Antibiotic Prophylaxis for Orthognathic Surgery: A Prospective, Comparative, Randomized Study between Amoxicillin-Clavulanic Acid and Penicillin

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Objective: *The present study was designed to evaluate the prophylactic efficacy after the correction of dentofacial deformities between short- and long-term penicillin and amoxicillin-clavulanic acid.*
Material and Method: *The present study was prospective, randomized, and double blinded. Patients were separated into four groups randomly: short-term and long-term (5 days) penicillin and short-term and long-term (5 days) amoxicillin-clavulanic acid.*
Results: *One hundred twenty two patients were assigned randomly into the four groups. Infection developed in a patient in the short-term amoxicillin-clavulanic acid group and in a patient in the long-term penicillin group.*
Conclusion: *There were no differences in infection between the two groups of antibiotics. Based on the present study, short-term penicillin is still the most appropriate choice for prophylactic antibiotic in orthognathic surgery.*

Keywords: *Antibiotic prophylaxis, Orthognathic surgery*

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Orthognathic surgery is the art and science of combining orthodontics and oral and maxillofacial surgery to normalize the relationship of musculoskeletal, dento-osseous, and soft tissue deformities of the jaw and the craniofacial complex. Orthognathic surgery, though being of great benefit to dentofacial-deformed patients, like most other surgeries contains risks and complications from the surgery. Some are serious and uncontrollable and some are trivial and controllable. One of the complications that surgeons often encounter and try to avoid is infection. Intraoral orthognatic surgery is classified as a "clean-contaminated" operation for which it is accepted that the infection rate for such clean-contaminated operations in the head and neck region vary from 10-15%[1,2]. Generally, the infection rate can be reduced if aseptic techniques and antibiotic prophylaxis are used[3]. In spite of this, the incidence of infection in orthognatic surgery varies from 0-60% with the various protocols of antibiotic[4-8].

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The principle of antibiotic prophylaxis is that the drug has to be distributed in the tissue and reach a therapeutic level before the procedure starts and be maintained for the shortest period after the procedure where there is a risk of infection[9,10]. Though most surgeons know the principles of antibiotic prophylaxis very well, some surgeons still prescribe antibiotics to prevent wound infection in order to be protected from being sued by the patients who don't understand failure to use antibiotics and get infected[9]. Antibiotics have been prescribed with various durations ranging from immediately before surgery to 8 days postoperatively[11,12]. The administration of prophylactic antibiotic differs among oral and maxillofacial surgeons. Some use them in the parenteral form for a specific period such as 1 dose, 1 day, 3 days, or until the patients are discharged from the hospital, and then switch to the oral form, which may continue for 3-8 days.

The chosen antibiotics for prophylaxis must be bactericidal, effective against the bacteria that are most likely to cause infection, and the least toxic agent available. For intraoral orthognatic surgery, the organisms most likely to cause infection are Streptococci, anaerobic Gram positive cocci and anaerobic Gram-negative rods[12] all of which make the prophylactic antibiotics of choice penicillin, amoxicillin-clavulanic acid and clindamycin[1,3,5-7,11-17].

The use of prophylactic antibiotics for a prolonged period provides no additional benefit in preventing post-operative infection[13,15]. Moreover, this may be related to the wide range of postoperative infection rates, a predisposition to develop bacterial resistant strains, and the potential for unusual post-operative consequences such as hemorrhage[1,11,13,16,18].

Though the authors have been using antibiotics for a long time and there are several existing studies regarding antibiotic prophylaxis in the orthognatic surgery, a comparison of study results and their conclusions is difficult due to the differences in surgical techniques, type, dosage and the duration of antibiotics and the criteria for diagnosis of infection[1,2,7,9,14-16,19]. Some studies have reported the benefit of antibiotic prophylaxis whereas some studies have shown indifferent results[1,14] or even have a higher infection rate from the study of Yrastorza in the antibiotic prophylaxis group when compared to the non-prophylaxis group[16]. Therefore, some authors use prophylactic antibiotics only in patients with metabolic diseases that have a lower resistance to infection, for the surgery that requires a sizable bone graft[16] and a potential exists for opening of fascial space or the formation of a large hematoma[5,9].

Penicillin has been used since 1929 and is still used for some bacterial infections, although the development of penicillin-resistance in several pathogenic bacteria now limits its effectiveness. Furthermore, the development of new antibiotics with improved antibacterial potency has challenged its position.

The purpose of the present study was to evaluate the efficacy of the short- and long-term of penicillin that is commonly used in our institution and amoxicillin-clavulanic acid, which is widely accepted as the drug of choice for controlling microbial infection in the oral and maxillofacial region[17].

