Evaluation of Effectiveness of 0.2% Chlorhexidine Gluconate and Amoxycillin+Clavulanate Potassium on the Prevention of Alveolar Osteitis Following Mandibular Third Molar Extractions¶

%0.2'LİK KLORHEKSİDİN GLUKONAT VE AMOKSİSİLİN + POTASYUM KLAVULANAT KOMBİNASYONUN MANDİBULAR ÜÇÜNCÜ MOLAR ÇEKİMLERİ SONRASI ALVEOLİTİN ÖNLENMESİNDEKİ ETKİNLİĞİNİN ARAŞTIRILMASI

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Summary

Purpose: The first purpose of this study is to evaluate the use of 0.2% chlorhexidine gluconate and amoxycillin+ clavulanate potassium combination as a prophylactic therapy for the prevention of alveolar osteitis. The other purposes are to assess smoking and oral contraceptive use as risk factors in alveolar osteitis and to examine advers reactions to chlorhexidine.

Materials and Methods: This randomized, placebo-controlled, parallel group study was conducted among 125 subjects and a total of 156 teeth were extracted. 3 groups were formed. First group (n=44) received 0.2% chlorhexidine gluconate, second group received 0.2% chlorhexidine gluconate and amoxycillin + clavulanate potassium combination and third group (n=47) received %0.09 sterile saline solution. All patients were recalled for alveolar osteitis diagnosis on the third and seventh postoperative days.

Results and Conclusion: When antibiotic group is compared with the other two groups, a significant reduction in alveolar osteits can be noted. Smoking did not increase the incidence of alveolar osteitis. 4 oral contraceptive using female patients were excluded at the end of the study because the number is not enough to do analysis. Alteration in tasting, bad taste of the solution and staining of dentures and oral tissues were the major complaints about chlorhexidine.

Key Words: Alveolar Osteitis, Third molar surgery, Chlorhexidine, Augmentin

T Klin J Dental Sci 2001, 7:29-34

Özet

Amaç: Bu çalışmanın ilk amacı, %0.2'lik klorheksidin glukonat ve amoksisilin+potasyum klavulanat kombinasyonunun alveolitin önlenmesinde proflaktik tedavi olarak etkinliğinin araştırılmasıdır. Ayrıca, sigara ve oral kont-raseptif kullanımının alveolit gelişmesinde risk faktörleri olarak değerlendirmesi ve klorheksidine karşı gelişe-bilecek yan etkilerin incelenmesi diğer amaçlarımızdır.

Materyal ve Metod: Rastgele örnekleme, plasebo kontrollü, paralel grup esasına göre planlanan çalışmaya dahil edilen 125 hasta 3 gruba ayrıldı ve toplam 156 diş çekimi yapıldı. Birinci gruba (n=44) %0.2'lik klorheksidin glukonat, ikinci gruba (n=30) %0.2'lik klorheksidin glukonat ve amoksisilin + potasyum klavulanat kombinasyonu, üçüncü gruba (n=47) %0.09'luk steril NaCl solüsyonu uygulandı. Bütün hastalar postoperatif üçüncü ve yedinci günde kontrole çağrıldı.

Bulgular ve Sonuç: Antibiyotik uygulanan grup diğer iki grup ile karşılaştırıldığında alveolit insidansında belirgin bir azalma saptandı. Sigara içmenin alveolit gelişmesinde belirgin bir etkisi bulunamadı. Oral kontaseptif kullanan 4 kadın hasta sayının istatistiksel analiz için az olması nedeniyle çalışmadan çıkartıldı. Tat almada değişiklik, solüsyonun kötü tadı ve ağız içinde renklenmeye neden olması hastaların klorheksidinden başlıca şikayetleriydi.

Anahtar Kelimeler: Alveolit, Üçüncü molar cerrahisi, Klorheksidin, Augmentin

Alveolar osteitis (AO) is an important postoperative problem especially after removal of mandibular third molars (1-4). The average reported incidence is 25% to 30% (5,6). The peak age of occurrence is from 20 to 40 years and has female propensity (6,7). Several risk factors have

Geliş Tarihi: 12.02.2001

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¶*This study was presented in 5th Congress of the Balkan Stomatological Society 13-16 April 2000, Thessaloniki-GREECE*

been identified in association with AO. These include infection, trauma to bone during surgery, experience of surgeon, tobacco and oral contraceptive use, inadequate blood supply and poor oral hygiene (2,8-10). Fibrinolysis with subsequent loss of blood clot is believed to be the general cause of AO. As the primary role of bacteria in this process has been repeated, the most effective method for reducing AO has been through the use of agents that systematically or topically reduce the oral microbes within the wound (7,8,11-13). Antibiotics and antibacterial rinses have been used with some effectiveness, the rationale being that infection is the ethiologic factor in the genesis of AO (13-16). Chlorhexidine (CHX) is effective against both aerobic and anaerobic, Gr (+) and Gr (-) organisms, as well as yeast. It has a high affinity for the cell wall of microorganisms and induces changes in the surface structures, resulting in the loss of osmotic equilibrium and precipitation of the cytoplasm (7,15,17-19). Oral rinsing with CHX has been shown to reduce the quantity of oral microbial populations and thus may be effective in reducing the incidence of AO (7,8,20,21).

