

Efficacy of Amoxicillin Rinse on Bacteriemia Prior to Dental Extraction

Diş Çekimi Öncesi Amoksisilin Gargara Kullanımının Bakteriyemi Üzerine Etkileri

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ÖZET Amaç: Dental enfeksiyonlar ve özellikle enfekte diş çekimlerini takiben kana karışan oral bakteriler hastaların genel sağlık durumunu kötü yönde etkileyebilir. Bu çalışmanın amacı, jel ve süspansiyon formunda hazırlanan amoksisilin gargaranın özellikle enfekte diş çekimlerinden önce farklı zaman aralıklarında kullanılmasının ağız içinde ve periferik kan sirkülasyonunda bulunan aerobik ve anaerobik bakteri varlığına etkisini araştırmak ve böylece hastaların genel sağlık durumlarının korunmasına veya var olan sorunların artmamasına katkıda bulunmaktır. **Gereç ve Yöntemler:** Bu çalışmada, diş çekimi yapılan toplam 105 hasta ve yedi farklı alt grup (n=15) yer almıştır. Hastalardan 45'ine amoksisilin jel, diğer 45'ine amoksisilin süspansiyon uygulanmış, kontrol grubuna dahil olan son 15 hastaya ise uygulama yapılmamıştır. Toplanan örneklerde kan kültürü yapılarak bakteriyemi araştırılmıştır. **Bulgular:** Anaerobik bakteri üremesindeki azalma, kontrol ve diğer gruplar arasında istatistiksel olarak anlamlı bulunmuştur (p<0.05). Bu anlamlı farklılık özellikle Grup A ve D (kontrol-2, 15 ve 30 dakika süspansiyon) ve Grup A ve E (kontrol-15 dakika jel) arasında belirgindir. **Sonuç:** Diş çekimi öncesinde uygulanan topikal amoksisilin oral kavitede anaerobik bakteri üremesini anlamlı olarak azalttığı saptanmıştır. Bununla beraber, topikal antibiyotik kullanımı dirençli bakterilerin artışına da neden olabileceğinden kullanımı dikkat gerektirmektedir.

Anahtar Kelimeler: Amoksisilin; aerobik bakteriler; anaerobik bakteriler; gargara

ABSTRACT Objective: Dental infections may worsen medical health status by spreading the oral bacteria into the bloodstream, especially following infected tooth extraction. The aim of this study was to determine the effect of amoxicillin rinse applied in gel and suspension form at different time intervals prior to tooth extraction to decrease the incidence of aerobic and anaerobic bacteria in the oral cavity and peripheral blood circulation in order not to worsen or trigger unknown health problems in patients. **Material and Methods:** In this study, a total of 105 dental patients who requested tooth extraction were participated. There were seven different subgroups (n=15). Forty five patient received amoxicillin suspension while other 45 received amoxicillin gel. Amoxicillin suspension was applied as one time 15 minutes (Group B), 30 minutes (Group C) and three times 2, 15, 30 minutes before the extraction (Group D). Group D received three applications. Same procedure was carried out for the gel application, in groups E, F and G respectively concerning time intervals. The last 15 subjects received no rinse as the control group (Group A). Blood culture was performed to determine the bacterial growth. **Results:** There was a significant decrease between control and each study group for anaerobic bacterial growth (p<0.05). The difference was particularly more obvious between Group A and D (control-2, 15 & 30 min suspension), and between Group A and E (control-15 min gel). **Conclusion:** The results of this study indicate that the use of topical amoxicillin prior to dental extraction is significantly effective to decrease the anaerobic bacterial growth in the oral cavity. However, topical antibiotic use may cause selection of resistant bacteria, therefore, consideration of its use necessitates discretion.

