Surgical Site Infection Following Orthognathic Surgery

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Abstract

The aim of this study is twofold: to compare the prophylactic effect of single versus multiple dose antibiotic regimens and to determine factors related to a surgical site infection in orthognathic surgery. 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 information, American Society of Anesthesiologists (ASA)-classified past medical history, surgical procedure, antibiotic regimen, postoperative infection, and maxillary rhinosinusitis. The records also contained 30-day follow-up information, following Centers for Disease Control and Prevention criteria for surgical site infection. Of the 168 patients, three developed signs of infection and four presented maxillary rhinosinusitis. In the infected group, one received a 1.2g single-dose intravenous amoxicillin-clavulanate at induction while the remaining two patients were administered with a 1.2g intravenous penicillin G every 4 hours perioperatively and one out of two received 1g oral amoxicillin twice a day postoperatively. No significant association was found between the type of prophylaxis and 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 variables namely age, gender, ASA score, smoking status, number of operated jaw(s), blood loss, blood transfusion, bone grafting and bad split. Of significance, there was a significant relationship between active smokers and maxillary rhinosinusitis (p = 0.047). The results suggest that the single-dose antibiotic prophylaxis can be sufficient in preventing infections. Active smoking should also be considered a significant risk for postoperative maxillary rhinosinusitis.

Keywords**:** *antibiotic prophylaxis, surgical site infection, smoking, maxillary rhinosinusitis, orthognathic surgery*

1. Introduction

Dentofacial deformities can cause several problems including improper function and unaesthetic appearance. Correction of these problems requires an integrated approach between an orthodontic treatment to decompensate for natural adaptation and an orthognathic surgery to reposition facial skeleton to a proper relationship (Pogrel, Kahnberg, & Andersson, 2014). However, one of the most common complications of orthognathic surgery is postoperative infection with prevalence as high as 53% (Bays & Bouloux, 2003). 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. Oral infection is polymicrobial in nature which is comprised of Gram-positive cocci, *Streptococci* in particular, and anaerobes. Most of these bacteria are sensitive to penicillins (Peterson, 1990). However, *Bacteroides*, and normal microflora in the maxillary sinus, namely *Streptococcus pneumoniae*, *Haemophillus influenza*, and *Moraxella catarrhalis*, are resistant to penicillins. Thus, the integration of a penicillin derivative and beta-lactamase inhibitor like amoxicillin-clavulanate is usually selected (Rosenfeld et al., 2015).

There are two critical issues that motivated the present study. First, previous findings on antibiotic prophylactic regimens have yielded mixed results. It has been demonstrated that the benefits of preoperative antibiotic administration that may last for as long as two hours depending on pharmacological properties of that antibiotic agent (Classen et al., 1992; World Health Organization, 2016). Retrospectively, one group of studies has shown that single-dose preoperative antibiotic prophylaxis is sufficient (e.g., Lindeboom, Baas, & Kroon, 2003; Zijderveld, Smeele, Kostense, & Tuinzing, 1999) while another has demonstrated superior benefits of multiple-dose perioperative prophylaxis with duration for 2-4 days (e.g., Bentley, Head, & Aiello, 1999; Jansisyanont, Sessirisombat, Sastravaha, & Bamroong, 2008). 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 (Berrios-Torres et al., 2017). Nonetheless, there has been no study to date

directly comparing single-dose amoxicillin-clavulanate with conventional prophylaxis. We took the first step in this direction by performing a retrospective study which offers insights into the effectiveness of single dose amoxicillin-clavulanate versus conventional multiple-dose penicillin.

Second, surgical wound infection can be compounded by various factors. To this end, the CDC highlighted factors other than antibiotic prophylaxis that affect the risk of infection. They include age, nicotine consumption, systemic condition, specific typed surgical procedure, and surgical techniques (Mangram, Horan, Pearson, Silver, & Jarvis, 1999). A meta-analysis revealed the incidence of surgical site infection in developing countries was greater than developed countries (Allegranzi et al., 2011). However, there has been only a handful of epidemiological studies from the South East Asian region (World Health Organization, 2016). Thus, we conduct a retrospective cohort study to first assess the prevalence of these factors.

