7).

1.1.1.2 Mandibular procedure

Several treatment options for orthognathic surgery in mandible has been proposed. Bilateral sagittal split ramus osteotomy (BSSRO), originated from Obwegeser and Trauner in 1955, is the most common operation in the mandible. This technique separates mandible bilaterally into proximal and distal portions. The distal portion includes most of mandibular body and ramus anterior to lingular fossa whereas the proximal portion contains the rest of mandible. Although BSSRO is the most common procedure among mandibular procedures, some other surgical techniques are performed in particular cases. The subapical osteotomy aims to correct anterior open bite, supra-eruption of posterior dentoalveolar segment, or ankylosed tooth. The genioplasty is indicated for esthetic reason and asymmetry of lower face. This surgical technique optimized the chin position in three-dimension including horizontal, vertical

and transverse directions. The genioplasty can be operated concomitantly as part of mandibular procedure. Pre-treatment model surgery and cephalometric analysis of facial structure are useful for the accurate assessment, diagnosis and planning steps (4, 7, 8).

1.1.1.3 Maxillary procedure

Le Fort I osteotomy (LF) is a famous operation employed for the three-dimensional repositioning of the maxilla. Horizontal osteotomy is performed to separate the maxilla from the relevant bony structures. The landmark of LF is parallel to maxillary occlusal plane. The nasal, maxillary antral and oral mucosa are reflected from the bone. The maxilla is separated, down-fractured and re-oriented with an internal rigid fixation. If the limited fragment mobilization, limited orthodontic tooth movement or various maxillary occlusal schemes are presented from an examination, the segmental Le Fort I osteotomy is the treatment option to increase the dimension of bone movement (5, 7, 9). Autogenous bone graft from anterior iliac crest or other grafting materials may be used as interpositional block to replace the residual bony defects (10).

In some type of deformities, anterior or posterior maxillary osteotomies are indicated. Anterior maxillary segmental osteotomy is considered to correct horizontal maxillary discrepancies in bimaxillary protrusion. In contrast, posterior maxillary osteotomy has a role in an extrusion of posterior maxilla. In severe transverse maxillary discrepancies with crowding, surgically assisted rapid palatal expansion (SARPE) is considered. SARPE is also indicated in patient with anterior arch length discrepancies. This technique separates maxilla into 2 fragments at the intermaxillary suture. Bone formation is induced by progressive callous distraction. The outstanding advantage of SARPE over the segmental Le Fort I osteotomy is a long-term stability in the transverse plane. In addition, no need of tooth extraction, less complication, improved facial appearance and a large degree of maxillary expansion are considered as greater benefits of SARPE. (7, 10).

1.1.2 Surgical site infection (SSI) following orthognathic surgery

1.1.2.1 Signs and symptoms of oral cavity and maxillary sinus infection

Surgical site infection (SSI), former name as surgical wound infection, is an infection of surgical area with or without placement of non-human implantable material (11). The signs and symptoms of SSI including elevated body temperature, pain, erythema over the surgical area, progressive swelling, purulent exudation and muscle trismus. In case of maxillary sinus infection, pressure and swelling at the overlying skin, pain, hypersensitivity of maxillary teeth, nasal and postnasal purulent discharge, and bad odor may present. Thus, early detection of these signs and prompt treatment are essential. Culture and sensitivity test, pus drainage, copious irrigation and appropriate antibiotic therapy are performed if indicated (12).

1.1.2.2 Factors associated with surgical site infection

The origin of infection consists of host, microorganism, and environment. There are several factors related to SSI which are categorized into patient and operation factors (Table 1). Patient factors are host or endogenous determinant. Current guidelines considered these potential factors including advanced age, poor nutritional status, diabetes, nicotine consumption, coexisting remote infection, microbial colonization, altered immune response, and length of pre-operative hospital admission, as patient-related factors. On the other hand, operation-related factors are environmental or exogenous determinant including surgical antimicrobial prophylaxis, surgical technique, duration of surgical operation, foreign material at surgical area, and operation room technique (11, 13).

Table 1 Patient-related and operation-related factors in surgical site infection (modified
from Mangram (11) with permission of use from RightsLink/Elsevier)

Patient factor	Operation factor
- Advanced age	- Inadequate preoperative skin preparation
- Poor nutritional status	- Inappropriate preoperative shaving
- Diabetes	- Inadequate surgical team preoperative hand and forearm antisepsis
- Smoking	- Contaminated operating room environment
- Obesity	- Inappropriate surgical attire and drapes
- Colonization with microorganisms	- Inadequate sterilization of instruments
- Coexisting infection at a remote body site	- Excessive duration of operation
- Altered immune response	- Poor surgical technique: excessive blood loss, hypothermia, tissue trauma, entry into a hollow viscus, devitalized tissues, presence of surgical drains and suture material, dead space
- Preoperative hospitalization	- Inappropriate or untimely antimicrobial prophylaxis

Some related surgical procedures associated with SSI. Removal of mandibular third molar increased a risk of periodontal disease of adjacent second molar in a long-term evaluation (14). However, there was no significant difference in an SSI rate between presence and absence of lower third molar during surgery (15, 16). If a bad

bone split was occurred, this might lead to SSI, particularly at the ramus of mandible (17). Steenen and colleagues also found no distinctive relationship between a bad split in a mandibular sagittal split osteotomy and a presence of lower third molar while Mehra reported the contradictory result (18, 19). To provide a stability in Le Fort I maxillary advancement, interpositional bone grafting using autogenous or synthetic materials provide a higher stability, acting as mechanical stabilizer in osteotomy gap and meshwork for a new bone formation(20-22) . Interestingly, the maxillary sinusitis was significantly found in Le Fort I osteotomy with demineralized bone matrix grafting (21). After the repositioning of jaw fragments, there are 3 methods to stabilize the fragments including lag screw, positional screw, and miniplate with monocortical screw placement. These materials can cause the SSI and may lead to a hardware removal (23-25).

1.1.2.3 Diagnosis of surgical site infection

Many organizations launched similar guidelines for prevention and management of the SSI (11, 13). However, CDC guideline for surgical site infection is the most widely used as diagnostic criteria and management protocols for SSI. CDC classifies SSI depending on the depth of incision through tissue layers (Table 2 to 4). SSI is divided into incisional and organ/space infection. The infection of intra-oral orthognathic surgical wound is categorized into a group of organ/space infection. The following diagnostic criteria are used (26, 27):

1. The SSI manifests within 30 days after surgical operation where the operation date is the first follow-up day and

2. At least one of the following situations:

1) Evidence of infection such as abscess, purulent discharge from a drain, or other finding related to the organ/space is found on invasive, gross anatomic, or histopathological examination.

2) Microorganisms are specified from fluid or tissue in the organ/space by microbiologic method.

3) Attending physician administers antimicrobial agent within 2 days of onset or worsening of symptoms.

Furthermore, maxillary surgery such as Le Fort osteotomy may involve maxillary sinus. Current clinical practice guideline launched by American Academy of Otolaryngology defines the term acute rhinosinusitis (ARS) as inflammation of paranasal antral and nasal mucosa with duration less than 4 weeks. This condition can result from a bacterial or viral infection which an initiation of antimicrobial therapy is essential. Thus, the etiology of ARS should be identified to differentiate acute bacterial rhinosinusitis from virus associated ARS and non-infective cause. Furthermore, the guideline do not recommend to use the radiographic imaging in the patient with distinctive signs and symptoms. The diagnostic criteria for ARS are (28):

1. Duration less than 4 weeks

2. Pus discharge from nasal cavity with at least one of these manifestations:

1) Nasal obstruction, congestion, blockade or stuffiness

2) Localized or diffuse headache, facial pain, pressure, or fullness

Table 2 Classification and diagnostic criteria of organ/space infection (26)

Classification	Criteria
Organ/Space SSI	- Infection occurs within 30 or 90 days after the operation depended on the list in table 3 and 4
	- Infection involves any part of the anatomy deeper than muscle and fascia (e.g. organs or spaces), which is opened or manipulated during an operation
	- At least one of the following:
	1. Purulent drainage from a drain that is placed into the organ/space
	2. Microorganism is specified from fluid or tissue by microbiologic testing
	3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination
	- At least one of the following criteria for specific organ/space infection listed in table 4

Table 3 Follow-up period for organ/space surgical site infection (26)

30-day surveillance	90-day surveillance
Abdominal aortic aneurysm repair,	Breast surgery,
Limb amputation,	Cardiac surgery,
Appendix surgery,	Coronary artery bypass graft with both chest and donor site incisions,
Shunt for dialysis,	
Bile duct, liver or pancreatic surgery,	Coronary artery bypass graft with chest incision only,
Carotid endarterectomy,	
Gallbladder surgery,	Craniotomy,
Colon surgery,	Spinal fusion,
Cesarean section,	Open reduction of fracture,
Gastric surgery,	Herniorrhaphy,
Heart transplant,	Hip prosthesis,
Abdominal hysterectomy,	Knee prosthesis,
Kidney transplant,	Pacemaker surgery,
Laminectomy,	Peripheral vascular bypass surgery,
Liver transplant, Neck surgery,	Ventricular shunt
Kidney surgery, Ovarian surgery,	
Prostate surgery, Rectal surgery,	
Small bowel surgery, Spleen surgery,	
Thoracic surgery,	
Thyroid and/or parathyroid surgery,	
Vaginal hysterectomy,	
Exploratory Laparotomy	

Table 4 Specific sites of organ/space surgical site infection.

(*) note that oral cavity and sinusitis are categorized in this group. (26)

Site	
Osteomyelitis	Other infections of the respiratory tract
Breast abscess or mastitis	Mediastinitis
Myocarditis or pericarditis	Meningitis or ventriculitis
Disc space	*Oral cavity (mouth, tongue, or gums)*
Ear, mastoid	Other infections of the male or female reproductive tract
Endometritis	Periprosthetic Joint Infection
Endocarditis	Spinal abscess without meningitis
Eye, other than conjunctivitis	*Sinusitis*
GI tract	Upper respiratory tract
Hepatitis	Urinary System Infection
Intraabdominal, not specified	Arterial or venous infection
Intracranial, brain abscess or dura	Vaginal cuff
Joint or bursa	

1.1.2.4 Surveillance program for surgical site infection

Although there are multi-modalities to decrease incidence of SSI, surveillance program is the most commonly used (11). Surveillance composes of systematic collection, analysis, evaluation and circulation of the risk data (29). These risk factors in specific operation are screened and send a feedback to a surgical team to monitor an at-risk patient (30). However, the accuracy of the program depends on the activation (31). These principles are recommended for initiating surveillance (11, 29, 32):

1. Uses CDC definitions of SSI for identifying SSI.

2. For patient during hospitalization (in-patients), uses direct examination of surgical site, indirect detection via patient and laboratory records, or combination methods.