Key Words: Amoxicillin; bacteria, aerobic; bacteria, anaerobic; mouthwashes

Dental infections may worsen the medical health status by spreading the oral bacteria into bloodstream, especially following infected tooth extraction. Tooth enamel surface is one of the best places for the colonization of different types of microbial species in the oral cavity. A dental plaque is also a complex aggregation of microorganisms. It has been reported that 1 mg of dental plaque contains nearly 10^{11} microorganisms.¹ These microorganisms mostly consist of Streptococcus and anaerobes with a low virulence. However, even low virulent bacteria might be detrimental when a patient's general condition is weakened for some reasons. In addition, it is also reported that nearly 80% of microorganisms in dental plaque can cause wide variety of microbial infections in the body.² These infectious processes include common problems such as urinary tract infections, catheter infections, middle-ear infections, coating contact lenses, and less common but more lethal processes such as endocarditis, infections in cystic fibrosis, and infections of permanent devices such as joint prostheses and heart valves.^{3,4}

Oral bacteriemia may also occur after dental extraction. Thus, antibiotic prophylaxis (AP) is recommended to dental patients who are at risk of bacteraemia following oral surgery.⁵ Antibiotics reduce the prevalence and magnitude of bacteriemia⁶ and alter the adhesion of bacteria to cardiac valves⁷ by eliminating the microorganisms that reach endocardium.⁸ It was reported that 14% to 20% of the bacteriemia cases are associated with a possible oral origin⁹ and 70% of the bacteriemia cases are occurred following dental extraction, subgingival scaling or intraligamentary injection.¹⁰

Oral antibiotics are the simplest approach when it is effective. Intravenous antibiotics are usually reserved for more serious cases. Antibiotics may sometimes be administered topically, such as eye drops or ointments. The aim of this study is to evaluate the effect of topical amoxicillin application in the form of gel and suspension at different time intervals prior to tooth extraction to decrease the incidence of anaerobic and aerobic bacterial growth in the oral cavity in order not to worsen or trigger known/unknown medical status in dental

patients by spreading the oral bacteria into the bloodstream, especially following infected tooth extraction.

MATERIAL AND METHODS

The study was conducted at the Gazi University, School of Dentistry, Department of Oral and Maxillofacial Surgery. The protocol of the study was composed according to declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, and it was also approved by the ethic committee of Gazi University, School of Medicine. All the participants of this study have been asked to sign a consent form prior to topical antibiotic application and blood drawing.

In this study, a total of 105 dental patients who requested tooth extraction were participated. Patients receiving antibiotics or immunosuppressive therapy or the any one who previously had bacterial endocarditis, rheumatic fever or congenital heart disease were not included to this study. All the patients had a dental extraction. There were seven different subgroups (n=15). The study was designed as a randomized, single-blinded trial. Participants were randomly assigned to one of the seven groups. Of these 105 patients, 45 of them received amoxicillin suspension, 45 of them received amoxicillin gel and the last 15 received no rinse as a control group. Amoxicillin suspension was applied as one time rinse application 15 minutes (Group B), 30 minutes (Group C) and three time rinse application 2, 15, 30 minutes before the extraction (Group D). Group D received three applications. Same procedure was carried out for the gel application, in groups E, F and G respectively concerning time intervals. The last 15 subjects received no rinse as the control group (Group A) (Table 1).

Suspension form of topical amoxicillin contained 2% amoxicillin trihydrate and 1ml mint flavour while the gel form of topical amoxicillin contained 2% amoxicillin trihydrate, 1ml mint flavour and 0.75% Carbopol 934 P NF (BF Goodrich Company, USA) gel. First of all, patients were asked to sit straight possible on the dental chair in order not to swallow the mouthwashes. Decision of using

TABLE 1: Time intervals of amoxicillin suspension and gel applications according to study groups.

Time intervals	Suspension	Gel
15 minutes before the extraction	Group B	Group E
30 minutes before the extraction	Group C	Group F
2, 15 & 30 minutes before the extraction (3 times)	Group D	Group G

Group A is the control group.

80ml of mouthwash was made after testing by plain water on one of the study co-worker. Patients first asked to rinse their mouth properly for the first couple of seconds until mouthwash reaches all the places in the oral cavity than keep the mouthwash particularly at the area where the extraction will take place for the rest of the time. Both mouthwash applications, suspension and gel, were asked to be applied in the same manner. Following the mouthwash application, patients were not allowed to rinse their mouth by plain water. Amoxicillin mouthwash was the only kind of application applied before the dental extraction. There has been no any kind of antimicrobial or topical disinfectant used prior to amoxicillin mouthwash application. In the control group, no mouthwashes were used to be able to get a normalized ratio for the statistical comparison. Each mouthwash applications of 80ml amoxicillin suspension or gel containing 2% amoxicillin retained 2 min in the oral cavity (Table 1).