2. Objectives

The objectives of the present study were as follows:

1. To compare the anti-infective effect of single-dose versus multiple-dose antibiotic prophylaxis; and

2. To determine the other factors impacted on surgical site infection including age, gender, American Society of Anesthesiologists (ASA) score, smoking status, number of operated jaw(s), total operation time, total blood loss, blood transfusion, bone grafting, and bad split in orthognathic surgery patient.

3. Materials and Methods

This study was performed in a retrospective manner. Medical records of patients who underwent an orthognathic surgery at the Faculty of Dentistry, Chulalongkorn University between 2014 and 2016 were retrieved. We excluded records from patients who were not available for at least 30-day follow-up postoperatively. Likewise, for patients who either demonstrated marked healing impairment, attended fewer than 3 follow-ups in a month, or underwent distraction osteogenesis (DO) and surgically assisted rapid palatal expansion (SARPE), their records were excluded.

3.1 Medical data collection

In-patient and out-patient medical records were screened and the following information was extracted:

1) General data: hospital number, gender, age, ASA classification, and history of smoking.

2) Surgical procedure: maxillary and mandibular procedures, number of operated jaw(s), total operation time, total amount of blood loss, blood transfusion, bone grafting, and marked bad split.

3) Prophylactic antibiotic regimen: class of antibiotic, dosage form, dose, route, duration, frequency, and type of prophylaxis (single/multiple).

4) Follow-up visit: at least one visit per week for at least three weeks per month.

5) Surgical site infection and acute maxillary rhinosinusitis: area, date, and surgical and therapeutic management.

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 a sign of infection during a prophylactic period, the antibiotic administration following the infectious exacerbation was defined as an antibiotic therapy.

3.2 Diagnostic criteria for surgical site infection and maxillary rhinosinusitis

Current CDC diagnostic criteria updated in 2016 were used to evaluate the surgical site infection that followed orthognathic surgery within the 30-day period. One of the following situations must be met: purulent discharge, identified microorganism from fluid or tissue, or antibiotic administration within 2 days of symptom worsening. For maxillary rhinosinusitis, purulent discharge with nasal congestion/obstruction or headache/facial pain/pressure/fullness must be met.

3.3 Data analysis

Descriptive statistics were calculated to display patient characteristics. Due to small samples in some cases (n < 5), the relationships between type of antibiotic prophylaxis and postoperative infection were tested using a Fisher's exact test. This test was also applied to other categorical variables, namely gender, ASA class, smoking status, number of operated jaw, blood transfusion, bone grafting and bad split. For continuous variables (e.g., age, total operation time, total blood loss, duration of postoperative prophylaxis in multiple dose group), a Mann-Whitney test was employed since normality assumptions were violated. Moreover, the relationships between age, gender, smoking status, type of antibiotic prophylaxis, and maxillary rhinosinusitis was tested using Fisher's exact test.

4. Results

257 patients' medical records were screened. 85 patients were excluded due to insufficient data collection or follow-up. 4 patients were excluded because DO (n = 3) and SARPE (n = 1) were performed. As a result, 168 records were included (67 male and 101 female). Patient age ranged from 17 to 52 years with a mean 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; the others showed a significant underlying disease, namely thalassemia trait (n = 4) and G-6-PD (n = 3), which compromised the healing process. 99 patients were operated in one-jaw surgery and 69 patients underwent bimaxillary surgery. Table 1 presents surgical procedures performed in the patients. Mean 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. Mean total blood loss was 502 ± 368.86 ml (one-jaw procedure = 327 ± 169.36; two-jaw procedure = 752 ± 430.23); 36 patients needed blood transfusion. The autogenous bone grafting materials were used in 17 patients: mandible (n = 12), mandible (n = 3), and both jaws (n = 2). Bad bone split was also found in four for maxilla and nine for mandible.

Table 1 Orthognathic surgery performed during 2014-2016

Operation	n
One-jaw surgery	99
A. Maxilla	
- Le Fort	7
- Segmental Le Fort	1
B. Mandible	
- BSSRO	76
- Genioplasty	1
- Lower anterior subapical osteotomy	1
- BSSRO and genioplasty	12
- BSSRO and lower anterior subapical osteotomy	1
Two-jaw surgery	69
- Le Fort and BSSRO	38
- Le Fort and BSSRO and genioplasty	3
- Le Fort and BSSRO and lower anterior subapical osteotomy	2
- Segmental Le Fort and BSSRO	15
- Segmental Le Fort and BSSRO and genioplasty	3
- Segmental Le Fort and BSSRO and lower anterior subapical osteotomy	7
- Upper posterior subapical osteotomy and BSSRO	1