3. For post-discharge patient (out-patients), uses direct examination during follow-up visit, or indirect surveillance by mail or telephone depended on hospital needs. However, a definite consensus for outpatients is not available.

4. Records patient and operation related risk factors.

5. Periodically investigates operation-specific SSI rate by related risk factor.

6. Addresses the feedback to surgical team. The optimal frequency and format for comparisons of SSI rate are determined by the case-dependent rates and initiation of continuous quality improvement.

1.1.3 Surgical antibiotic prophylaxis in orthognathic surgery

1.1.3.1 General consideration

Surgical site infection is a preventable consequence by excellent surgical technique and antibiotic prophylaxis, reducing an infection rate to less than 1% (33). However, every cases of post-operative infection cannot be avoided by only using prophylactic antibiotic agent (34). Antibiotic prophylaxis should be offered only to patient if an evidence of benefit is beyond risk (35). These following factors should be considered including a significant risk of infection, an appropriate antibiotic agent, a high plasma concentration of antibiotic agent, and the proper timing with shortest duration of antibiotic administration. Peterson proposed a high degree of wound contamination, an operative time exceeded 3 hours, and an insertion of foreign material as indications of antibiotic prophylaxis (33). Additionally, The minimum inhibitory concentration that inhibits a growth of 90 percent of bacterial pathogens (MIC$_{90}$) should be achieved perioperatively to retain an adequate prophylactic level (36). The selection of proper antibiotic agents should meet these following criteria including residential bacterial flora, patient's allergy, toxicity, costs, bactericidal effect, diffusion ability into tissue at the surgical site, therapeutic tissue concentration, bioavailability of antibiotic, drug dosing and re-administration, and drug delivery (37).

1.1.3.2 Microorganisms associated with the surgical site infection following orthognathic surgery

The characteristic of infection following orthognathic surgery is polymicrobial (38). The source of microbial pathogen is endogenous from the surgical area (32). Haug (2003) reviewed the related literatures in oral and maxillofacial microbiology and found that 30-60% of oral residential bacteria were *Streptococci* (39). In trans-oral orthognathic surgery, the associated microorganism are *Streptococci*, anaerobic Gram-positive cocci, and anaerobic Gram-negative rods (33). Chow and colleagues examined the microbiological cultures of 58 orthognathic patients with post-operative infection, and reported that the most frequent isolated species were *Bacteroides, Streptococci, Pseudomonas, Enterobacter, Actinomyces, Staphylococcus aureus,* methicillin-

resistant *Staphylococcus aureus,* and *Candida albicans*, respectively. With an exception of *Bacteroides*, these bacterial species are susceptible to penicillin as first-line agent, and cephalosporin if significant extra-oral procedure is indicated. Most of the oral anaerobes including *Bacteroides* indicate the co-formulated regimen with metronidazole or the use of amoxicillin-clavulanate (12, 38). On the other hand, clindamycin is advocated in patient with beta-lactam allergy, which also covered microorganism similar to penicillin (40).

If nasal cavity and maxillary sinus are involved in the surgical procedure, *Haemophilus influenza*, *Diphtheroids* and *Peptostreptococci* may be present. In bacterial maxillary sinusitis, the most isolated species are *Streptococcus pneumoniae* and *Haemophilus influenzae*. Other species also found such as *S. aureus, Moraxella catarrhalis*, alpha-hemolytic *Streptococci, Bacteroides* and *Peptostreptococci*. Unfortunately, the emergence of beta-lactamase producing strains are found in *S. pneumoniae, H. influenzae* and *M. catarrhalis*, which exhibited a resistance to most of penicillins. Thus, the penicillin integrated with beta-lactamase inhibitor, such as clavulanic acid, is indicated (28, 34, 39).

1.1.3.3 Prophylactic antibiotic agents

According to previous literatures related to orthognathic surgery, there were three classes frequently selected as prophylactic antibiotic agents namely beta-lactam derivatives, amoxicillin-clavulanic acid and clindamycin.

Beta-lactam derivatives are the first-line chemotherapeutic agents for oral and maxillofacial infection. Its fundamental structure composes of beta-lactam ring with acryl side chain as a functional group (Figure 1), or thiazolidine ring with carboxyl side chain (Figure 2). Mechanism of action of these agents target at peptidoglycan synthesis interrupting transpeptidation process. The antibiotic molecule penetrates through the cell wall, attaches to a specific receptor, penicillin binding protein, and inhibits the cross-linking process between N-acetylglucosamine and N-acetylmuramic acid of peptidoglycan synthesis. As a result, the bacterial cell wall cannot be established and leads to cell death that active growing bacteria are only affected. However, its

antibacterial activity can be lost if either acryl or carboxyl side chain is hydrolyzed. Penicillins are well-effective against Gram-positive bacteria, Gram-negative cocci, and non-beta-lactamase-producing anaerobes with a slight effect against Gram-negative rods (33, 41).
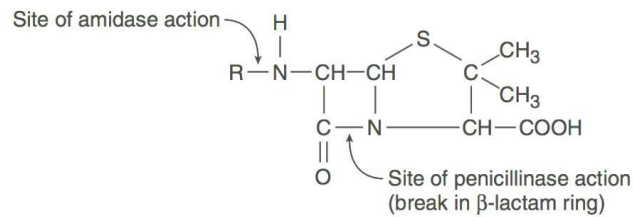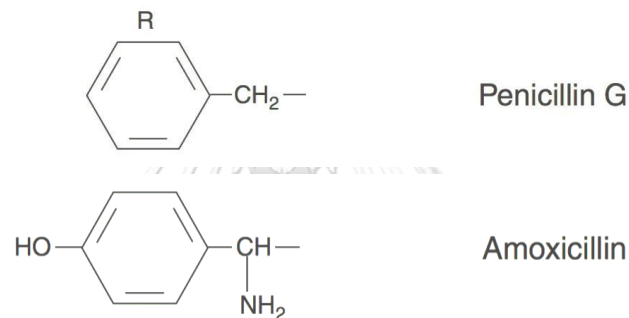
Figure 1 Molecular structure of penicillins (41)

[with permission of use from McGraw-Hill]
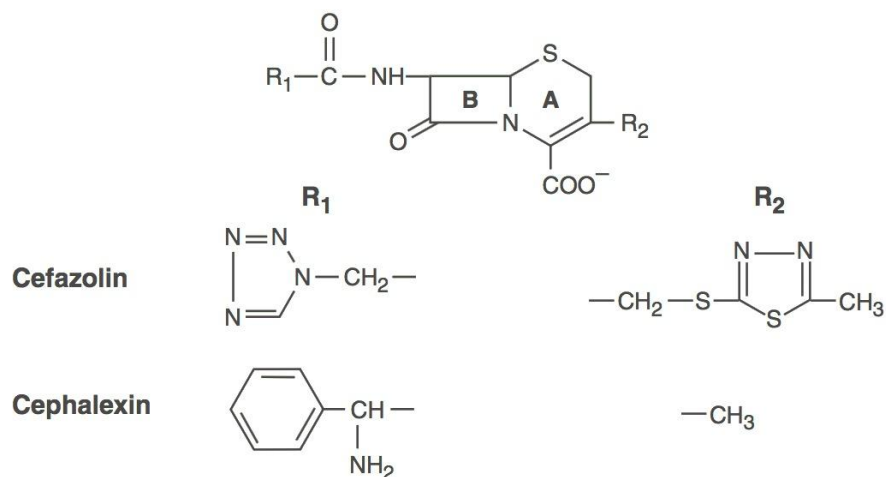
Figure 2 Molecular structure of cephalosporins (41)

[with permission of use from McGraw-Hill]

Penicillins are classified into 4 major groups. Natural penicillin and amino-penicillin are preferred groups in the oral and maxillofacial surgery. Penicillin G sodium or benzylpenicillin sodium (PGS), a parenteral form of natural penicillin, is the first-line antibiotic therapy for oral and maxillofacial infection (Figure 1) (12, 42). Its half-life is 30 minutes, so in 5 half-lives or 2.5 hours, PGS is totally eliminated from the human body (43). A double concentration of usual therapeutic dose with intravenous infusion of 2 million units PGS are suggested preoperatively to ascertain a peak plasma concentration. A peak soft tissue concentration is acquired within 15-30 minutes after administration. This concentration can be remained for 2 hours. Thus, PGS should be re-administered every 2-4 hours (7, 12).

Amino-penicillin or extended-spectrum penicillin has a greater activity against gram-negative microorganisms than natural penicillin but cannot resist the bacterial beta-lactamase (Figure 1) (41). Its mechanism of action is a competitive inhibitor at the active site of beta-lactamase, preventing this enzyme reactivation. The beta-lactamase inhibitors such as clavulanic acid and sulbactam, can be incorporated to extend its antibacterial activity against beta-lactamase producing bacteria (Figure 3). Amoxicillin-clavulanate, well-known trade name as Augmentin® or Co-amoxiclav®, is the combination form between amino-penicillin and beta-lactamase inhibitor (44). Amoxicillin-clavulanic acid 1.2 gram is recommended for intravenous infusion with repeated dose every 8 hours (45).
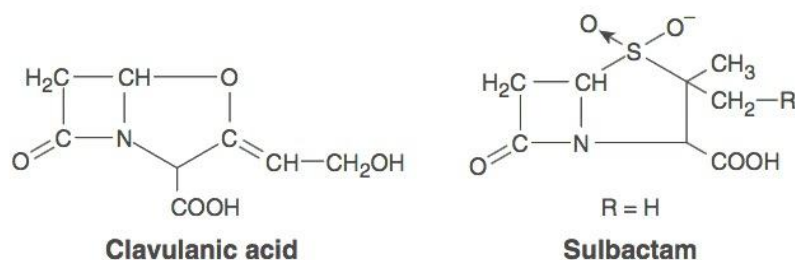
Figure 3 Molecular structure of beta-lactamase inhibitors (41)

[with permission of use from McGraw-Hill]

Cephalosporin is a synthetic agent from 7-aminocephalosporanic acid as an intermediate substance (Figure 2) (46). Replacement of a five-membered ring by a six-membered thiazolidine ring in the molecular structure causes cephalosporin less reactive, even though cephalosporin has similar mechanism to penicillin. Cephalosporins are classified into four generations depending on spectrum of activity and stability to beta-lactamases. Newer generations have a greater Gram-positive with lesser Gram-negative activity (44). The recommended dose for antibiotic prophylaxis is 1-2 grams cefazolin by parenteral infusion with repeated dose every 4 hours. This agent can be used as single dose or 24-hour duration (12, 46).