Peripheral blood was collected by venipuncture using 21g venoject needle (Terumo Europe NV, Belgium) into two BD Bactec plus aerobic/F and plus anaerobic/F vacutainer tubes (Becton, Dickinson and Company-USA) containing soybean-casein. First, forearm was cleaned twice by povidone-iodine then by 70% alcohol to prevent any contamination and then blood sample was drawn within 2 min following the extraction. The blood samples were processed in the same day for anaerobic and aerobic isolation with BacT-Alert system (Organon Teknika) at Gazi University, Medical School, Department of Microbiology. The bottles were incubated at 37°C with the caps loose in a 10% carbon dioxide for up to 10 days. If bacteria were in the patient's blood, they would produ-

ce CO₂ while they were growing and the sensor would change from blue-green to yellow. Subculture was performed whenever macroscopic inspection suggested a positive broth. In addition, routine subcultures were carried out after 1, 5, 7, and 10 days' incubation. Subcultures were performed using a syringe and needle to transfer about 0-1 ml of mixed broth onto fresh blood agar plates, which were incubated for 48 h in a carbon dioxide incubator. Bacteremia was defined as the presence of any viable bacteria subcultured on standard bacteriological media from the blood culture bottle and identified by conventional microbiological test methods.

Fisher's exact test was performed for the statistical evaluation (SPSS statistical software, Version 11.0).

RESULTS

There were total of 45 female and 60 male otherwise healthy volunteers participated in this study. Ages of the participants were ranging between 16 and 70 years (mean=38.2 years). There were 15 subjects at each group and total of seven groups to determine aerobic and anaerobic bacteria. Statistically the difference between the control and rest of the groups for aerobic bacteria was not significant ($p > 0.05$). However, there was a significant difference for anaerobic bacteria growth ($p < 0.05$).

There was no anaerobic bacteria growth determined in Group D (suspension form). Therefore, the difference for the positive anaerobic bacteria growth between Group A and Group D was statistically significant ($p < 0.05$). In addition, there was also a significant decrease for anaerobic bacteria growth in Group E (gel form) when compared to Group A which is the control group ($p < 0.05$) (Table 2).

DISCUSSION

Dental infections can be particularly harmful in medically compromised patients. Certain medical problems such as cardiac and brain infarction,¹¹ stroke,¹² coronary heart diseases, and also problems of the hip & knee prosthesis¹³ have already been reported to be associated with an increased number

TABLE 2: Distribution of aerobic and anaerobic bacteria by groups.

	Aerobic Bacteria			Anaerobic Bacteria		
	Count	Percentage	Count	Count	Percentage	Count
GroupA	10	66.7%	5	15	80%	3
		33.3%	100%	20%	100%	15
GroupB	9	60%	6	15	60%	6
		40%	100%	40%	100%	15
GroupC	9	60%	6	15	86.7%	2
		40%	100%	13.3%	100%	15
GroupD	12	80%	3	15	100%	0
		20%	100%	100%	0%	15
GroupE	12	80%	3	15	93.3%	1
		20%	100%	6.7%	100%	15
GroupF	13	86.7%	2	15	80%	3
		13.3%	100%	20%	100%	15
GroupG	11	73.3%	4	15	66.7%	5
		26.7%	100%	33.3%	100%	15
Total	76	72.4%	29	15	81%	20
		27.6%	100%	19%	100%	15

Aerobic Bacteria; $p=0.534$, ($p>0.05$)Anaerobic Bacteria; $p=0.032$, ($p<0.05$)

of foci of odontogenic infections. Furthermore, Rajasuo et al¹⁴ stated clearly the role and importance of anaerobic bacteremia which triggers adverse systemic reactions. Infections and anaerobic bacteremia seems to play an important role in systemic diseases. In the present study, results displayed a significant decrease for the anaerobic bacteria growth when amoxicillin suspension was applied 2, 15 and 30 min before the dental extraction or amoxicillin gel was applied 15 min before the extraction ($p < 0.05$).

