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ORIGINAL ARTICLE

Prevalence of bacteraemia following dental extraction – efficacy of the prophylactic use of amoxicillin and clindamycin

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ABSTRACT

Objectives: To evaluate the efficacy of single-dose antibiotic prophylaxis (AP) in the prevention of bacteraemia following tooth extractions at our clinic.

Material and methods: Fifty patients undergoing tooth extractions were enrolled. The need of AP was determined according to the health status and possible allergies of the patients. Blood culture samples were collected at baseline, 5 min after the first tooth extraction and 20 min after the last extraction.

Results: The majority (76%) received prophylactic oral amoxicillin or intravenous ampicillin (AMX/AMP) (2 g), 12% received clindamycin (CLI) (600 mg) and 12% received no prophylaxis (NO AP). All baseline blood cultures were reported negative. The prevalence of bacteraemia was significantly higher in the CLI and NO AP groups compared to the AMX/AMP group 5 min after the first tooth extraction ($p < .0001$ and $p = .015$, respectively). Twenty minutes after the last extraction positive blood cultures were reported only for CLI ($p = .0015$) and NO AP groups. There was no significant difference in the prevalence of positive blood cultures between CLI and NO AP groups.

Conclusions: Appropriately administered AMX/AMP proved its efficacy in reducing both the prevalence and duration of bacteraemia following tooth extractions whereas CLI was not effective in preventing bacteraemia following tooth extractions.

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Introduction

Bacteraemia can be caused by any dental manipulation including daily oral activities. The reported prevalence of bacteraemia after dental procedures has ranged from 58% to 100% [1–9]. Bacteraemia is typically transient rather than continuous although persisting bacteraemia lasting up to 1 h has been reported [7]. However, instead of the incidence or duration, the intensity of bacteraemia seems to play a significant role in systemic spread of infections [6]. The presence of chronic infection of the periodontal tissue seems to provoke the entry of oral microorganisms into the blood stream elevating the intensity of bacteria [4,5,10–14]. The cumulative burden of bacteraemia due to daily oral activities especially on infected sites predisposes to systemic spread of oral microorganisms [13,15].

Viridans group streptococci and anaerobic bacteria are the most commonly isolated bacteria in blood cultures after dental procedures [2,4–7]. In healthy patients, oral microorganisms are eradicated from the blood by the reticuloendothelial system [6,8]. If this fails, microorganisms can enter any organ system through blood circulation. Hence, systemic and distant site infections due to oral source have been reported in various sites of the body [10,16–18].

Antibiotic prophylaxis (AP) has been shown to reduce the incidence and duration of bacteraemia in several studies [1,5,8,19,20]. According to the latest Cochrane Review in 2013 there is still no firm evidence whether AP is effective in patients at risk in invasive dental procedures [21]. The aim of this study was to investigate the efficacy of single-dose AP in the prevention of bacteraemia following tooth extractions at our clinic and to evaluate the antimicrobial sensitivities of bacteria isolated in post-extraction blood cultures.

Materials and methods

Study design

A total of 60 consecutive patients undergoing tooth extractions at the Department of Oral and Maxillofacial Surgery, Helsinki University Hospital during 2006–2008 were enrolled in the study. Patients were identified from the weekly theatre lists by the research team members. Most patients seen at this secondary care referral hospital have complex medical histories and underlying conditions requiring treatments at other departments of the hospital (i.e. Haematology/Oncology, Rheumatology, Infectious Diseases). The need of

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Table 1. Patient demographics in the different patient groups. Data are presented as number or mean (range).

	All	NO AP	AMX/AMP	CLI	*p*
Total number	50	6	38 (28 i.v. / 10 p.o.)	6	
Female:male	23:32	1:5	17:21	3:3	NS
Age (years)	55 (21–89)	43 (33–50)	56 (21–89)	51 (36–61)	.048
Female	57 (31–89)	45	59 (31–89)	47 (36–57)	NS
Male	54 (21–79)	42 (33–50)	54 (21–75)	54 (44–61)	NS
No. of teeth extracted	8 (1–27)	3 (1–12)	9 (1–27)	8 (1–21)	.043
Duration of extractions (minutes)	40 (4–89)	33 (21–61)	42 (4–89)	36 (11–66)	NS

Mean and range are shown.