Clindamycin is the chlorine-substituted derivative of lincomycin, extracted from *Streptomyces lincolnensis* (Figure 4). The main antibacterial action of this agent is targeted on the 50s bacterial ribosomal subunit in the pathway of protein synthesis (41). The recommended dose is 600 milligrams. The effective tissue concentration at surgical site does not exceed 8 hours after infusion. This agent should be re-administered every 4-8 hours perioperatively (36, 47).
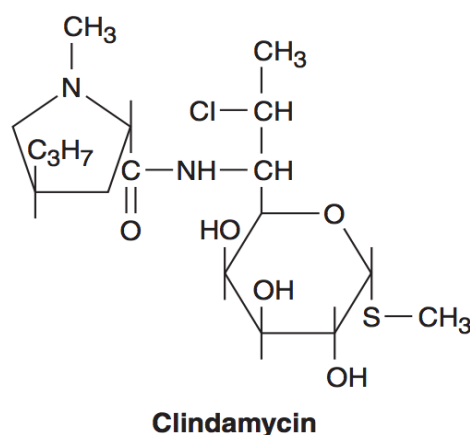
Clindamycin

Figure 4 Molecular structure of clindamycin (41)

[with permission of use from McGraw-Hill]

1.1.3.4 Duration of antibiotic prophylaxis

Surgical antibiotic prophylaxis (SAP) is considered to be one of the operation-related factor in the prevention of SSI (11). The purpose of SAP is to prevent preoperative contamination at the beginning of surgery and the chance of postoperative recontamination (34). SAP can be categorized into 3 periods, single-dose preoperative, short-term multiple-dose, and extended multiple-dose prophylaxis. The global guideline for the prevention of SSI, launched by WHO in 2016 strongly recommended the use of antibiotic prophylaxis within 120 minutes preoperatively based on the half-life of the antimicrobial agent (13). On the other hand, the effect of multiple-dose SAP has been disputed (33, 48, 49). Nevertheless, there is no definitive consensus in the optimal length of SAP.

1.1.3.5 Adverse events and management of inappropriate administration of antibiotic agents

The inappropriate use of antibiotic agent may lead to several consequences including antibiotic related diarrhea, allergic reactions, and antibiotic resistance (41). Antimicrobial resistance results in a life-threatening infection, a longer hospital admission, and other severe complications. In addition, a severe infection caused by multidrug-resistant bacterial strains, has been widely presented. Current evidences showed that antimicrobial resistance could be found not only in developing country, but also in developed country. Countries with profound antimicrobial consumption have a higher rate of antibiotic resistance. There is no systematic data of antimicrobial resistance in South East Asian zone have not been investigated properly. However, some information provided that the drug resistance has been risen. Avoidance of under-treatment, patient complaints, and medico-legal problem, are the major reason for the antibiotic resistance particularly in hospitalized patient (50, 51). Thus, SSI surveillance, infection control protocol, and obligatory antibiotic prescription are essential to reduce the resistance bacterial strain (52). Other factors related to antibiotic prescription are cultural aspects, socio-economic status, cultural beliefs of the patient and the prescriber, patient requirement, clinical autonomy, and diagnostic uncertainty. Some authors suggest that experience of physician, medical specialty and

perceived patient satisfaction are physician characteristics for an overprescription (53). Llor and Bjerrum released recommendations for decreasing antibiotic over-prescription as follows (50):

    1. prescribing antibiotic agents as needed

    2. enforcing laws restricting over-the-counter antibiotic sale

antibiotic stewardship programs by giving educational campaign through publications, guidelines, sessions, and mass media

    4. supporting evidenced-based antibiotic therapy from pragmatic research

    5. enhancing the use of proper diagnostic tools

    6. promoting delayed antibiotic prescription

    7. enhancing communication skills between doctor and patient
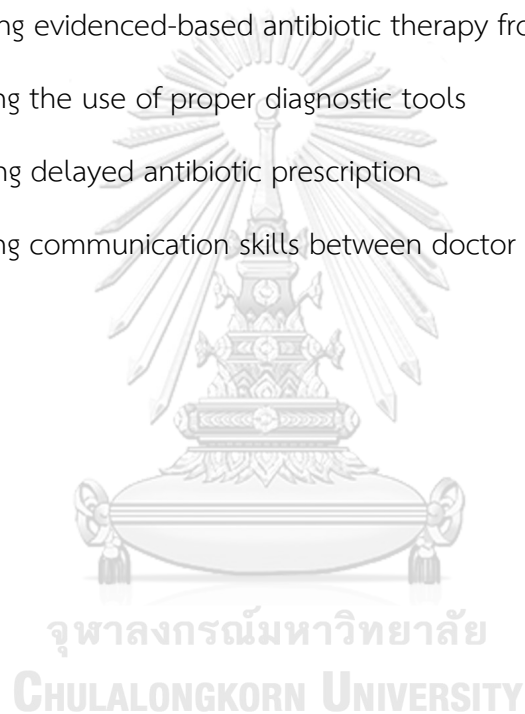
1.2 Rationale

Dentofacial discrepancies are the forms of dentofacial deformities. These problems resulted in several problems including poor oral hygiene, improper dentofacial function, facial imbalance and unaesthetic facial appearance. Management of these problems requires a combination approach between an orthodontic treatment to decompensate a natural adaptation and an orthognathic surgery to realign facial skeletal structures to an appropriate alignment. An orthognathic surgery is a surgical management of dentofacial deformities (54). Several complications related to orthognathic surgery are discussed. Nevertheless, one of the most common complications of orthognathic surgery is surgical site infection with prevalence as high as 53% (55). An intra-oral orthognathic surgery is categorized as a clean-contaminated surgical wound due to gastro-intestinal tract involvement. The 10-15% estimated infection rate can be reduced by antibiotic prophylaxis. Infection in the oral cavity is polymicrobial in nature which is comprised of Gram-positive cocci, *Streptococci* in particular, and anaerobes. Most of these bacteria are sensitive to penicillin and its derivatives (33). However, *Bacteroides*, and normal microflora in the maxillary sinus, such as *Streptococcus pneumoniae*, *Haemophillus influenza*, and *Moraxella catarrhalis*, are resistant to penicillins. Thus, the integration of penicillin and beta-lactamase inhibitor namely amoxicillin-clavulanate is usually selected (28).

There are two critical issues that motivated the present study. First of all, previous findings on antibiotic prophylactic regimens have yielded mixed results. Prophylactic antibiotic is commonly used in orthognathic surgery. It has been demonstrated that the benefits of preoperative antibiotic administration that may for last as long two hours depended on pharmacological properties of that antibiotic agent (13, 56). Some previous studies revealed that a single-dose preoperative antibiotic prophylaxis is sufficient (e.g., 36, 57) while some has demonstrated superior benefits of multiple-dose postoperative prophylaxis for 2-4 days (e.g., 45, 58). The Centers for Disease Control and Prevention (CDC) recently released a 2017 updated guideline for the prevention of surgical site infection in various surgical operations. It is recommended that subsequent antibiotic dose, even in the presence of a drain, not

be used (59). Nonetheless, there has been no study to date directly comparing a single-dose amoxicillin-clavulanate prophylaxis with a multiple-dose penicillin prophylaxis. Hence, the authors would like to perform a retrospective study in the effectiveness of a single dose versus a multiple-dose antibiotic prophylaxis.

Secondly, surgical site infection can be contributed by various factors. CDC highlighted factors other than antibiotic prophylaxis that effect the infection. They include age, nicotine consumption, systemic condition, specific typed surgical procedures, and surgical techniques (11). A meta-analysis revealed incidence of surgical site infection in developing countries was greater than developed countries (60). However, there has no epidemiological study of surgical site infection following orthognathic surgery from the South East Asian region (13). Thus, we conduct a study to assess the prevalence of these factors.

1.3 Research question

1.3.1 Are there differences in the infection rates following orthognathic surgery between single-dose and multiple-dose antibiotic prophylaxis?

1.3.2 Do any contributing factors related to an orthognathic surgery impact on surgical site infection?

1.4 Objective

1.4.1 To compare the efficacy between a single-dose and a multiple-dose antibiotic prophylaxis in prevention of surgical site infection.

1.4.2 To determine the other factors impacted on surgical site infection including age, gender, ASA score, smoking status, orthognathic surgical procedures and intraoperative complications, total operation time, total blood loss, blood transfusion, and bone grafting in orthognathic surgical patients.

1.5 Hypothesis

Ho_1: There is no difference in the infection rate between a single-dose and a multi-dose antibiotic prophylaxis.

Ha_1: There is difference in the infection rate between a single-dose and a multi-dose antibiotic prophylaxis.

Ho_2: Age, gender, ASA score, smoking status, orthognathic surgical procedures and intraoperative complications, total operation time, total blood loss, blood transfusion, and bone grafting do not impact on the surgical site infection in orthognathic surgery patient.

Ha_2: These factors impact on the surgical site infection in orthognathic surgery patient.

1.6 Keywords

Antibiotic prophylaxis, Orthognathic surgery, Surgical site infection

1.7 Study design

A retrospective cohort study.

1.8 Conceptual framework

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┌──────────────┐          ┌──────────────────┐
│ Single-dose  │          │ Operation factors│
└──────────────┘          └──────────────────┘
        │                          │
┌──────────────────────┐          │              ┌────────────────────────┐
│ Antibiotic prophylaxis│─────────┼─────────────▶│ Surgical site infection│
└──────────────────────┘          │              └────────────────────────┘
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│ Multiple-dose│          │ Patient factors  │
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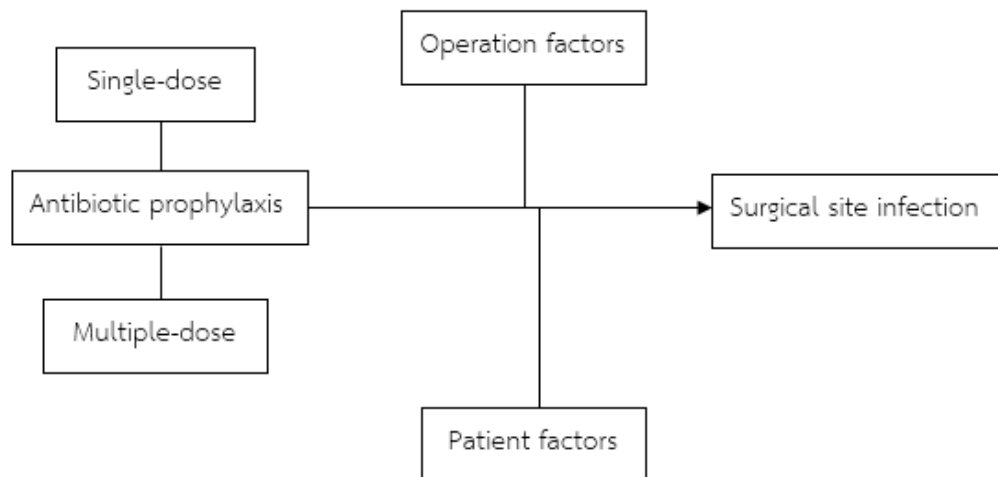
1.9 Potential benefits

The following issues were considered as benefits of this research project:

1. The rationale in antibiotic use will be promoted. This study will advocate to decrease the possibility of adverse events including potentially severe allergic reaction and antibiotic resistance due to epidemically antimicrobial overuse.