Materials and methods

This is a prospective, comparative, randomized, and double blinded study. The purpose of the present study is to evaluate the efficacy of penicillin and amoxicillin-clavulanic acid as antibiotic prophylactics in patients who have undergone orthognatic surgery. The operations performed were standard techniques including Lefort I osteotomies (including one-piece and multi-segments), sagittal split ramus osteotomies, segmental osteotomies or combined or solitary genioplasty and adjunctive surgeries such as symphysis osteotomy, third molar removal, and tooth extraction. All the operations in the present study were performed by four staff in the departments and senior residents under close supervision. The operations were conducted at the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Chulalongkorn University and Oral and Maxillofacial Surgery Unit at the Police General Hospital between July 2002 and September 2005. The present study protocol was approved by the ethics committee of the Faculty of Dentistry, Chulalongkorn University (number 10/2005). All the patients who participated in the present study were clearly informed about the experiment and consent was given by all the participants.

The authors conducted a prospective randomized trial comparing the short term (pre-operative and 1 dose post-operative) and the long term (pre-operative and 5 days post-operative). The patients were divided into four groups randomly. In group 1, the patients were given 1.2 gm of intravenous amoxicillin-clavulanic acid 30 minutes pre-operatively and every 8 hours during the operation and then one more single dose 8 hours post-operatively. In group 2, the patients were given an antibiotic regimen consisting of 2 million units of aqueous penicillin G (IV) 30 minutes preoperatively which was continued every 4 hours during the surgery and then one more single dose 4 hours after the surgery. In group 3, the patients were given 1.2 gm of intravenous amoxicillin-clavulanic acid 30 minutes pre-operatively and every 8 hours during the operation, followed by a 625 mg tablet amoxicillin-clavulanic acid orally every 8 hours postoperatively for 5 days. In group 4, the patients were given the same antibiotic regimen as group 2, and then the post-operative antibiotic was changed to 500 mg oral amoxicillin every 8 hours for 5 days. This is due to the better absorption, less gastrointestinal irritation, and better compliance of amoxicillin, which is more available in most general hospitals. There was no control group.

Patients were excluded from the present study if they met the following criteria. 1) If patients presented with metabolic diseases or low resistance to infection. 2) If the patients needed a bone graft for the correction of dentofacial deformity. 3) If the patients sustained

perioperative complications that make antibiotic usage more crucial, such as unfavorable fractures or excessive bleeding that can cause a large hematoma. 4) If the patients had received an antibiotic within 4 weeks of surgery. 5) If the patients had been treated by a distraction osteogenesis device or surgically assisted rapid palatal expansion. And, 6) If the patients had a history of allergy to penicillin.

During hospitalization, each patient was examined daily. After discharge, the patients were recalled to the clinic for post-operative examination at 1, 2, 4, 6, 8 and 12 weeks.

The criteria for postoperative infection were based on the definition of the infection by the Center for Disease Control[12]. The infection had to be present at the surgical site within 42 days (6 weeks) of surgery (this being the normal period for soft tissue and bone healing). A diagnosis of infection was made if there was 1) purulent discharge from the surgical site. 2) serosanguineous drainage and a wound culture proved positive for a known pathogen 3) an elevation of temperature to more than 38.5 C after more than 48 hours and the patients had been ruled out from other causes of infection by complete blood count, chest x-ray, and urinary analysis. 4) pain or tenderness, localized swelling, and redness of the wound margin and surrounding tissue.

If there were any signs of post-operative infection, gram stains, cultures, and evidence of antibiotic sensitivity, test were obtained, and the methods and the results of treatment were recorded.

For the relation between the type of operation and operating time will be investigated by Brown-Forsythe and the multiple comparison by Tamhane method and the relation between the incidence of infection and the group of antibiotic will be tested by the Pearson Chi-square test by exact method.

Results

One hundred thirty seven patients participating in the present study but 15 patients were excluded for various reasons; allergy to penicillin (5 patients), loss of follow up (1 patient), intra-operative complications (6 patients), and being treated by distraction osteogenesis devices (3 patients). One hundred and twenty two patients participated in the present study; 40 male and 82 female. The patients' age ranged from 17.10 - 47.60 years with an average age of 26.52 years. The majority of the patients were found to be between 15-25 years old (60 out of 122; 49.18%) (Table 1). There were no patients younger than 15 years (Table 1). All the operations were done by intraoral approach using rigid fixation (Table 2). For the relation between the type of operation and operating time, Brown-Forsythe and the multiple comparisons by Tamhane method showed that the mean operating time was statistically different between BSSRO and Lefort combined with BSSRO and between BSSRO and BSSRO combined with genioplasty. The mean operating time of all surgical procedures were associated in the median level from the ETA analysis ($p = 0.600$). The 122 patients were assigned randomly into four groups. However, because some patients were excluded from the study, the four groups were not equal. There were 33, 29, 28, and 32 patients in group 1, 2, 3, and 4, respectively (Table 1). The means operating time ranged from 2.99 to 4.57 hours (Table 3). Patients were followed-up for more than 10 months in all groups (Table 3). Infection developed in two patients.