AP was determined according to the health status and possible allergies of the patients. AP was administered to patients with increased risk for infection complications. Patients who had received antimicrobial agents (i.e. antibiotics, antifungals, or antiviral agents) within the past 30 days, had an oral abscess, or had been diagnosed with a haematological malignancy (i.e. leukaemia, lymphoma), neutropenia ($<0.5 \times 109$/l) or human immunodeficiency virus were excluded. All patients were over the age of 18. The extractions were performed during a single session. Complete blood count was requested preoperatively to assess thrombocyte and leukocyte levels. The age, sex, general health status, underlying diseases and medications in use were recorded. All participating subjects signed an informed consent before inclusion. The study has been approved by the Ethics Committees of the Helsinki University Central Hospital (Dnro 277/E6/06).

Collection of blood cultures

Peripheral venous blood cultures, approximately 8 ml each, were drawn from the patients into aerobic and anaerobic vacuum bottles; BacT/ALERT FA aerobic culture media (30 ml peptone-enriched TSB, supplemented with brain heart infusion (BHI) solids and activated charcoal) and BacT/ALERT FN anaerobic culture media (40 ml peptone-enriched TSB, supplemented with BHI solids and activated charcoal) (bioMérieux, Marcy l'Etoile, France). The blood cultures were drawn at baseline (before the administration of any antimicrobial agents and before any dental manipulation) (time point I), 5 min after the first tooth extraction (time point II) and 20 min after the end of the last extraction (time point III). The blood cultures were collected from the antecubital fossa or dorsum of the hand after the disinfection of the venepuncture site by scrubbing with 70% alcohol. The samples were immediately transported to the laboratory. The blood cultures were analyzed according to routine protocols at the Department of Clinical Microbiology, Helsinki University Central Hospital HUSLAB, an accredited reference laboratory.

Statistical methods

Data was analyzed by using GraphPad Prism version 5.00 (GraphPad Inc. San Diego, CA). The two-tailed Mann–Whitney test and the one-way ANOVA, Bonferroni post-test and Fisher's exact test were used for the comparisons between groups. *p* Values of less than .05 were considered statistically significant.

Results

Subjects

Of the 60 patients recruited in the study 10 were excluded (AMX/AMP $n = 8$, CLI $n = 0$, NO AP, $n = 0$). Reason for exclusions was failure in the collection of blood cultures at the right time points. The patient demographics and characteristics are summarized in Table 1. Thirty-eight patients (76%) received prophylactic oral amoxicillin or intravenous ampicillin 2 g (AMX/AMP), six patients (12%) received oral or intravenous clindamycin 600 mg (CLI) and six patients (12%) did not receive any prophylactic antimicrobial agents (NO AP). The mean duration of the extractions was 41 min (range 4–89 min). There was no statistical difference in the mean duration of the extraction procedures among the different patient groups. The mean time between the blood cultures at time point II and time point III was 55 min (range 19–104 min). The underlying medical conditions of the patients in the different groups are presented in Table 2.

Prevalence of bacteraemia

Time point I (baseline)

All of the blood cultures at time point I were negative.

Time point II (5 min after the first extraction). At time point II, 83% of the blood cultures in the CLI group, 67% of the blood cultures in the NO AP group and 5% of the blood cultures in the AMX/AMP group had bacterial growth (Table 3). The proportion of positive blood cultures was significantly higher in CLI and NO AP groups compared to AMX/AMP group as presented in Figure 1 ($p < .0001$ and $p = .015$, respectively). There was no significant difference in the prevalence of positive blood cultures between CLI and NO AP groups.

Time point III (20 min after the end of the last extraction). At time point III, 50% of the blood cultures in the CLI group and 17% of the cultures in the NO AP group were reported with bacterial growth. All blood cultures at this point were negative in the AMX/AMP group. The difference in the proportion of positive blood cultures at time point III was statistically significant between AMX/AMP group and CLI group ($p = .0015$) but not compared to the NO AP group.

Characteristics of bacteria detected in blood cultures

A total of 66% of all the positive blood cultures were polymicrobial. There was no significant difference in the prevalence

Table 2. The underlying diseases of the patients in the different patient groups.