2. The cost of treatment will be reduced with highly effective antibiotic administration.

3. The epidemiological study of contributing factors of surgical site infection in orthognathic surgery will be enhanced the strength of the current guideline.

PART II

REVIEW OF LITERATURE

2.1 Prevalence of surgical site infection

Most orthognathic surgical procedure are performed intraorally. The degree of wound contamination of this procedure classifies as class II or clean-contaminated wound (Table 2). An infection rate for this class was approximately 10-15% (33). However, there are various reports in the infection rate following different procedures of orthognathic surgery.

Panula *et al.* (61) reviewed complications in orthognathic surgery. They included 655 orthognathic patients operated in Finland during 1983 to 1996. This study revealed that 26 patients (4%) manifested signs of infection up to 24th post-operative week due to bony sequestrum and loosening screws. Six patients (0.9%) had maxillary sinusitis after surgery. Five patients (7.6%) had a fistula at skin overlying mental nerve.

Chow *et al.* (38) conducted a 16-year study in prevalence of infection following orthognathic surgery. All patients underwent orthognathic surgery at University of Hong Kong between 1990 and 2004 were recruited. They found similar rate of infection between maxilla (51%) and mandible (49%). Le Fort II osteotomy (5.9%), sagittal split osteotomy (5.7%) and Le Fort I osteotomy (5.1%) were remarkable in SSI patients. The overall infection rate was 7.4% which was lower than an estimate rate for clean-contaminated wound class (10-15%). Note that duration of antibiotic prophylaxis was varied from a single dose to 14 days postoperatively.

Iannetti *et al.* (62) studied postoperative complications in 3,236 patients undergoing orthognathic surgery at University of Rome, Italy. Two percent patients developed signs of infection and found contributing factors including poor oral hygiene and smoking. Most cases were well responsive to antibiotics with only 0.2% which needed a surgical drainage. Thus, they suggested the prevention of infectious complication using prophylactic antibiotic.

Table 5 Classification, characteristics and estimated infection rates of surgical wound (modified from Mangram and Peterson (11, 33) with permission of use from RightsLink/Elsevier)

Class	Degree of contamination	Characteristics	Infection rate
I	Clean	- no respiratory, gastrointestinal and genitouinary involvement - primary wound closure	2%
II	Clean-contaminated	- respiratory, gastrointestinal and genitouinary involvement - no evidence of infection - no break in aseptic technique	10-15%
III	Contaminated	- gross contamination from gastrointestinal tract - a major break in aseptic technique	20-30%
IV	Dirty-infected	- clinical infection - perforated visceral tissue - existing microorganism in the surgical field	50%

Bouchard *et al.* (63) conducted an experiment in 336 patients in Canada from 2008-2013. They compared BSSRO with other operations. Patients were followed up for at least 3 months. As a consequence, 11.3% of patients were infected which 3% of patients required hardware removal. Furthermore, a longer length of operation and type of surgical procedure had an impact on the incidence of infection. Logistic regression analysis demonstrated that a combination surgery between Le Fort I osteotomy and BSSRO had a lower rate of infection than BSSRO. On the other hand,

age and a presence of third molar during surgery were not related to post-operative infection.

Davis *et al.* (15) conducted an epidemiological study in the prevalence of post-operative infection following orthognathic surgery in Canada during 2005 to 2013. This study demonstrated that both primary (62%) and recurrent (78%) surgical site infection frequently found in the lower jaw which 26% of the recurrent group still expressed signs and symptoms of infection after antibiotic therapy. Two-jaw surgery showed a significantly higher mean prevalence of infection than single-jaw surgery (9.2% vs. 5.3%). A single-jaw maxillary osteotomy (3.5% in single-piece group, 4.3% in multiple-piece group) demonstrated a lower prevalence of infection than mean prevalence (3.9% vs. 8.0%).

2.2 Duration of antibiotic prophylaxis

Ruggles and Hann (64) conducted a randomized controlled trial of penicillin G in the United States during 1979 to 1980. They included 40 patients underwent intraoral orthognathic surgery and allocated into 2 groups. Both groups received 1 million units penicillin G preoperatively via intramuscular injection and repeated with 2 million units intravenous penicillin G every 3 hours perioperatively. The final dose was given 3 hours after the last intraoperative dose. Experimental group was administered with 2 million units intravenous penicillin G every 4 hours for 2 days whereas placebo group was given 5 % dextrose in water. As a result, 3 patients in placebo group showed signs of infection within 7-14 days, while another group did not. However, no evidence of follow-up period was shown in the study.

Fridrich *et al.* (65) launched a randomized controlled study of penicillin G in patients underwent transoral orthognathic surgery in 1994. 30 patients were allocated into 2 groups. Two million units penicillin G was given to both groups preoperatively and every 4 hours perioperatively for a day. One group was administered with 500 mg penicillin V four times a day for a week while another was not. Patients were observed for at least a month. One patient from each group showed signs of infection at the

mandible. However, there was no statistical significance between antibiotic regimens and SSI.

Zijderveld *et al.* (57) performed a randomized controlled trial of amoxicillin-clavulanate and cephalosporin in the Netherlands during 1992-1996. Fifty-four patients underwent bimaxillary surgery were randomized into 3 groups receiving single-dose normal saline as placebo, 2.2 g amoxicillin-clavulanic acid and 1.5 g cefuroxime. Each regimen was administered 30 minutes preoperatively via intravenous infusion. A 30-day period was used to follow up with unclear diagnostic criteria. Overall infection rate was 27%, 11.1% for amoxicillin-clavulanate group, 17.6% for cefuroxime, and 52.6% for placebo. Statistically significant difference was found between prophylactic and placebo group but not different between two antibiotics.

Kang *et al.* (66) launched a study of the third-generation cephalosporin in the South Korea in 2009. Fifty-six patients underwent Le Fort I osteotomy with bilateral intraoral vertical ramus osteotomy were randomly distributed into 2 groups. Both groups received 1 g cefpiramide 30 minutes preoperatively by intravenous infusion. One group received 1 g cefpiramide two times daily for 3 days postoperatively and another group was not given. They followed up patients for 2 weeks using CDC criteria. The result showed no significant difference between single-dose (3 infected patients) and multiple-dose (2 infected patients) groups.

Lindeboom *et al.* (36) conducted a randomized controlled study of clindamycin in the Netherlands in 2003. Seventy patients underwent BSSRO were recruited and allocated into 2 groups. Clindamycin 600 mg was intravenously infused 15 minutes before incision placement. Experimental group was given every 6 hours for a day. They monitored SSI using unknown source of diagnostic criteria for 3 months. No statistical significance was found between single-dose (5.6% infected) and one-day (2.8% infected) groups.

Jansisyanont *et al.* (45) compared the prophylactic effect of penicillin G and amoxicillin-clavulanate in Thailand during 2002-2005. One hundred and twenty-two patients were allocated into 4 groups including group I perioperative penicillin, group

II 5-day penicillin, group III perioperative amoxicillin-clavulanate and group IV 5-day amoxicillin-clavulanate regimens. For penicillin regimens (group I and II), 2 million units penicillin G was given intravenously 30 minutes prior to surgery and every 4 hours perioperatively. Group I was given the final dose at 4 hours postoperatively. Group II was prescribed additionally with 500 mg oral amoxicillin every 8 hours for 5 days. For the amoxicillin-clavulanate regimens (group III and IV), patients were intravenously infused with 1.2 g amoxicillin-clavulanate 30 minutes prior to surgery and every 8 hours perioperatively. The final dose for group III was given at 4 hours postoperatively. Group IV was prescribed with 625 mg amoxicillin-clavulanate orally every 8 hours for 5 days. They monitored SSI using CDC criteria for 6 weeks. Consequently, an infection rate was 2/122 (1.64%). Two infected patients represented from extended penicillin group and short-term amoxicillin-clavulanate. However, a statistical significant difference was not achieved between SSI and prophylactic antibiotic regimens.

Danda *et al.* (67) performed a prospective randomized experiment of ampicillin, a parenteral form of broad-spectrum penicillin, in India between 2005 and 2007. One hundred and fifty orthognathic surgery patients were recruited and divided into 2 equal groups. At induction, both groups received 1 g ampicillin via intravenous infusion. Group 1 received 500 mg ampicillin intravenously every 6 hours for one day while group 2 infused with normal saline solution as a placebo by the same manner. They evaluated SSI using CDC criteria for 30 days. The result showed 9.3% and 2.7% infection rates in the group 1 and 2 respectively. The statistical significance was not found, however, it seemed to be clinical significance in SSI reduction for one-day prophylaxis. They recommended to use ampicillin due to its better activity on gram-negative bacilli than penicillin.

Wahab *et al.* (68) launched a randomized controlled trial of amoxicillin in India in 2013. Sixty patients underwent BSSRO setback or advancement were allocated into 2 groups. All patients were administered with 1 g amoxicillin intravenously at induction. The first group was given with 500 mg amoxicillin every 4 hours for 2 additional doses. The second group was given with normal saline in the same manner. They reviewed patients for 2 months using CDC diagnostic criteria. Six patients in the single-dose group

manifested signs of infection while a patient in the triple-dose group did not. The statistical analysis showed significant difference in infection rate between two groups, but there was no difference in direction of mandibular repositioning. They also found *Bacteroides* and *S. aureus* in 7 infected patients ($n_{group\ 1}$ = 5, $n_{group\ 2}$ = 2). Thus, they suggested to use short-term antibiotic prophylaxis in BSSRO surgery.

Eshghpour *et al.* (69) published a prospective clinical study of cephalosporin and amoxicillin in Iran in 2014. Fifty patients underwent Le Fort I osteotomy and BSSRO, were allocated into 2 groups. All patients were intravenously infused with 1 g cefazolin in 30 minutes before surgery and repeated at 4 hours after the first injection. For experimental group, 500 mg amoxicillin syrup was given per oral every 8 hours for 7 days while control group received a placebo in the same regimen. They observed patients for 6 weeks with unknown source of diagnostic criteria. No infected patient was found in this study. Therefore, this could be implied that extended antibiotic prophylaxis might not be necessary.