Abbreviation: Le Fort (Le Fort I osteotomy), BSSRO (bilateral sagittal split ramus osteotomy)

Per type of prophylaxis (see Table 2), 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 perioperatively received 1.2g IV penicillin G, 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 1.2g IV penicillin G

and 1.2g IV amoxicillin-clavulanate (n = 10) or 600mg IV clindamycin (n = 1) if indicated. In case of prolonged length of operation, the patients were re-dosed with the same antibiotic given at induction depending on its half-life. Penicillin G dose was repeated every 4 hours while clindamycin was infused every 6 hours. None in amoxicillin-clavulanate regimen was re-administered perioperatively. Postoperative prophylaxis was given in the multiple-dose group. The same agent was infused until the feeding was possible. Penicillin G and amoxicillin-clavulanate were extended respectively with 1g oral amoxicillin and 1g amoxicillin-clavulanate twice a day whereas 300mg clindamycin was given orally thrice daily. Each agent was given for at least 7 days after discharge. A range of multiple-dose antibiotic administration was between 3 and 20 days postoperatively (Figure 1). Patients in multiple-dose regimen were continuously infused with a prophylactic antibiotic until oral feeding was possible. The intravenous antibiotic agent was replaced by an oral antibiotic. Prolongation of intravenous and oral antibiotic prophylaxis in multiple-dose group were shown in Table 2

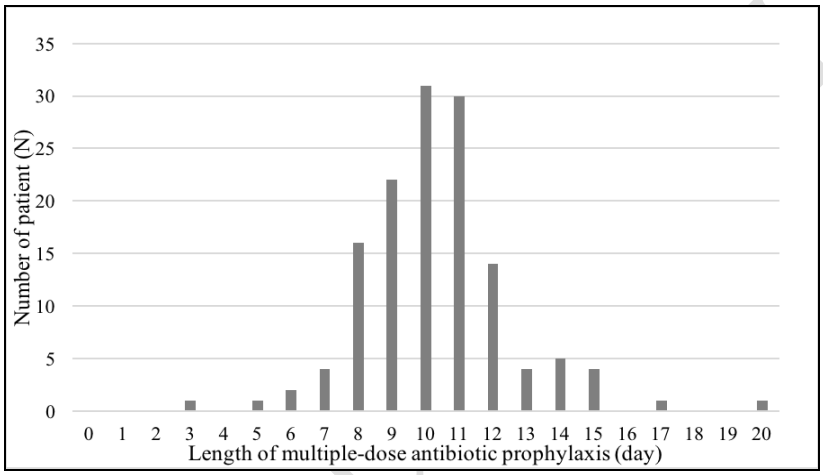

Figure 1 Length of multiple-dose antibiotic prophylaxis in orthognathic surgical patients

Table 2 Length 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				

Per CDC criteria, three patients had signs of infection (see Table 3). Significant difference was found between total operation time and post-operative infection (p = 0.030, Mann-Whitney test). No significant relationship was found between surgical site infection and 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, different antibiotic regimens (Table 4). Concerning the maxillary sinus-related procedure, four patients undergoing bimaxillary surgery showed signs of acute maxillary rhinosinusitis. They received multiple-dose penicillin prophylaxis ranging from 5 to 17 days postoperatively. There were statistically significant associations between patients' smoking behavior and acute maxillary rhinosinusitis (p = 0.046, Fisher's exact test); current smokers were more likely to exacerbate the postoperative maxillary rhinosinusitis. (Table 5).

Table 3 Infected patients underwent orthognathic surgery

Patient characteristics	Details of operation	Antibiotic prophylaxis	Signs of infection	Management
Patient LD male 21 years old	Le Fort I osteotomy and BSSRO 285 minutes blood loss 1100 ml	1.2 g amoxicillin-clavulanate IV at induction	At day 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 minutes blood loss 500 ml	1.0 g penicillin G at induction and 3 days post-operatively	At day 4 -Right parapharyngeal 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 minutes blood loss 200 mL	1.0 g penicillin G at induction and 3 days post-operatively and 500 mg oral amoxicillin three times daily for additional 7 days	At day 12 - Vestibular space abscess at right mandible - Right retromolar fistula	- stitch off - copious irrigation with normal saline - given 1g oral amoxicillin-clavulanate for 7 days