Underlying diseases predisposing to systemic complications	NO AP	AMX/AMP	CLI
Diabetes mellitus (type 2)		8	2
Previous sepsis (Streptococcal)		1	
Psoriasis (infliximab treatment)		1	
Waldeström's macroglubulinemia			
Systemic lupus erythematosus			
Recent infective endocarditis		1	
Rheumatoid arthritis		2	
Cirrhosis		1	
Hepatic encephalopathy			
Other underlying organic diseases	NO AP	AMX/AMP	CLI
Arterial hypertension	1	17	2
Cardiac arrhythmia		6	
Cardiac insufficiency		3	
Recent cardiac thrombosis		1	
Heart valve disease		1	
Cardiomyopathy		1	
Previous cardiac infarction		2	
Arteriosclerosis		1	
Chronic obstructive pulmonary disease		5	
Pulmonary insufficiency		1	
Asthma	1	4	1
Pyelonephritis		1	
Nephropathy		1	
Hyperlipidaemia		7	2
Previous cerebral infarction		2	1
Sjögren's syndrome			
Myasthenia gravis		1	
Hypothyroidism	1		
Solid malignant tumours (pre-treatment)	NO AP	AMX/AMP	CLI
Lung carcinoma			1
Laryngeal carcinoma		2	
Oral carcinoma		1	
Salivary gland carcinoma		1	
Squamous cell carcinoma of skin		1	
Renal carcinoma		1	
Mammary carcinoma		2	
Malignant mesothelioma		1	
Immunosuppressive drugs	NO AP	AMX/AMP	CLI
Infliximab		1	
Methotrexate and intravenous corticosteroid		1	
Sulphasalazine and methotrexate		1	
Prednisolone		1	

of aerobic (49%) and anaerobic bacteria (46%) in the blood cultures. Overall, 5% of the cultures contained normal oral flora. In total, 39% were aerobic Gram-positive bacteria, 7% aerobic Gram-negative bacteria, 32% anaerobic Gram-positive bacteria and 17% anaerobic Gram-negative bacteria. The most frequently isolated bacterial species were *Streptococcus* species found in 20% of all the positive blood cultures. *Streptococcal* species isolated were *Str. anginosus*, *Str. mutans*, *Str. viridans*, *Str. oralis* and *Str. mitis.* All the *Streptococcus* species were susceptible to AMX/AMP. All *Streptococci* were isolated 5 min after the first tooth extraction. The bacterial findings in the blood cultures are demonstrated in Table 3.

Antimicrobial sensitivities of bacteria isolated in post-extraction blood cultures

All of the bacteria in the positive blood cultures in the AMX/AMP group were sensitive to AMX/AMP and CLI. In the CLI group 72% of the bacteria from the blood cultures collected at time point II were sensitive to CLI, 17% were resistant to CLI and 11% were dose dependently sensitive to CLI, whereas all were susceptible to AMX/AMP. All of the bacteria in the blood cultures at time point III in the CLI group were resistant to clindamycin (100%). Of the bacteria in the positive blood cultures in the NO AP group 100% were susceptible to AMX/AMP and 23% to CLI at time point II. At time point III, the isolated bacteria in the NO AP group were susceptible to CLI.

Discussion

Amoxicillin, with a dose of 2 g, has been found to have high efficacy in reducing both the prevalence and duration of bacteraemia following tooth extractions in several studies [1,5,8,9]. This was confirmed in our study, as 95% of the blood cultures collected after tooth extractions in patients that had received AMX/AMP were negative. A study by Reis et al. demonstrated a significantly higher amount of positive blood cultures in patients who did not receive AP compared to patients receiving AMX. However, when samples were analyzed with qPCR there were no significant differences in the incidence or the magnitude of bacteraemia in the two patient groups. However, molecular detection methods detect DNA and not viable cells and, therefore, provide indirect measure of bacteraemia [22].

There are few studies that have evaluated the effect of CLI on the prevention of bacteraemia following dental procedures, but the results have not been able to confirm its efficacy [23]. Yet, the prophylactic use of CLI seems to be fairly wide [5,24]. We were surprised by the small amount of patients allergic to penicillin and, therefore, the CLI group unfortunately remained small. However, with this small number of patients the results of our study confirm the inefficacy of CLI in the prevention of bacteraemia. All of the patients in the CLI group had positive blood cultures; 83% of blood samples were positive for bacterial growth 5 min after the first tooth extraction and 50% 20 min after the end of all the extractions. The prevalence of bacteraemia was significantly higher in the CLI group compared to AMX/AMP group both 5 min and 20 min after the tooth extractions.