Bentley *et al.* (58) launched a randomized controlled study of penicillin G and V in Canada in 1999. Thirty patients were separated into 2 equal groups. All patients were administered with 2 million units penicillin G at the time of incision and followed by 1 million units penicillin G every 3 hours intraoperatively. An additional dose was given 3 hours following the final intraoperative dose. Experimental group was infused with 1 million units penicillin G every 6 hours for 2 days and received 300 mg oral penicillin V every 6 hours for 2 additional days. Control group received placebo in the same manner. Patients was monitored for 30 days using CDC criteria. One patient in experimental group (6.7%) and nine patients in control groups (60%) showed signs of SSI. The study showed statistically significant infection between two groups. Additionally, most infection (9 of 10) occurred in the mandible. The cause of infection might be due to an epinephrine effect to support bacterial accumulation, a collection of saliva and food debris in the incision, and a gravitational effect against wound drainage. However, a small sample size should be considered as a significant factor. Finally, they suggested 5-day antibiotic regimens as a proper prophylaxis.

Baqain *et al.* (70) conducted a randomized controlled trial of amoxicillin in patients underwent intraoral orthognathic surgery. Thirty patients were enrolled and randomly assigned into 2 groups. All patients received intravenous infusion with 1 g amoxicillin at induction and 500 mg amoxicillin 3 hours postoperatively. Group 1 was prescribed with 500 mg oral amoxicillin every 8 hours for 5 days. Group 2 was given a placebo with the same direction. If a patient was allergic to penicillin, the prophylactic agent was replaced by clindamycin. They followed up patients for 6 weeks with unclear diagnostic criteria. They also evaluated infection score using facial swelling (score 0-3), pain (score 0-4), skin redness (score 0 or 5), pus exudate (score 0 or 10), identified microorganisms (score 0 or 10), fever (score 0 or 10), and wound dehiscence (score 0 or 10). The total infection score was 52. As a consequence, 4 patients in group 1 and 2 patients in group 2 were diagnosed as SSI, but statistical significance was not found. The infection score was higher in one-day regimen (405 compared to 264). Cultures of patient exudation showed *Bacteriodes* in 2 cases and *S. aureus* mixed with anaerobes in a case. In conclusion, extended antibiotic prophylaxis might not reduce infection rate, but they supported extended prophylaxis due to reduction in surgical morbidity as shown in the infection score.

In summary, 11 mentioned studies could be categorized into 3 prophylactic groups; single dose, short-term multiple dose, and extended multiple dose. Zijderveld, Lindeboom, Kang, and Danda supported the use of single-dose antibiotic prophylaxis. Fridrich, Baquin, Jansisyanont, Wahab, and Eshghpour promoted short-term regimens which duration of prophylaxis did not exceed a day. Ruggle and Hann, Bentley and Baqain encouraged the use of extended antibiotic prophylaxis which duration of administration ranged from 2 to 4 days. Furthermore, 2 meta-analytical studies in the effect of post-operative antibiotic prophylaxis published in 2011 concluded the contradictory results. Tan et al. (48) supported the use of single-dose prophylactic regimen whereas Danda (71) advocated extended prophylactic duration. A meta-analysis conducted by Brignardello-Petersen in 2015, could not summarize the benefit of single-dose over short-termed prophylactic regimen due to insufficient evidences (72).

PART III

MATERIALS AND METHODS

3.1 Sample recruitment

3.1.1 Study population

Patient's medical records who underwent orthognathic surgery in the Faculty of Dentistry, Chulalongkorn University

3.1.2 Inclusion criteria

1) The patient who underwent any orthognathic surgical procedures between 2014 and 2016

2) The patient had no marked underlying diseases impairing a healing process such as diabetes, osteoporosis, or renal diseases

3.1.3 Exclusion criteria

1) The patient who was not available for 30-day follow-up after surgery

2) The patient who was not available for at least one visit per week for at least three weeks per month

3) The patient who underwent distraction osteogenesis (DO) and surgically assisted rapid palatal expansion (SARPE)

3.2 Data extraction

In-patient and out-patient medical records were reviewed. The following data was extracted and filled in the data collecting form using Microsoft® Excel 2016:

3.2.1 General data

1) Hospital number (HN) and admission number (AN)

2) Year of operation (A.D.)

3) Gender (male/ female)

4) Age (year)

5) Medical history including underlying disease, current medication, history of smoking, allergy of ß-lactam derivative. These records were integrated to give ASA class for each patient.

3.2.2 Surgical operation

1) Maxillary procedure (single-piece Le Fort I osteotomy, multiple-piece Le Fort I osteotomy or subapical osteotomy)

2) Mandibular procedure (bilateral sagittal split ramus osteotomy, genioplasty, or subapical osteotomy)

3) Type of surgical operation (single-jaw or dual-jaw)

4) Total operation time (minute)

5) Total amount of blood loss (ml)

6) Blood transfusion (autologous blood, packed red cell or both types)

7) Bone grafting site (maxilla, mandible, or both jaws)

8) Marked bad split (maxilla, mandible, or both jaws)

3.2.3 Prophylactic antibiotic regimen

1) Type of antibiotic agent (PGS, amoxicillin, amoxicillin-clavulanate, clindamycin, or others)

2) Dose (mg or unit)

3) Route of administration (per oral or per intravenous)

4) Frequency of administration

5) Duration of administration for each dosage form (at induction or day)

6) Total duration of administration (day)

7) Type of prophylaxis (single-dose or multiple-dose)

3.2.4 Surgical site infection

1) Date of follow-up

2) Area of infection (maxilla, mandible, both jaws, or maxillary sinus)

3) Date of post-operative infection

4) Management including

4.1) Intervention (surgical drainage, antibiotic therapy, or both)

4.2) Class of antibiotic agent (PGS, amoxicillin, amoxicillin-clavulanate, clindamycin or others)

4.3) Dose (mg)

4.4) Route of administration (per oral or per intravenous)

4.5) Frequency of administration

4.6) Duration of administration (day)

Note that the antibiotic prophylaxis in this study referred to a course of perioperative and postoperative antibiotic administration for the prevention of surgical site infection. If a patient manifested signs of infection during a prophylactic period, the antibiotic administration following the infectious exacerbation was defined as an antibiotic therapy.

3.3 Diagnostic criteria for surgical site infection in orthognathic surgery

These criteria must be met in the subject to diagnose as oral infection (26, 27):

1. The SSI exacerbates within 30 days after surgical operation

2. At least one of the following situations is investigated:

   1) Evidence of infection such as abscess, purulent discharge from a drain, or other finding related to the organ or fascial space found on invasive, gross anatomic, or histologic examination

   2) Microorganisms inoculated from fluid or tissue in the organ/space

   3) Attending physician administered antibiotic medication within 2 days after onset or worsening of symptoms

The following diagnostic criteria are used to evaluate the maxillary sinusitis after orthognathic surgery (28):

1. Duration less than 4 weeks

2. Purulent discharge from nasal cavity with at least one of these manifestations:

   1) Nasal obstruction, congestion, blockade or stuffiness

   2) Localized or diffuse headache, facial pain, pressure, or fullness

3.4 Statistical hypothesis

Ho_1: There are no significant differences in the infection rate between single-dose pre-operative and multi-dose antibiotic prophylaxis (p1=p2)

Ha_1: There are significant differences in the infection rate between single-dose pre-operative and multi-dose antibiotic prophylaxis (p1≠p2)

Ho_2: There are no significant association between surgical site infection and factors including age, ASA class, type of operation, total operation time, total blood loss, and intraoperative complications (p1=p2)

Ha_2: There are significant association between surgical site infection and factors including age, ASA class, type of operation, total operation time, total blood loss, and intraoperative complications (p1≠p2)

3.5 Statistical analysis

The data were analyzed using Statistical Package for the Social Science for Mac (SPSS for Mac) version 22.0. Descriptive statistics were calculated to display patient characteristics. The relationships between antibiotic prophylactic regimens and surgical site infection were compared using Fisher's exact test. Other factors including gender, age, ASA class, smoking status, number of operated jaw(s), total operative time, total amount of blood loss, blood transfusion, bone grafting, bad split and length of postoperative prophylaxis compared to surgical site infection will be compared using Fisher's exact test for categorical data and Mann-Whitney test for continuous data. The relationships between age, gender, smoking status, type of antibiotic prophylactic regimens and acute maxillary rhinosinusitis were analyzed using Fisher's exact test. The p-value less than 0.05 will be judged as statistical significance.

CHAPTER IV
RESULTS

Two hundred and fifty-seven patients' medical records were screened. Eighty-five patients were excluded due to insufficient data collection (n = 10) or follow-up (n = 75). Four patients who underwent DO (n = 3) and SARPE (n = 1) were also excluded. Therefore, 168 patients were included (67 male and 101 female). Patient age ranged from 17 to 52 years with an average age of 26 ± 6 years. The majority of patients were categorized as ASA class I; only nine of the patients (5.35%) were ASA class II. Two out of nine ASA-class II patients were active smokers while the rest showed a significant underlying disease which compromised the healing process including thalassemia trait (n = 4) and G-6-PD (n = 3). Ninety-nine patients were treated by single-jaw surgery and 69 patients underwent bimaxillary surgery. Table 6 revealed surgical operations performed in the patients. Average total operation time was 255 ± 125.90 minutes, with 195 ± 76.37 and 341 ± 133.28 minutes for one-jaw and two-jaw groups, respectively. Average total amount of blood loss was 502 ± 368.86 ml (one-jaw procedure = 327 ± 169.36; two-jaw procedure = 752 ± 430.23); Thirty-six patients needed blood transfusion. The autogenous bone grafting was performed in 17 patients comprising of twelve at the maxilla, three at the mandible, and the rest at both jaws. Bad bone split was also found in four cases at the maxilla and nine cases at the mandible.