5. Discussion

In 1990, Peterson proposed the principles of antibiotic prophylaxis for oral and maxillofacial surgery. Prophylactic antibiotic administration could reduce the infection rate of the intra-oral surgery from 10-15% to under 1%. 3-year prevalence of surgical site infection in this study was 1.79% (or 0.6 for average prevalence per year). Same as previous findings, the antibiotic prophylaxis yielded an effectively anti-infective benefit for orthognathic surgery. As one recommendation, beta-lactam penicillin was administered perioperatively; a final dose was given at a recovery room (Peterson, 1990). This principle has been widely accepted. Nevertheless, because orthognathic surgery usually involved the maxillary sinus, beta-lactamase producing bacteria from the sinus might be an inevitable source of infection (Rosenfeld et al., 2015). Moreover, in two studies that examined the microbiologic culture of patients' abscess (Baqain, Hyde, Patrikidou, & Harris, 2004; Wahab, Narayanan, Nathan, & Madhulaxmi, 2013), *Bacteroides* species was found in seven out of eleven patients and the remaining was mixed culture of *Staphylococcus aureus* and anaerobes. Penicillin has been selected as an antibiotic of choice for the anaerobic bacterial infection. Unfortunately, many anaerobes including *Bacteroides* and *S. aureus* could produce beta-lactamase; thus, the co-formulation regimen like amoxicillin-clavulanic acid could play an important role in both situations (Brook, Wexler, & Goldstein, 2013).

Table 4 Surgical site infection in patients underwent orthognathic surgery list by factors.

Characteristic	Non infected n.	Infected n (% compared to 168)	*p*-value
Gender			
- Male	65	2 (1.19)	0.349
- Female	100	1 (0.60)	
Age			0.509
ASA classification			
- class I	156	3 (1.79)	0.847
- class II	9	0	
Smoking			
- former/non-smoker	163	3 (1.79)	0.964
- active smoker	2	0	
Number of operated jaw			
- one jaw	97	2 (1.19)	0.538
- two jaw	68	1 (0.60)	
Operation time			0.030*
Blood loss			0.871
Blood transfusion			
- no	129	3 (1.79)	0.483
- yes	36	0 (0.60)	
Bone grafting			
- no	148	3 (1.79)	0.725
- yes	17	0	
Bad split			
- no	152	3 (1.79)	0.784
- yes	13	0	
Type of antibiotic prophylaxis			0.472
- single dose	31	1 (0.60)	
- multiple dose	134	2 (1.19)	
Duration of multiple dose			0.209

Table 5 Acute maxillary rhinosinusitis in patients underwent orthognathic surgery list by factors

Characteristic	Non-sinusitis n	Sinusitis n (% compared to 168)	*p*-value
Gender			
- Male	66	1 (0.60)	0.476
- Female	98	3 (1.79)	
Age			0.256
Smoking			
- former/non-smoker	163	3 (1.79)	0.047*
- active smoker	1	1 (0.60)	
Type of antibiotic prophylaxis			0.453
- single dose	32	0	
- multiple dose	132	4 (2.38)	
Duration of multiple dose			0.606

Jansisyanont et al. (2008) directly compared penicillin and amoxicillin-clavulanate in perioperative and five-day prophylactic regimens and found that penicillin was appropriate in orthognathic surgery. Lindeboom et al. (2003) investigated the microbiologic culture of purulent secretion from infected patients who received clindamycin prophylaxis. The sensitivity test revealed penicillin-sensitive pathogens were successfully treated with 500 mg amoxicillin for 5 days. However, in the present study, the researchers

found that various antibiotic agents were used. Thus, an additional study comparing each antibiotic agent by controlling the similarity of other variables was needed.