The most frequently isolated bacterial species were streptococci found in 20% of the positive blood cultures. This was in line with previous studies [1,4,5,7,8]. In the AMX/AMP group, the bacteria that could be isolated consisted of *Streptococcus* species and *Propionibacterium* species. In the CLI group, species from aerobic and anaerobic as well as Gram-positive and Gram-negative bacteria could be detected. *Streptococcal* species isolated were *Str. anginosus*, *Str. mutans*, *Str. viridans*, *Str. oralis* and *Str. mitis,* which are frequently detected in infective endocarditis (IE) [9]. Most of the positive blood cultures were polymicrobial. The positive blood cultures isolated 5 min after the first extraction were more frequently polymicrobial than the positive blood cultures isolated 20 min after the end of the operation reflecting the different eradication rate of the bacteria by the host.

AP is given preoperatively in order to achieve peak concentrations at the onset of the dental procedure. Yet, a notable proportion of patients with evident bacteraemia despite adequately administered AP are recorded reflecting the

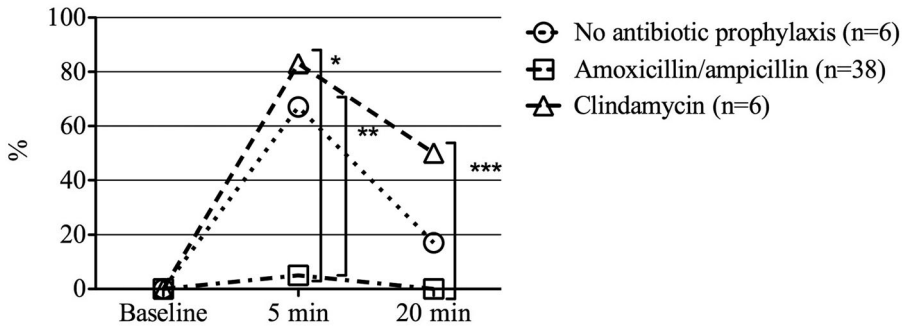
Table 3. Characteristics of the patients with positive blood cultures five minutes after the extraction of the first tooth (timepoint II) or 20 min after the end of the extractions (timepoint III).

Age	iv/po	No. of extracted teeth	Duration of extractions (min)	Underlying diseases	Bacterial findings at timepoint II	Bacterial findings at timepoint III
Amoxicillin or ampicillin						
21	iv	4	89	–	*Propionibacterium acnes*	–
36	po	16	63	Arterial hypertension	*Streptococcus anginosus, Streptococcus mutans, Streptococcus viridans,* mixed oral flora	–
Clindamycin						
44	iv	19	66	Arterial hypertension, psoriasis, gout	*Streptococcus viridans, Staphylococcus epidermidis, Veillonella,* two different unidentified gram-positive rods, mixed oral flora	An anaerobic Gram-positive coccus
57	iv	21	24	Lung cancer (pretreatment), psoriatic arthritis	*Streptococcus viridans, Haemophilus* spp, three different unindentified gram-positive rods, mixed oral flora	A Gram-positive rod
49	iv	3	49	–	–	*Neisseria mucosa, Propionibacter acnes*
36	iv	3	39	–	*Lactobacillus gasseri, Dialister* spp., mixed oral flora	–
57	iv	1	44	Diabetes mellitus II, arterial hypertension, hyperlipidaemia, asthma, Meniere's disease, osteoporosis, neuropathy	*Streptococcus mutans, Micromonas micros, Bulleidia/ Solobacterium moorei*	–
61	iv	2	11	Diabetes mellitus (type II), arterial hypertension, hyperlipidaemia, previous cerebral infarction, epilepsy	*Actinomyces* spp.	–
No AP						
40	–	1		–	*Staphylococcus epidermidis, Micrococcus* spp., *Propionibacter acnes,* mixed oral flora	–
47	–	?		–	*Streptococcus anginosus, Actinomyces* spp., *Atopobium parvulum, Anaerobobus geminatus, Dialister pneumosintes, Veillonella parvula*	–
42	–	1	28	Arterial hypertension	*Streptococcus viridans, Streptococcus anginosus*	*Veillonella* spp,
33	–	12	21	–	*Neisseria elongata, Fusobacterium nucleatum*	–

iv: intravenous; po: per oral.