Per type of prophylaxis (see table 7), 32 patients were administered a single-dose antibiotic; the rest received multiple-dose prophylaxis. In the single-dose group, most patients received 1.2g intravenous (IV) amoxicillin-clavulanate at induction. Two patients were given 600mg IV clindamycin due to a penicillin allergy. While most patients in the multiple-dose group received 2 million units IV penicillin G perioperatively, nine received 1.2g IV amoxicillin-clavulanate and six were given 600mg IV clindamycin due to the penicillin allergy. Eleven patients received a combination of regimens between 2 million units IV penicillin G and 1.2g IV amoxicillin-clavulanate (n = 10) or 600mg IV clindamycin (n = 1) if indicated. In case of prolonged operation,

Table 6 Orthognathic surgery performed during 2014-2016

Operation	n
Single-jaw surgery	**99**
A. Maxilla	8
- Le Fort I osteotomy	7
- Multiple-piece Le Fort I osteotomy	1
B. Mandible	91
- BSSRO	76
- Genioplasty	1
- Lower anterior subapical osteotomy	1
- BSSRO and genioplasty	12
- BSSRO and lower anterior subapical osteotomy	1
Bimaxillary surgery	**69**
- Le Fort I osteotomy and BSSRO	38
- Le Fort I osteotomy, BSSRO and genioplasty	3
- Le Fort I osteotomy, BSSRO and lower anterior subapical osteotomy	2
- Multiple-piece Le Fort I osteotomy and BSSRO	15
- Multiple-piece Le Fort I osteotomy, BSSRO and genioplasty	3
- Multiple-piece Le Fort I osteotomy, BSSRO and lower anterior subapical osteotomy	7
- Upper posterior segmental osteotomy and BSSRO	1

the patients were additionally administered with the same antibiotic depending on its half-life. Penicillin G was repeated every 4 hours while clindamycin was infused every 6 hours. None of case with amoxicillin-clavulanate regimen was re-administered perioperatively. Postoperative prophylaxis with the same agent was given in the multiple-dose until the oral feeding was possible. Penicillin G and amoxicillin-clavulanate were extended with 1g oral amoxicillin and 1g amoxicillin-clavulanate twice a day respectively whereas 300mg clindamycin was given orally three times daily. Each agent was given for at least 7 days for home medication. A range of multiple-dose antibiotic administration was between 3 and 20 days postoperatively (Figure 5). Duration of intravenous and oral antibiotic prophylaxis in multiple-dose group were shown in table 7. Most of patients received intravenous antibiotic for 3-5 days postoperatively and oral antibiotic for 5-7 days.
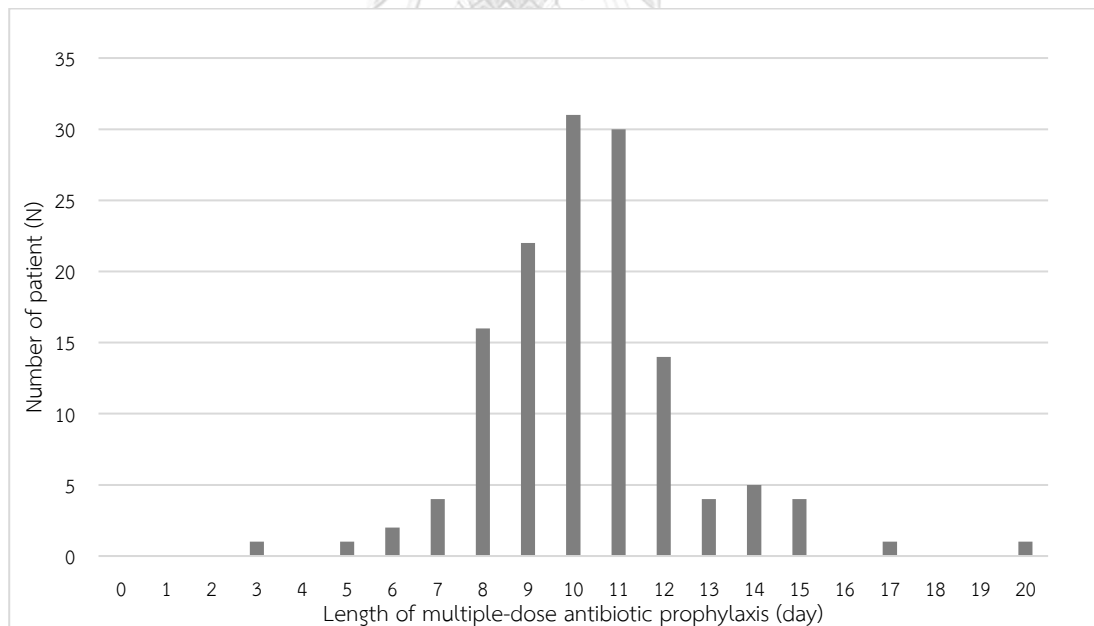
Figure 5 Length of multiple-dose antibiotic prophylaxis in orthognathic surgical patients

Table 7 Duration of intravenous and oral antibiotic prophylaxis in orthognathic surgical patients list by regimens

	N	Day length of IV antibiotic prophylaxis										Day length of oral antibiotic prophylaxis												
		0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	10	11	12
Single dose prophylaxis	32																							
- Amoxicillin-clavulanate	30	30										30												
- Clindamycin	2	2										2												
Multiple dose prophylaxis	136																							
- IV penicillin G and oral amoxicillin	110			1	31	47	24	5	2			2			2	8	39	11	29	13	1	5		
- IV and oral amoxicillin-clavulanate	9				5	2	1		1			1							3	1			3	1
- IV and oral clindamycin	6				2	4										1	1		3	1				
- IV penicillin G and oral amoxicillin-clavulanate	10		1		2	4		2			1				2		3		3		1		1	
- IV penicillin G and oral clindamycin	1						1													1				

According to CDC criteria, three patients had signs of infection (see Table 8 for details). Significant relationship was found between the operation time and post-operative infection (p = 0.030, Mann-Whitney test). No significant relationship was found between surgical site infection and other factors including age groups of patients, gender, ASA class, current smoking status, number of operated jaw(s), total blood loss, blood transfusion, placement of autogenous bone graft, presence of bad split, and different antibiotic regimens (Table 9). Concerning the maxillary sinus-related procedure, four patients undergoing bimaxillary surgery showed signs of postoperative maxillary sinusitis. They received multiple-dose penicillin prophylaxis ranging from 5 to 17 days postoperatively. There were no statistically significant associations between factors and postoperative maxillary sinusitis (Table 10).

Table 8 Infected patients underwent orthognathic surgery

Patient characteristics	Operation	Operation Time (minute)	Blood Loss (ml)	Antibiotic prophylaxis	Surgical site infection		Management
					Day	Signs and symptoms	
Patient LD male 21 years old	Le Fort I osteotomy and BSSRO	285	1,100	1.2 g amoxicillin-clavulanate IV at induction	18	- Left buccal space abscess due to wound dehiscence at left maxilla - Fixation plate exposure	- Copious irrigation with normal saline - Given 1g oral amoxicillin-clavulanate for 7 days
Patient CW female 27 years old	BSSRO	120	500	1.0 g penicillin G at induction and 3 days post-operatively	4	-Right lateral pharyngeal swelling - Fever	- Stitch off - Copious irrigation with normal saline - Given 600mg IV clindamycin for 5 days and 600mg oral clindamycin for additional 5 days
Patient PP male 41 years old	BSSRO	120	200	1.0 g penicillin G at induction and 3 days post-operatively and 500 mg oral amoxicillin three times daily for additional 7 days	12	- Vestibular space abscess at right mandible - Abscess at right retromolar area	- Stitch off - Copious irrigation with normal saline - Given 1g oral amoxicillin-clavulanate for 7 days

Table 9 Surgical site infection in patients underwent orthognathic surgery

list by factors.

Characteristic	Non-infected (n)	Infected (n)	*p*-value
Gender			
- Male	65	2	0.349
- Female	100	1	
Age			0.509
ASA classification			
- class I	156	3	0.847
- class II	9	0	
Smoking			
- former/non-smoker	163	3	0.964
- active smoker	2	0	
Number of operated jaw			
- one jaw	97	2	0.538
- two jaw	68	1	
Operation time			*0.030
Blood loss			0.871
Blood transfusion			
- no	129	3	0.483
- yes	36	0	
Bone grafting			
- no	148	3	0.725
- yes	17	0	

Characteristic	Non-infected (n)	Infected (n (%))	p-value
Bad split			
- no	152	3	0.784
- yes	13	0	
Type of antibiotic prophylaxis			
- single dose	31	1	0.472
- multiple dose	134	2	
Duration of multiple dose			0.209

Table 10 Maxillary sinusitis in patients underwent orthognathic surgery list by factors

Characteristic	Non-sinusitis (n)	Sinusitis (n)	p-value
Gender			
- Male	30	1	0.644
- Female	43	3	
Age			0.248
Smoking			
- former/non-smoker	73	3	0.052
- active smoker	0	1	
Type of antibiotic prophylaxis			
- single dose	20	0	0.568
- multiple dose	53	4	
Duration of multiple dose			0.916

CHAPTER V

DISCUSSION

5.1 The Appropriateness of antibiotic prophylaxis in orthognathic surgery

In this study, 3-year prevalence of surgical site infection following orthognathic surgery who received antibiotic prophylaxis was 1.79% (or 0.6% per year). The infection rate in this study was low and relative to previous study (0.46-1.88% per year) (15, 38, 61-63, 73). Therefore, the use of antibiotic prophylaxis was a promising intervention in reduction of post-operative infection following orthognathic surgery. As shown in Peterson's study (33), prophylactic antibiotic administration could reduce the infection rate in the intraoral surgery, as a clean-contaminated wound, from 10-15% to less than 1%. Also in systematic review by Bay (55), the infection rate of trans-oral orthognathic surgery was 0-18% in patients who received a prophylactic antibiotic agent while it could be 53% in non-prophylactic patients. Focusing on non-prophylactic situation, surgeons want to reduce the risk of postoperative infection. All cases underwent orthognathic surgery in the Faculty of Dentistry, Chulalongkorn University must receive antibiotic prophylaxis. As a result of this study, prevalence of infection in non-prophylactic case could not be evaluated.

5.2 Infection following maxillary surgery

For the maxilla, a patient (patient LD) who received a single-dose amoxicillin-clavulanate, manifested signs of the left buccal space abscess. An intraoral examination showed a flap dehiscence at the left posterior maxilla. This case underwent a bimaxillary surgery that usually involved a maxillary sinus. Both maxillary sinus was cut through during Le Fort I osteotomy. There was a blood collection which was controlled by pressure or hemostatic agent. As a consequence, the environment within the sinus cavity was change due to direct communication between oral and antral cavities. Endogenous bacteria of the maxillary sinus could be an inevitable source of infection, leading to postoperative bacterial maxillary sinusitis and/or surgical site infection at the maxilla. Furthermore, some bacterial species in the maxillary sinus

including *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*, showed resistance to penicillin, therefore the use of amoxicillin-clavulanate as prophylactic and therapeutic agent was appropriate (28).