Table 1. Age distribution

Groups	Age range (years)					
	15-25	25-35	35-45	> 45	Total	Mean ± SD
I	18	14	0	1	33	25.56 ± 5.36
II	12	16	1	0	29	26.40 ± 4.55
III	12	13	3	0	28	27.56 ± 5.86
IV	18	10	4	0	32	26.73 ± 6.67
Total	60	53	8	1	122	26.52 ± 5.65

group I (the short term amoxicillin-clavulanic acid group), group II (the short term penicillin group), group III (the long term amoxicillin-clavulanic acid group) and group IV (the long term penicillin group)

Table 2. Number and type of operations

Type of operations	Number
Lefort I	8
Lefort I, BSSRO	22
Lefort I, genioplasty	4
Lefort I, BSSRO, genioplasty	3
BSSRO	55
BSSRO, genioplasty	18
Segmental surgery	10
Segmental surgery, genioplasty	1
Combination surgery	1
Total	122

BSSRO: bilateral sagittal split ramus osteotomy

Table 3. Age, operating time and follow-up period

Groups	Mean age (years)	Mean operating time (hours) (range)	Mean follow-up period (months) (range)
I	25.54	3.43 (1.25-8.45)	11.19 (3-26)
II	26.40	3.53 (1.50-8.00)	10.10 (3-36)
III	27.56	4.57 (2.00-9.00)	11.04 (3-27)
IV	26.72	2.99 (1.35-6.35)	11.75 (2-29)

Case of postoperative infection

Case 1, a male patient who was in the short-term amoxicillin-clavulanic acid group underwent bilateral sagittal split ramus osteotomy for correction of mandibular laterognathia. On the 7th post-operative day, serosanguinous discharge was found in the left posterior mandibular region. The wound was explored and curreted under local anesthesia. This patient was successfully treated with 625 mg of amoxicillin-clavulanic acid orally every 12 hours for 5 days.

Case 2, a male patient who underwent Lefort I osteotomy and bilateral sagittal split ramus osteotomy using the long-term penicillin protocol, experienced bleeding when brushing his teeth from the left lower molar region on the 5th week after the surgery. Upon clinical examination, pus discharge was found at the left first molar wound margin. He was then treated with 500 mg amoxicillin orally three times a day for 7 days. The localized infection resolved within 7 days.

In both infected cases, the osteotomy was performed within 2.30 hours. The infection rate in all patients was 1.64% and the infection rate when compared intra-group in groups 1 and 4 was 1/33; 3.03% and 1/32; 3.13%, respectively. The incidence of infection between the two groups was not statistically different according to the chi-square test by Fischer's exact method ($p > 0.05$).

Discussion

Antibiotics may cause a variety of untoward effects[20]. These can be classified into four groups. First, allergic reaction ranges from a minor skin rash to an anaphylactic reaction[1,12,17]. Second, toxic reactions may occur including neural, renal, hepatic, hematopoietic, and gastrointestinal toxicity[1,17]. Third, secondary infections can range from a mild oral or vaginal candidiasis to a severe Gram-negative pneumonia[1,17]. Finally, the misuse of antibiotics may cause the growth of resistant bacteria[12,13,17]. Because of these undesired effects, surgeons should use them cautiously.

The factors that influence the use of prophylactic antibiotics are the location of the operation, the condition of the host tissue (normal or infected tissue), the type and degree of difficulty of the operation and the health status of the individual. The operating time also plays a role in the decision to use antibiotics. Some studies recommend using antibiotics when the operative time is longer than 4 hours[5,9].

A variety of prophylactic antibiotic regimens for orthognathic surgery has been investigated revealing many different conclusions[1,4,6,7,11-15,17,21-24]. Surgical techniques evolve and the criteria for infection differ among authors or institutions. Furthermore, most prospective studies were comparisons between types or durations of antibiotic used except the study by Zijderveld et al, which used a placebo as the control group[17]. The incidence of infection in the placebo-controlled group of Zijderveld's study was quite high (52.6%)[17]. This result was contradictory to the study by Yrastorza and Ridge that found 0% infection rate in the placebo-controlled group[16]. However, most surgeons are likely to prescribe an antibiotic if the operations are done intraorally due to the clean-contamination environment of the intraoral orthognathic surgery[9].

For intraoral procedures, penicillin is the first choice according to Peterson[2] even though it has been challenged by the up-and-coming antibiotics. Penicillin is the antibiotic commonly used including the present study. The studies by Fridrich and Conover revealed that the incidences of infection in the use of short-term penicillin group were 6.2 and 11%, respectively[6,14]. The infection rate with the use of long-term penicillin with different durations from 3-8 days was between 0-60%[4,6,7,14,15,22,24]. The infection rates in the short-term and long-term penicillin in the present study were 0% and 3.13%, respectively.