Amoxycillin has enhanced penetration into Gr (-) bacilli and enterococci, but like penicillin V, is inactivated by ß-lactamase. The spectrum of activity includes most organisms sensitive to penicillin, with the addition of some non ß-lactamase producing Gram (-) rods. Approximately 50 % of Bacterioides species other than B. Fragilis are inhibited by amoxycillin. Clavulanic acid is a naturally occuring ß-lactam compound with little intrinsic antibacterial activity, but it binds irreversibly to ß-lactamases, inactivating these enzymes (22-24). A combination of amoxycillin and clavulanate potassium (A + CP) is available as Augmentin. It has antimicrobial activity against all organisms mentioned for amoxycillin, as well as ß-lactamase producing strains for Bacterioides, Staphylococci and Gram (-) bacilli (16,22,25).

This study seems to be the first one in English language literatures that evaluates the effects of CHX and amoxycillin + clavulanate potassium together on the prevention of AO following mandibular third molar extractions.

The purposes of this study is to evaluate the use of 0.2% chlorhexidine gluconate and amoxycillin + clavulanate potassium combination as a prophylactic therapy for the prevention of alveolar osteitis. Furthermore, we aim to assess smoking and oral contraceptive use as risk factors in alveolar osteitis and to examine advers reactions to chlorhexidine.

Materials and Methods

125 patients (41 male, 84 female), mean aged 24 years were enrolled for this study. To be eligible, patients had to be in good general health and to have at least one extraction-planned mandibular third molar. Patients who had pericoronitis or were taking antibiotics for other infections were excluded. Pregnant or breast feeding women were also excluded, but oral contraceptives use was not a criteria for exclusion. 4 female patients were using oral contraceptives. The number is too small to come to a conclusion, therefore they were excluded. The analysis was done with 121 patients (41 male, 80 female) and 151 teeth. The patients were referred for removal of these teeth and were divided into 3 groups. 30 bilateral patients were equally distributed among these groups. We obtained informed consent from all participants.

Group 1 (n=44): Patients first rinsed with 15 ml of CHX solution (Klorhex) for 30 sec. just prior to surgery. The surgery was performed under local anesthesia with Ultracain (Articain HCL: 40 mg/ml, epinefrin HCL: 0.012 mg/ml) and standard surgical procedures. Intraoperatively, 15 ml CHX diluted with 15 ml sterile saline was used as irrigation. The soft tissue was closed with 3/0 silk suture for transalveolar procedures. The day after surgery, the patients started home use of the rinse (15 ml for 30 sec) twice daily for 7 days.

Group 2 (n=30): The second experimental group was treated similar to that of group 1. However, the patients were prescribed Augmentin BID (500 mg Amoxycillin trihidrate, 125 mg clavulanate potassium) twice daily for 5 days use postoperatively.

Group 3 (n=47): The control group was similarly treated as in group 1 with the substitution

Table 1. Patients in each group

	Group 1	Group 2	Group 3
Male	14	13	14
Female	30	17	33
Mean age (years)	24.2	24.7	24.1
Smoking			
Yes	10	5	9
No	34	25	38

of sterile saline solution (0.09 % NaCl) for CHX.

All 3 groups were advised to use 500 mg paracetamol (Minoset) for postoperative pain relief. A postoperative examination was performed on the third and seventh days to determine any adverse reactions and presence of AO diagnosed by presence of a necrotic blood clot or the absence of a blood clot, fetid breath, increase in pain unrelieved by analgesics and exposed bone. Chi-square test was used for statistical analysis.

Results

121 patients were included in this study and a total of 151 mandibular third molars were extracted. The 3 groups were well balanced with respect to age and gender, they all had similar male to female ratios and mean ages ($p>0.05$) (Table 1). The difficulty of extractions and surgeon experience were examined with respect to treatment groups because surgical trauma has been reported to be a risk factor in AO. Tooth removal was performed by the two same experienced oral and maxillofacial assistants. Erupted and soft tissue impacted teeth accounted for 40.4%, partial and fully bone impactions accounted for 59.6% of all extractions (Table 2). Most patients needed unilateral tooth removal (75.2%). In extraction site-level analysis, the incidence of AO was 20.3% in CHX group (Group 1), 2.5% in CHX and A+ CP group (Group 2), 22.8% in saline group (Group 3). In subject level analysis the incidence of AO is; 20.4% in Group 1, 3.3% in Group 2, and 23.4 % in Group 3. There is statistically significantly reduction ($p< 0.05$) of AO in Group 2 whereas there is no significant difference between Group 1 and 2 ($p>0.05$). Although level of impaction which determines surgical trauma is considered to be a risk factor in AO, we could not find a significant correlation between characterization of teeth and incidence of AO ($p>0.05$). We also evaluated smoking as predisposing factor in AO. A current smoking habit was reported by 24 subjects, representing 19.8% of the total population. Incidence of AO in subject-level analysis is 29.1% (7/24) and 29.6% (8/27) in extraction site-level analysis. Smoking was not related to a statistically significant increase in AO ($p>0.05$) (Table 3). Slight complaints about CHX was noted in this study. Of the total subjects in Group 1and 2, 54.5% and 66.6% respectively were pleasant with the CHX solution (Table 4).