5.3 Infection following mandibular surgery

Two patients (patient CW and PP) received multiple-dose penicillin G prophylaxis. One (patient CW) was found the right submandibular and lateral pharyngeal swelling with an elevated body temperature to 38.1 $^{\circ}$C on the 4th postoperative day. Other signs of infection like trismus and dysphagia were also found. The patient was treated with stitch removal, copious saline irrigation and given 5-day oral clindamycin. Another (patient PP) had an abscess at the vestibule of lower right premolar and retromolar region. Both cases suggested that the infection had a tendency to occur in the sagittal split site. To concentrate on the anatomical aspect, the mandible only had a major blood supply from inferior alveolar artery which was fewer than maxilla. Oral mucosa of the mandible was supplied by lingual and facial arteries. The gravitational force and poor cleaning efficacy during intermaxillary fixation also facilitated a deposition of saliva and food debris in the osteotomy site. According to the evidences mentioned above, it could be implied that the mandible was generally more susceptible to infection than maxilla (58, 68, 74).

5.4 Single-dose vs. multiple-dose antibiotic prophylaxis

The infection rates were 3.13% in single-dose group and 1.47% in multiple-dose group. Nevertheless, no significant difference was found between the two groups. This study demonstrated the efficacy of single-dose regimen had no different prophylactic effect compared to a multiple-dose regimen in both single-jaw (p = 0.753; Fisher's exact test) or bimaxillary surgery (p = 0.275; Fisher's exact test). Furthermore, a prolonged duration of antibiotic prophylaxis did not alter the rate infection (p = 0.811; Mann-Whitney test). This could be implied that single-dose prophylaxis was effective and sufficient in patient underwent orthognathic surgery

There have been no definitive consensus concerning the proper duration of antibiotic prophylaxis in orthognathic surgery. There are some studies in the online

database. The systematic review of 7 randomized controlled trials (472 participants) concluded a better outcome of multiple-day over one-day regimens, but did not demonstrate value of single-dose versus one-day prophylaxis (72). Only two studies of this review did a comparison between single-dose and single-day regimens and revealed no significant advantage of single-day over single-dose (36, 67). The systematic reviews by Tan *et al.* in 2011 and Oomens *et al.* in 2014 concluded that there was a greater benefit of the single-dose preoperative over extended dose for post-operative prophylaxis (48, 49). However, no study directly compared between single-dose and extended antibiotic prophylaxis. Our study conducted an observation in this gap and showed no significant difference. Due to retrospective design of this study, a RCT would be more relevant to support the result.

5.5 Other contributing factors of surgical site infection in orthognathic surgery

Longer operation time was presented in orthognathic surgery due to complicated hard tissue management. Most of the patients were young adult with healthy or non-immunocompromised systemic disease. Some medical conditions such as Thalassemia and Glucose-6-phosphate dehydrogenase deficiency (G-6-PD) could increase the risk and severity of infection (75). Four patients with thalassemia trait and three G-6-PD patients were found in this study. Regarding to the patients with abnormalities in red blood cells, hemoglobin concentration lower than 12-13 g/dl was considered as guideline for diagnosing an anemia (76). At least 10 g/dl hemoglobin level was accepted before elective surgery (77). The patient had 10.7-15 g/dl hemoglobin concentration, 35.1-45.6% Hematocrit, and 4.37-6.01 million red blood cells/mm^3. Two patients found hypochromic microcytic anemia while the others were not. ASA score were established from these medical condition and used to compare among each patient. However, our study found no significant association between these systemic conditions and the postoperative infection.

Other contributing factors might lead to the postoperative infection. For autogenous bone grafting and bad splitting, our study showed no association between bone grating, bad split and surgical site infection. A half of infected patients had a higher perioperative blood loss than mean total blood loss (323 and 757 ml for single

and two-jaw operation). If excessive blood loss occurred, oxygen concentration would decrease and disturb a normal cellular function. Peterson suggested that the operation time longer than 180 minutes had a tendency of infection from tissue traumatization. The longer operation time could increase the risk of infection (15). In our study, mean operation time of single-jaw (194 minutes) and bimaxillary (340 minutes) surgery was higher than the recommended time from Peterson's study. However, the operation time in infected patients was lower than 180 minutes except one patient (patient LD, 285 minutes) who underwent the bimaxillary surgery.

5.6 Rationale antibiotic use

There were no sign of adverse reaction from the patients in this study. An administration of broad-spectrum antibiotic, primarily clindamycin and beta-lactam derivatives, increased the risk of *Clostridium difficile* associated diarrhea. Hansen et al. reported that a patient underwent Le Fort I osteotomy developed *C. difficile* colitis on the 8th postoperative day by the prophylactic administration of the 1st generation cephalosporin perioperatively (78). While other studies did not demonstrate that none of the patients developed such adverse reactions following antibiotic prophylaxis (36, 79). In general, the prophylactic antibiotic was administered as a brief course. The risk of antibiotic use in this purpose had a low risk from adverse drug reaction. However, due to the previous report on the adverse reaction, prophylactic antibiotic may not be absolutely safe and should be used with a great caution.

One of the limitations in this study was the inability to trace back from the records whether patients complied with the surgeons' antibiotic prescription. Patient compliance should be considered as an important factor for the successful treatment. At Chulalongkorn University Dental hospital, surgeon usually prescribed additional oral antibiotic at least 5 days following the final dose of intravenous antibiotic. As a cause, examiners might not have recognized the importance of patients' compliance, with no record about patient compliance with the prescription. Other factors related to compliance could affect the treatment results. Duration of antibiotic use was inversely correlated with patient compliance, showed a better compliance in regimen shorter than 7 days significantly (80). Blinder et al. also found that only one-third of oral surgical

patients complied a prescribed antibiotic following verbal and written instructions, whereas the other two-third did not (81). Thus, doctor-patient communication and record in the follow-up visit did play a crucial role in the appropriate antibiotic administration.

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CHAPTER VI
CONCLUSION

This study demonstrated multiple-dose antibiotic prophylaxis did not have better benefits than single-dose antibiotic prophylaxis in prevention of postoperative infection in orthognathic surgery. The single-dose antibiotic prophylaxis is sufficient in the prevention of surgical site infection. This study can be a strong scientific evidence for the rationale antibiotic use in orthognathic surgery not only to save the country economy, but also patient safety from adverse drug reaction.

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APPENDIX

Chi-square test between gender and SSI

Crosstab

Count

		SSI		Total
		0	1	
Gender	F	100	1	101
	M	65	2	67
Total		165	3	168

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.914[a]	1	.339		
Continuity Correction[b]	.130	1	.718		
Likelihood Ratio	.892	1	.345		
Fisher's Exact Test				.564	.349
N of Valid Cases	168				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.20.

b. Computed only for a 2x2 table

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Phi	.074	.339
	Cramer's V	.074	.339
	Contingency Coefficient	.074	.339
N of Valid Cases		168	

Chi-square test between age, total operation time, total blood loss, duration of multiple dose prophylaxis and SSI

Case Processing Summary

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Age	136	81.0%	32	19.0%	168	100.0%
Op time	136	81.0%	32	19.0%	168	100.0%
Blood loss	136	81.0%	32	19.0%	168	100.0%
duration_multidose	136	81.0%	32	19.0%	168	100.0%

Descriptives

			Statistic	Std. Error
Age	Mean		26.25	.502
	95% Confidence Interval for Mean	Lower Bound	25.26	
		Upper Bound	27.24	
	5% Trimmed Mean		25.81	
	Median		24.50	
	Variance		34.322	
	Std. Deviation		5.859	
	Minimum		18	
	Maximum		52	
	Range		34	
	Interquartile Range		7	
	Skewness		1.347	.208
	Kurtosis		2.266	.413
Op time	Mean		277.17	10.986
	95% Confidence Interval for Mean	Lower Bound	255.44	
		Upper Bound	298.90	
	5% Trimmed Mean		270.56	
	Median		257.50	
	Variance		16415.075	

	Std. Deviation	128.121	
	Minimum	90	
	Maximum	640	
	Range	550	
	Interquartile Range	195	
	Skewness	.675	.208
	Kurtosis	-.274	.413
Blood loss	Mean	547.06	32.830
	95% Confidence Interval for Mean — Lower Bound	482.13	
	95% Confidence Interval for Mean — Upper Bound	611.99	
	5% Trimmed Mean	503.68	
	Median	400.00	
	Variance	146583.878	
	Std. Deviation	382.863	
	Minimum	100	
	Maximum	2200	
	Range	2100	
	Interquartile Range	400	
	Skewness	1.863	.208
	Kurtosis	4.435	.413
duration_multidose	Mean	10.30	.191
	95% Confidence Interval for Mean — Lower Bound	9.92	
	95% Confidence Interval for Mean — Upper Bound	10.68	
	5% Trimmed Mean	10.24	
	Median	10.00	
	Variance	4.938	
	Std. Deviation	2.222	
	Minimum	3	
	Maximum	20	
	Range	17	
	Interquartile Range	2	
	Skewness	.652	.208
	Kurtosis	3.089	.413

Tests of Normality

	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Age	.164	136	.000	.891	136	.000
Op time	.119	136	.000	.941	136	.000
Blood loss	.181	136	.000	.812	136	.000
duration_multidose	.163	136	.000	.936	136	.000

a. Lilliefors Significance Correction

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of Age is the same across categories of Infect_no_sinus.	Independent-Samples Mann-Whitney U Test	.509	Retain the null hypothesis.
2	The distribution of Op time is the same across categories of Infect_no_sinus.	Independent-Samples Mann-Whitney U Test	.030	Reject the null hypothesis.
3	The distribution of Blood loss is the same across categories of Infect_no_sinus.	Independent-Samples Mann-Whitney U Test	.871	Retain the null hypothesis.
4	The distribution of duration_multidose is the same across categories of Infect_no_sinus.	Independent-Samples Mann-Whitney U Test	.209[1]	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

[1] Exact significance is displayed for this test.