Use of antibiotic is quite common for the management of dental infections. Antibiotics can be categorized according to their target specificity; 'narrow-spectrum' antibiotics target particular types of bacteria, such as gram-negative or gram-positive bacteria, whilst 'wide-spectrum' antibiotics affect a larger range of bacteria. Oral antibiotics are the simplest approach when effective, however intravenous antibiotics reserved for more serious cases. The frequently used protocols for AP are put forward by the American Heart Association (AHA) and British Society of Antimicrobial Chemotherapy (BSAC). AHA guidelines propose using of 2 g amoxicillin, whereas BSAC guidelines propose using 3 g of amoxicillin two hours before the surgical procedure. Amoxicillin is semisynthetic oral

penicillin that fights with bacteria. However, it is well known that prophylactic administration of antibiotics does not significantly lower the incidence or magnitude of bacteremia following tooth extraction.¹⁵ It only interrupts by bacterial attachment or bacterial growth. Therefore, in the present study entirely the incidence of bacterial growth has been investigated. It is not clear whether the potential harms, such as anaphylactic reactions/ hypersensitivity, developing resistant microorganisms¹⁶ outweigh any of the beneficial effects. Thus, practitioners need to well consider both the potential benefits and harms of antibiotic prophylaxis before any decision is made for antibiotic administration. On this ground, topical application of amoxicillin may be the choice of dental practitioners to decrease the number and magnitude of oral bacteria in the oral cavity before any dental procedure which may cause bleeding is performed as penicillin-like antibiotic may stop growth of bacteria. Nevertheless, it should also be considered that topical antibiotic application may cause selection of resistant bacteria. However, it has been already well known that the major risks are unnecessary if antibiotics are used under-dosed.¹⁷ Therefore, using amoxicillin mouthwash in form of suspension or gel only for once and swallowing the some amount

of it during rinsing may not cause any serious complications such as anaphylactic reaction.

Moreover, numerous aerobic and anaerobic bacteria are colonized on the mucosal and epithelial surfaces including the oropharynx. Anaerobes outnumber their aerobic counterpart in a ratio of 10:1–100:1. The predominant anaerobes are streptococci, veillonella, bacteroides and anaerobic gram-negative bacilli.¹⁸ These organisms can participate in a variety of chronic infections in and around the oropharynx including dental abscesses. Anaerobes can also reach large numbers in the oropharynx in patients with poor dental hygiene, caries, or periodontal disease. Previous findings revealed that the majority of bacterial species found in blood samples after dental treatment are anaerobic which may also explain why there was no significant difference for the aerobic bacteria growth in the present study.^{19,20}

The application of antiseptic or topical amoxicillin mouthwashes can decrease the prevalence of bacteriemia of oral origin, peculiarly when they applied to gingival sulcus of the teeth.²¹ However, sulcular irrigation in patients with poor dental hygiene may also cause bacteriemia.²² In addition, it has been already reported that mouthwashes with chlorhexidine do not significantly altered the number of positive blood cultures or the nature of the organisms applied prior to the single-tooth extraction which was expected to cause a bacteraemia regardless of the status of the dentition or periodontium.²³ Thus, in this study use of mouthwash were preferred instead of sulcular irrigation. In addition, application of mouthwashes in both

forms was found to be successful to decrease the prevalence and magnitude of oral bacteria before they reach the blood and disperse into the body circulation. There was no significant increase for the growth of aerobes and anaerobes. Statistical results demonstrated that there was a significant decrease for the anaerobic bacteria growth, particularly following the application of amoxicillin suspension at 2, 15 & 30 min before the dental extraction in Group D or following the application of amoxicillin gel at 15 min before the dental extraction in Group E when compared to Group B which displayed the highest growth of anaerobic bacteria. This result may also demonstrate the importance of repetition times of the application and viscosity of topical solution applied (suspension or gel form) (Table 2).

The results of this study indicate that the use of topical amoxicillin prior to dental extraction is significantly effective decreasing the anaerobic bacteria growth in the oral cavity. Since, under dosed topical antibiotic use reported to be not causing any major contraindication such as its systemic use. Amoxicillin mouthwash can be used more confidently and safely especially for the dental patients who are under suspect of having medical problem. Nevertheless, topical antibiotic use may cause selection of resistant bacteria, therefore, consideration of its use still necessitates discretion.

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