Amoxicllin-clavulanic acid is widely used for major head and neck surgery including orthognatic surgery. However, only a few studies have been published for orthognathic surgery. There are two studies of amoxicillin-clavulanic acid for orthognathic surgery prophylaxis in the English literature. Both of them studied the short-term course where the infection rate was approximately 11%[17,22]. The infection rates for the short-term and long-term amoxicillin-clavulanic acid in the present study were lower, at 3.03% and 0%, respectively.

From the previous short-term antibiotic prophylaxis studies that used penicillin, clindamycin, amoxicillin-clavulanic acid, cefuroxime, penicillin with

oxacillin, and cefazolin, the infection rates ranged from 6 to 18%[11,12,14,22,24] while those in the long-term antibiotic group were from 0 to 60%[4,6-7,14,15,21,22,24]. The overall infection rate in the present study was 1.61% in both groups, which is lower than in the previous studies. However, there was a wide range of durations of antibiotic therapy in the long-term group; ranging from 3-8 days that made the comparison in terms of infection rates more difficult.

The use of a vasoconstrictor with local anesthesia, intermaxillary fixation, the failure of hardware, the sump-effect created by the sagittal wound and the problem from the closed suction drainage system which lead to the loss of an air-and water-tight seal, tissue reaction, dead space around the drain itself or contamination during drain removal have been suggested by several authors as the causes of infection in mandibular ramus osteotomies[4,12,25]. Both infected cases in the present study occurred at the sagittal split sites, which can be attributed by any of the above causes or the failure of antibiotic prophylaxis.

However, there was no statistical difference in infection rates among the four groups due to the small number of infection cases.

Conclusion

There were no differences in infection rates between the two groups of antibiotics, penicillin and the more potent and expensive amoxicillin-clavulanic acid. Based on the present study, short-term penicillin is still the most appropriate choice for prophylactic antibiotic in orthognathic surgery. The duration of antibiotic coverage also may have to be extended if there is any risk of bacterial contamination when the patients present with metabolic diseases or are immunocompromised, or when they need a bone graft or alloplastic implant for correction of dentofacial deformity.

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การใช้ยาต้านจุลชีพเพื่อป้องกันการติดเชื้อภายหลังการผ่าตัดแก้ไขความผิดปกติของกระดูกใบหน้าและฟัน: การศึกษาในลักษณะ prospective, เปรียบเทียบ และ สุ่ม ระหว่างอะม็อกซิซิลลิน-กรดคลาวูลานิค และเพนนิซิลลิน

พรชัย จันศิษย์ยานนท์, สมชาย เศรษฐศิริสมบัติ, ปาหนัน ศาสตรวาหา, พิมล บำรุง

วัตถุประสงค์: *รายงานนี้จัดทำเพื่อประเมินประสิทธิภาพในการป้องกันการติดเชื้อภายหลังการผ่าตัดเพื่อแก้ไขความผิดปกติของกระดูกใบหน้าและฟันโดยการใช้เพนนิซิลลิน และอะม็อกซิซิลลิน-กรดคลาวูลานิค ในช่วงเวลาสั้นและยาว (5วัน)*

วัสดุและวิธีการ: *การศึกษานี้เป็นลักษณะ prospective, สุ่ม และ double blinded โดยผู้ป่วยจะถูกแบ่งออกเป็น 4 กลุ่มแบบสุ่ม ซึ่งได้แก่ กลุ่มที่ให้เพนนิซิลในช่วงระยะเวลาสั้น และยาว (5 วัน) และกลุ่มที่ให้อะม็อกซิซิลลิน-กรดคลาวูลานิค ในช่วงระยะเวลาสั้นและยาว*

ผลการศึกษา: *ผู้ป่วยจำนวน 122 คนที่เข้าร่วมการศึกษานี้ได้ถูกแบ่งออกเป็น 4 กลุ่มตัวอย่าง โดยพบว่ามีการติดเชื้อเกิดขึ้นในผู้ป่วย 1 คนในกลุ่ม อะม็อกซิซิลลิน-กรดคลาวูลานิคที่ให้ช่วงเวลาสั้น และผู้ป่วยอีก 1 คนในกลุ่มที่ได้รับเพนนิซิลลินในช่วงเวลาที่ยาว*

สรุป: *พบว่าไม่มีความแตกต่างกันในการป้องกันการติดเชื้อของยาต้านจุลชีพทั้ง 2 กลุ่ม การให้เพนนิซิลลินในช่วงเวลาสั้น น่าจะยังคงเป็นยาต้านจุลชีพที่เหมาะสมที่สุดในการป้องกันการติดเชื้อในการผ่าตัด เพื่อแก้ไขกระดูกใบหน้า และฟัน*