Chi-square test between ASA class and SSI

Crosstab

Count

		SSI		Total
		0	1	
ASA	1	156	3	159
	2	9	0	9
Total		165	3	168

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.173[a]	1	.678		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.333	1	.564		
Fisher's Exact Test				1.000	.847
Linear-by-Linear Association	.172	1	.678		
N of Valid Cases	168				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .16.

b. Computed only for a 2x2 table

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Phi	-.032	.678
	Cramer's V	.032	.678
	Contingency Coefficient	.032	.678
N of Valid Cases		168	

Chi-square test between smoking and SSI

Crosstab

Count

		SSI		Total
		0	1	
Active smoker	0	163	3	166
	1	2	0	2
Total		165	3	168

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.037[a]	1	.848		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.073	1	.788		
Fisher's Exact Test				1.000	.964
Linear-by-Linear Association	.037	1	.848		
N of Valid Cases	168				

a. 3 cells (75.0%) have expected count less than 5. The minimum expected count is .04.

b. Computed only for a 2x2 table

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Phi	-.015	.848
	Cramer's V	.015	.848
	Contingency Coefficient	.015	.848
N of Valid Cases		168	

Chi-square test between number of operated jaw and SSI

Crosstab

Count

		SSI		Total
		0	1	
Op jaw	1	97	2	99
	2	68	1	69
Total		165	3	168

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.076[a]	1	.783		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.077	1	.781		
Fisher's Exact Test				1.000	.633
Linear-by-Linear Association	.075	1	.784		
N of Valid Cases	168				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.23.

b. Computed only for a 2x2 table

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Phi	-.021	.783
	Cramer's V	.021	.783
	Contingency Coefficient	.021	.783
N of Valid Cases		168	

Chi-square test between blood transfusion and SSI

Crosstab

Count

		SSI		Total
		0	1	
Blood_trans	0	129	3	132
	1	36	0	36
Total		165	3	168

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.833[a]	1	.361		
Continuity Correction[b]	.041	1	.839		
Likelihood Ratio	1.462	1	.227		
Fisher's Exact Test				1.000	.483
Linear-by-Linear Association	.828	1	.363		
N of Valid Cases	168				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .64.

b. Computed only for a 2x2 table

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Phi	-.070	.361
	Cramer's V	.070	.361
	Contingency Coefficient	.070	.361
N of Valid Cases		168	

Chi-square test between bone grafting and SSI

Crosstab

Count

		SSI		
		0	1	Total
Bone_graft	0	148	3	151
	1	17	0	17
Total		165	3	168

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.344[a]	1	.558		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.646	1	.421		
Fisher's Exact Test				1.000	.725
Linear-by-Linear Association	.342	1	.559		
N of Valid Cases	168				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .30.

b. Computed only for a 2x2 table

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Phi	-.045	.558
	Cramer's V	.045	.558
	Contingency Coefficient	.045	.558
N of Valid Cases		168	

Chi-square test between bad split and SSI

Crosstab

Count

		SSI		Total
		0	1	
Bad_split	0	152	3	155
	1	13	0	13
Total		165	3	168

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.256[a]	1	.613		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.488	1	.485		
Fisher's Exact Test				1.000	.784
Linear-by-Linear Association	.255	1	.614		
N of Valid Cases	168				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .23.

b. Computed only for a 2x2 table

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Phi	-.039	.613
	Cramer's V	.039	.613
	Contingency Coefficient	.039	.613
N of Valid Cases		168	

Chi-square test between type of antibiotic prophylaxis and SSI

Crosstab

Count

		SSI		Total
		0	1	
Prophylaxis type	1	31	1	32
	2	134	2	136
Total		165	3	168

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.404[a]	1	.525		
Continuity Correction[b]	.000	1	1.000		
Likelihood Ratio	.350	1	.554		
Fisher's Exact Test				.472	.472
Linear-by-Linear Association	.402	1	.526		
N of Valid Cases	168				

a. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .57.

b. Computed only for a 2x2 table

Symmetric Measures

		Value	Approx. Sig.
Nominal by Nominal	Phi	-.049	.525
	Cramer's V	.049	.525
	Contingency Coefficient	.049	.525
N of Valid Cases		168	

<u>Chi-square test between number of operated jaw and SSI (split case by type of prophylaxis)</u>

Prophylaxis type = 1

Case Processing Summary[a]

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Op jaw * SSI	32	100.0%	0	0.0%	32	100.0%

a. Prophylaxis type = 1

Op jaw * SSI Crosstabulation[a]

Count

		SSI		Total
		0	1	
Op jaw	1	13	0	13
	2	18	1	19
Total		31	1	32

a. Prophylaxis type = 1

Chi-Square Tests[a]

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.706[b]	1	.401		
Continuity Correction[c]	.000	1	1.000		
Likelihood Ratio	1.065	1	.302		
Fisher's Exact Test				1.000	.594
Linear-by-Linear Association	.684	1	.408		
N of Valid Cases	32				

a. Prophylaxis type = 1

b. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .41.

c. Computed only for a 2x2 table

Symmetric Measures[a]

		Value	Approx. Sig.
Nominal by Nominal	Phi	.149	.401
	Cramer's V	.149	.401
	Contingency Coefficient	.147	.401
N of Valid Cases		32	

a. Prophylaxis type = 1

Prophylaxis type = 2

Case Processing Summary[a]

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Op jaw * SSI	136	100.0%	0	0.0%	136	100.0%

a. Prophylaxis type = 2

Op jaw * SSI Crosstabulation[a]

Count

		SSI		Total
		0	1	
Op jaw	1	84	2	86
	2	50	0	50
Total		134	2	136

a. Prophylaxis type = 2

Chi-Square Tests[a]

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.180[b]	1	.277		
Continuity Correction[c]	.121	1	.728		
Likelihood Ratio	1.851	1	.174		
Fisher's Exact Test				.532	.398
Linear-by-Linear Association	1.171	1	.279		
N of Valid Cases	136				

a. Prophylaxis type = 2

b. 2 cells (50.0%) have expected count less than 5. The minimum expected count is .74.

c. Computed only for a 2x2 table

Symmetric Measures[a]

		Value	Approx. Sig.
Nominal by Nominal	Phi	-.093	.277
	Cramer's V	.093	.277
	Contingency Coefficient	.093	.277
N of Valid Cases		136	

a. Prophylaxis type = 2

Chi-square test between gender and maxillary sinusitis

Crosstab[a]

Count

		Sinusitis		
		0	1	Total
Gender	F	43	3	46
	M	30	1	31
Total		73	4	77

a. Op_Maxilla_01 = 1.0

Chi-Square Tests[a]

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.408[b]	1	.523		
Continuity Correction[c]	.013	1	.908		
Likelihood Ratio	.433	1	.510		
Fisher's Exact Test				.644	.468
N of Valid Cases	77				

a. Op_Maxilla_01 = 1.0

b. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.61.

c. Computed only for a 2x2 table

Symmetric Measures[a]

		Value	Approx. Sig.
Nominal by Nominal	Phi	-.073	.523
	Cramer's V	.073	.523
	Contingency Coefficient	.073	.523
N of Valid Cases		77	

a. Op_Maxilla_01 = 1.0

Chi-square test between age and maxillary sinusitis

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of Age is the same across categories of Sinusitis.	Independent-Samples Mann-Whitney U Test	.248[1]	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

[1] Exact significance is displayed for this test.

Chi-square test between smoking status and maxillary sinusitis

Case Processing Summary[a]

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
smoking * Sinusitis	77	100.0%	0	0.0%	77	100.0%

a. Op_Maxilla_01 = 1.0

Crosstabulation[a]

Count

		Sinusitis		Total
		0	1	
Smoking	0	73	3	76
	1	0	1	1
Total		73	4	77

a. Op_Maxilla_01 = 1.0

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Chi-Square Tests[a]

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	18.490[b]	1	.000		
Continuity Correction[c]	4.130	1	.042		
Likelihood Ratio	6.176	1	.013		
Fisher's Exact Test				.052	.052
Linear-by-Linear Association	18.250	1	.000		
N of Valid Cases	77				

a. Op_Maxilla_01 = 1.0

b. 3 cells (75.0%) have expected count less than 5. The minimum expected count is .05.

c. Computed only for a 2x2 table
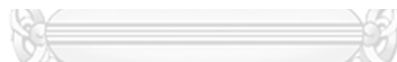
Symmetric Measures[a]

		Value	Approx. Sig.
Nominal by Nominal	Phi	.490	.000
	Cramer's V	.490	.000
	Contingency Coefficient	.440	.000
N of Valid Cases		77	

a. Op_Maxilla_01 = 1.0

Chi-square test between type of maxillary surgery and maxillary sinusitis

Case Processing Summary[a]

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
Op Maxilla * Sinusitis	77	100.0%	0	0.0%	77	100.0%

a. Op_Maxilla_01 = 1.0

Op Maxilla * Sinusitis Crosstabulation[a]

Count

		Sinusitis		Total
		0	1	
Op Maxilla	LFI	48	2	50
	Multipiece LFI	24	2	26
	UPSO	1	0	1
Total		73	4	77

a. Op_Maxilla_01 = 1.0

Chi-Square Tests[a]

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.529[b]	2	.768
Likelihood Ratio	.552	2	.759
Linear-by-Linear Association	.129	1	.720
N of Valid Cases	77		

a. Op_Maxilla_01 = 1.0

b. 4 cells (66.7%) have expected count less than 5.

The minimum expected count is .05.

Symmetric Measures[a]

		Value	Approx. Sig.
Nominal by Nominal	Phi	.083	.768
	Cramer's V	.083	.768
	Contingency Coefficient	.083	.768
N of Valid Cases		77	

a. Op_Maxilla_01 = 1.0

Chi-square test between type of antibiotic prophylaxis and maxillary sinusitis

Crosstab[a]

Count

		Sinusitis		Total
		0	1	
Prophylaxis type	1	20	0	20
	2	53	4	57
Total		73	4	77

a. Op_Maxilla_01 = 1.0

Chi-Square Tests[a]

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	1.480[b]	1	.224		
Continuity Correction[c]	.398	1	.528		
Likelihood Ratio	2.482	1	.115		
Fisher's Exact Test				.568	.292
Linear-by-Linear Association	1.461	1	.227		
N of Valid Cases	77				

a. Op_Maxilla_01 = 1.0

b. 2 cells (50.0%) have expected count less than 5. The minimum expected count is 1.04.

c. Computed only for a 2x2 table

Symmetric Measures[a]

		Value	Approx. Sig.
Nominal by Nominal	Phi	.139	.224
	Cramer's V	.139	.224
	Contingency Coefficient	.137	.224
N of Valid Cases		77	

a. Op_Maxilla_01 = 1.0

Chi-square test between duration of post-operative prophylaxis and maxillary sinusitis

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of Age is the same across categories of Sinusitis.	Independent-Samples Mann-Whitney U Test	$.248_1$	Retain the null hypothesis.
2	The distribution of Op time is the same across categories of Sinusitis.	Independent-Samples Mann-Whitney U Test	$.443_1$	Retain the null hypothesis.
3	The distribution of Blood loss is the same across categories of Sinusitis.	Independent-Samples Mann-Whitney U Test	$.075_1$	Retain the null hypothesis.
4	The distribution of duration_multidose is the same across categories of Sinusitis.	Independent-Samples Mann-Whitney U Test	$.916_1$	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

$_1$Exact significance is displayed for this test.

VITA

Teeraphat Pochana grew up in Bangkok, Thailand in August 1989 and graduated from the Faculty of Dentistry, Chulalongkorn University in March 2014. He spent two years working in Nakhon Prathom where he was a general practitioner at Samphran Hospital. In 2016 he started his Master's Degree in oral and maxillofacial surgery at Chulalongkorn University.