Discussion

Many clinical investigations and research have sought to prevent or decrease the problem of AO

Table 2. Characterization of teeth and alveolar osteitis.

	Group 1			Group 2			Group 3		
	*	**	***	*	**	***	*	**	***
Erupted	2	4	6	0	7	7	1	7	8
Soft tissue impaction	4	13	17	0	6	6	4	13	17
Partial bony impaction	4	15	19	0	12	12	6	10	16
Full bony impaction	1	11	12	1	14	15	2	14	16

* Symptomatic (alveolar osteitis)
** Asymptomatic
*** Total

Table 3. Risk factors and alveolar osteitis

	#patients	#AO cases
Smoking		
Yes	24	7
No	97	13
Treatment		
CHX	44	8
CHX + Augmentin	30	1
Sterile saline	47	10

Table 4. Advers reactions to chlorhexidine

	Group 1		Group 2	
	#patients	%	#patients	%
Allergy	0	0	0	0
Staining	3	6.8	3	16.6
Mucosal irritation	0	0	0	0
Alterations in tasting	10	22.7	3	10
GIS complaints	0	0	0	0
Bad taste	7	15.9	2	6.6
No adverse reactions	24	54.5	20	66.6

(5,26,27). The effect of oral bacteria causing a clot breakdown is thought to be significant. Attempts to prevent AO have focused on reducing oral microbes within the wound either through oral administration of antibiotics or local application of antiseptic solutions (11,13,28). Mac Gregor and Hart (20), have shown that extraction sites are routinely contaminated with bacteria. In a study of 71 mandibular third molar extractions, they found that all produced bacterial growth. The organisms most frequently found were; Streptococcus viridans, Corynebacterium xerosis, Staphylococcus lactis, Vibros fusobacteria, Bacterioides melaninogenicus, Neisseria pharyngis, and Staphylococcus aureus. The emergence of resistant strains of pathogenic organisms has also been noted (29,30). Hunt et al (30) reported increasing resistance of Streptococci to erythromycin (53 %), S. Aureus to penicillin and erythromycin (50 %) and increasing number of penicillin resistance of Bacterioides organisms isolated from oro-dental infections. The high prevalence of ß-lactamase producing bacteria is an important reason for the rise in bacterial resistance (22,29). Support in the literature for and against the effectiveness of antimicrobial solutions for irrigation or rinsing as preventive measure in AO formation is questionable. Several studies have demonstrated that preoperative rinsing with CHX does not influence outcome (7,20), whereas investigations of perioperative and postoperative rinsing have shown more consistent and striking reductions in the incidence of AO. Legarth et al (7,20) found a reduction from 13.7 % to 7.5% when twice daily postoperative rinses with 0.2 % CHX following third molar surgery. Ragno et al (5) used 0.12 % CHX similar to our study protocol. They found CHX useful in reduction of AO. However Brewick and Lessin (7) reported that CHX is no more effective than postoperative irrigation with normal saline. A study by Krekmanov and Nordenram (14) published in 1986, found decreased incidence with penicillin V in combination with CHX was not significant than that seen with CHX alone and the incidence of AO seen with both of these regimens was significantly less than that seen in control group. In our study, though a 11% reduction was found when CHX and sterile saline are compared, it is not statistically significant but antibiotic administered group has significantly less AO incidence. There is some evidence to suggest why CHX may be ineffective in preventing AO. Schiott et al (21) noted in their research concerning the effect of CHX mouth rinses on human flora that, whereas salivary bacterial counts were reduced up to 95%, the saliva still contained numerous bacteria. The bacterial levels following rinse may still be enough to initiate bacterial fibrinolysis and AO. The activity of CHX is decreased by blood and calcium. This would also reduce antimicrobial effect in the extraction site.

Smoking is said to be predisposing factor in AO but the trial findings are controversial. Bannie and Brighton (11), Larsen (8) found increase in AO in smokers but Hermsch et al (31) found no difference. Our result is consistent with the latter.

One of our purposes in this study is to examine any adverse reactions to CHX previously reported or informed by the manufacturer (5,31). Most of adverse reactions included bad taste of the solution, alterations in food tasting during treatment and staining of teeth, dentures and restorations. Staining could be managed easily by mechanical cleansing. Alterations in tasting was over with the completion of using. There were no systemic or other significant reactions to CHX.

We conclude that, CHX may not be effective alone in reducing AO following mandibular third molar extractions. It will be more rationale to use in combination with ß-lactamase containing antibiotic to overcome resistant microorganims.

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