complex interactions between the host and the micro-organisms [8,12]. Several national recommendations have been made for the identification and evaluation of the operative risk factors and 'at risk' patients [19,20,25–27,28]. However, these recommendations have been mainly aimed at the prevention of IE. Patients included in these studies have been immunologically heterogeneous and poorly defined for their comorbidities. As the scientific interest has mainly been focussed on IE, other distant site infections and their potential risk factors have been less studied.

In our study, the choice of AP regimen was determined by the risk stratification according the local clinical practice guidelines. At our hospital patients are categorized into four groups; none/minor, elevated risk, moderate risk and high risk based on their overall risk for infection complications. The risk is assessed by the medically trained members of the Maxillofacial surgery team and builds on full medical history and the assessment of immunological status of the patient as well as a detailed internal guideline. This is a different approach compared to US, UK and European guidelines, where these recommendations for AP are restricted to the prevention of IE. In a recent meta-analysis by Cahill and colleagues, the evidence base of AP for IE was analyzed. The most restricted guideline was presented by NICE in the U.K. as they restricted the use of AP totally in March 2008. However, after the restriction it was shown that the incidence of IE increased significantly [29,30]. Thereafter, in 2016, the recommendations were softened to state that AP should not be routinely used prior dental procedures. The guidelines stated by the European Society for Cardiology (ESC) and the American Heart Association/American College of Cardiology (AHA/ACC) restricted the use of AP to various



* Amoxicillin/ampicillin vs clindamycin $P<0.0001$
** Amoxicillin/ampicillin vs no antiobiotic prophylaxis $P=0.015$
*** Amoxicillin/ampicillin vs clindamycin $P=-0.0015$

Figure 1. Prevalence of bacteraemia as percentage of positive blood cultures per patient group at baseline, five minutes after the extraction of the first tooth and 20 min after end of the operation. *p* Values between the proportions of positive blood cultures between different patient groups are presented.

degrees and situations. The effect of these guidelines on the incidence of IE has also been studied, but no significant difference has been detected although a similar increasing trend was observed.

The majority of the patients in this study were considered having elevated risk for infection complication and AMX/AMP was the most common drug of choice. CLI was administered to patients allergic to penicillin as well as when the risk was considered moderate with the aim of covering broader range of oral bacteria. Unfortunately, the subgroup of patients receiving no AP and CLI remained small decreasing the statistical power of our results. The decision whether AP is administered is based on the immunological and medical status of the patient, the infection status of the operation site and invasiveness of the procedure. The majority of patients seen at our Department have complex medical histories and many are immunocompromised, and, thus, require AP. Further research is needed regarding the identification of the patients 'at risk' that benefit from AP prior to dental procedures. It is acknowledged that the cumulative burden of daily oral activities play a significant role in the risk for community acquired IE. However, on the ethical point of view, dental as well as other medical procedures conducted by health care professionals should not increase the patient's risk for IE or other distant site infections as there is evidence on the effect of AP in prevention of post-procedural bacteraemia and consequently IE. On the other hand, accountable and research-based use of antimicrobial agents is essential to minimize development of resistance. Stopping the use of ineffective antibiotics like clindamycin in dental prophylaxis is an obvious first step in antibiotic stewardship in dentistry.

In conclusion, appropriately administered AMX proved its efficacy in reducing both the prevalence and duration of bacteraemia following tooth extractions. Based on the results of our study, the use of CLI in the prophylactic setting can be recommended only in rare cases when other antibiotic regimens cannot be used, for example due to drug allergies. The most effective prevention is the maintenance of good oral health, which supports stabile and protective oral microbiota. Prevention of infection complications in the surgical setting in general should consist of high standard surgical techniques and perioperative aseptic procedures in addition to antibiotic prophylaxis.

Disclosure statement

The authors have none to declare.

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