There is no clear consensus concerning the proper duration of antibiotic prophylaxis with respect to orthognathic surgery. Cochrane systematic review of 7 randomized controlled trials (472 participants) demonstrated the advantages of multiday over one-day regimens, but the value of single-dose versus one-day prophylaxis was unresolved (Brignardello-Petersen et al., 2015). One limitation of Brignardello-Petersen *et al.*'s study was that one included study (Samman and Cheung, 2010) showed a high rate of infection (10 and 23 % in both antibiotic regimen groups) with reference to the estimated infection rate (10-15% without antibiotic) and the largest weight (63%) was given to Samman's study. Unfortunately, the researchers could not appraise this article further due to unknown source of publication. Only two of the included studies in this review paper performed a comparison between single-dose and single-day regimens and found no significant advantage of single-day over single-dose (Danda, Wahab, Narayanan, & Siddareddi, 2010; Lindeboom et al., 2003). No study directly compared between single-dose and extended prophylactic regimens, except our study with no significant difference found. With this summary, the RCT is needed to investigate the appropriateness of single-dose prophylaxis.

In this present study, we found none of the patients showed any signs of adverse effects (e.g., diarrhea, nausea, vomiting, or allergic reaction). A broad-spectrum antibiotic administration, primarily clindamycin and beta-lactam derivatives, increased the risk of *Clostridium difficile* associated diarrhea. Hansen, Pollan, and Fernando (2013) reported that a patient undergoing Le Fort I osteotomy developed *C. difficile* colitis on the 8th postoperative day during the prophylactic administration of the 1st generation cephalosporin perioperatively whereas other studies demonstrated that none of the patients expressed adverse reactions following antibiotic prophylaxis (Lindeboom et al., 2003; Tan, Lo, & Zwahlen, 2011). Consequently, the prophylactic antibiotic may not be entirely safe and should be used when indicated.

One of the limitations in this study was the inability to trace back from the records whether patients did follow the surgeons' antibiotic recommendation. Patient compliance should be considered as a significant factor for the successful prevention of surgical site infection. At Chulalongkorn University Dental Hospital, surgeons usually prescribe further 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, failing to record antibiotic consumption in the patients' medical chart. Other factors related to compliance could affect the treatment results. Duration of antibiotic use inversely correlated with patient compliance showed significantly better compliance in regimen shorter than 7 days (Kardas, 2002). Blinder, Rotenberg, Peleg, and Taicher (2001) also found that only one-third of oral surgical patients took prescribed antibiotic following verbal and written instructions while the majority of patients did not follow antibiotic instruction, consuming either shorter or longer duration depending on their severity of symptoms. Thus, doctor-patient communication did play a crucial role in the appropriate antibiotic administration.

To concentrate on the anatomical aspect, two infected patients in this study had a pus discharge in the mandibular region. Previous studies have attempted to describe the anatomically related contributing factors that the mandible had a fewer blood supply, moreover, the gravitational force facilitated a deposition of saliva and food debris in the mandibular osteotomy site, enhancing by poor cleaning efficacy during intermaxillary fixation. The mandible is more susceptible to infection than maxilla as a result (Davis, Gregoire, Davis, & Steeves, 2017; Wahab et al., 2013). However, the present study included various surgical operations, thus an experiment on the specific operation should be conducted.

Other contributing factors might lead to post-operative infection. Davis, Gregoire, Steeves, and Demsey (2016) found an association between a longer operation time and the risk of infection. Peterson suggested that the operation time longer than 180 minutes increased the incidence of infection (Peterson, 1990). In the present study, the significant association between total operation time and surgical site infection was found. The operation time in infected patients was below 180 minutes except one patient who underwent the bimaxillary surgery (285 minutes). An extended duration of surgery appeared to increase the tendency of surgical site infection from tissue traumatization. The significant relationship between smoking status and post-operative maxillary rhinosinusitis was also found. Cigarette smoking has been considered a risk factor for the impairment of oral wound healing and surgical site infection (Jones & Triplett, 1992; Kuhlefelt, Laine, Suominen, Lindqvist, & Thoren, 2012; Mangram et al., 1999). The rising of beta-

lactamase producing species like *S. aureus*, *M. catarrhalis* and *H. influenzae* was frequently found in smoking patients with acute maxillary rhinosinusitis (Brook et al., 2013), which referred to the importance of amoxicillin-clavulanate in sinus involved surgery and a smoking cessation before surgery.

5. Conclusion

We found that multiple-dose antibiotic prophylaxis did not yield greater benefits than single-dose prophylaxis. The single-dose antibiotic prophylaxis can be sufficient in the prevention of surgical site infections. The results thus provide support for a rational antibiotic use in surgical patients. Length of surgical operations had an impact on postoperative infection. Current smoking behavior should be considered as one significant infection risk. However, RCT should be conducted to further confirm our findings.

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