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Comparative efficacies of Amoxicillin and Moxifloxacin in Prevention of Bacteremia following Dental Extraction

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Abstract: AIM: *To compare efficacies of Amoxicillin and Moxifloxacin in prevention of bacteremia following dental extraction.*
MATERIAL & METHOD: *Thirty patients were randomly selected and allocated into 3 groups. Group 1: subjects receiving no antibiotics (controls); Group 2: subjects receiving capsule Amoxicillin (AMX); and Group 3: subjects receiving tablet Moxifloxacin (MXF). A peripheral venous blood sample (6 ml) was drawn 30 seconds and 1 hour after dental extraction and microbiological analysis was carried out.*
RESULT: *At baseline, the percentages of positive blood cultures detected were 40% in the control group, 40% in the AMX group, and 30% in the MXF group. The prevalence of bacteremia immediately after completion of the dental extraction was 80% in the control group, 70% and 60% in AMX and MXF groups respectively which were statistically significantly (P< 0.001) when compared to the control group. The prevalence of bacteremia at 1 hour after completion of the final dental extraction was 70% in the control group, 50% and 30% respectively in AMX and MXF groups respectively which were statistically significantly when compared to the control group. Significant differences were observed in the percentages of positive blood cultures between the control group and the AMX and MXF groups (63.33% versus 53.33% and 40%, respectively).*
CONCLUSION: *Moxifloxacin was found to be clinically efficacious for the prevention of bacteremia after dental manipulations whereas Amoxicillin was observed to be unsatisfactory in this regards.*
Keywords: *Antibiotics, Amoxicillin, Moxifloxacin, Bacteremia, Tooth Extraction,*

I. Introduction:

Bacteremia is a condition in which living bacilli are found free in the blood-stream. There are two classes of bacteremia: one in which the inhibitory power of the blood very rapidly destroys the bacteria, and in the second the inhibitory action of the blood is for some reason kept in abeyance.[1] The concern with occult bacteremia is that it could progress to a more severe local or systemic infection if left untreated.[2] Patients with prosthetic heart valve, cardiac structural like damage valves and damaged endocardium due to ischemic changes; glomerulo nephritis and individuals with recent prosthetic joint replacement surgery and bone prosthesis are at increased risk of developing bacterial infections because of bacteremia following dental procedures. Among this endocarditis is the major threat, as, in the majority of retrospective studies published during 1990's the oral cavity was identified as the portal of entry of causative microbial agent in 14-20 % of patients with bacterial endocarditis.[3]

Bacterial endocarditis (BE) is an uncommon infection of the cardiac endothelium, with an incidence ranging between one and five cases/100,000 population/yr.[4,5] The main complications resulting from BE are valvular destruction, heart failure, and emboli, requiring cardiac surgical treatment within 3 months for almost 30% of patients.[6] In 1995, for the first time, the oral origin of two cases of BE was demonstrated by molecular biological techniques, since a complete concurrence of identity was observed between the blood and oral cavity isolates.[7]

Streptococci, particularly the *viridans* group, continue to be the bacteria most frequently involved in bacterial endocarditis.[8,9] *Staphylococcus epidermidis* and *aureus* are other species most frequently involved,[10] and although these species are considered commensal microorganisms of the skin or nosocomial pathogens, they have also been isolated from the oral cavity.[11,12] Consequently, these micro-organisms may also occasionally be responsible for bacterial endocarditis of oral origin.[13] Facultative anaerobic Gram-negative bacteria of the HACEK (*Haemophilus* spp., *Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, Kingella* spp.) group were infrequently implicated in early studies of bacterial endocarditis,[14] they may be responsible for 3-5% of cases of bacterial endocarditis.[15,16] The most frequently isolated HACEK micro-organism implicated is the periodontopathogen *Actinobacillus* (now *Aggregatibacter*) *actinomycetemcomitans.*[16] The obligate anaerobic bacteria were considered to be etiological agents in 2-16% of cases of bacterial endocarditis.[17] The oral cavity constitutes one of the principal ecological reservoirs for

some of these micro-organisms, principally *Fusobacterium* spp., *Bacteroides* (*Porphyromonas*) spp., and *Peptostreptococcus* spp.[18] In a recent analysis of 51 cases of bacterial endocarditis caused by Gram negative obligate anaerobic bacteria, the oral cavity was implicated in 40% of cases in which the portal of entry was identified.[19]

Amoxicillin continues to be the antibiotic of choice for patients "at risk" of BE and who are to undergo certain dental procedures; for patients allergic or intolerant to penicillin the antibiotic of choice is Clindamycin.[20,21,22] Moxifloxacin is a broad-spectrum antibacterial agent approved for use for the treatment of acute exacerbations of chronic bronchitis, community-acquired pneumonia, acute bacterial sinusitis, and uncomplicated skin and skin structure infections.[23] This fluoroquinolone shows good in-vitro activity against odontogenic pathogens.[24,25] It has been observed that all the streptococci isolated from a series of patients with iatrogenic bacteremia of oral origin showed a low MIC to Moxifloxacin.[26] Furthermore, they have demonstrated its efficacy in-vivo for the treatment of submucous layer dental abscesses, confirming its penetration into tissue in the oral cavity.[27]

In the following study efficacies of Amoxicillin and Moxifloxacin in prevention of bacteremia following tooth extraction were evaluated.

The study group was made up of 30 patients, including 17 (57%) males and 13 (43%) females, with a average age of males 40.64 years (age range, 20 to 72 years) and of females were 35.53 (age ranges from 22-62). The median number of teeth extracted per patient was 1.13. No significant differences were found between the different study groups with regard to age, sex, or number of teeth extracted.

II. Materials And Methods:

This study included 30 (17 males and 13 females) (age range: 20-72 years) systemically healthy subjects. Subjects were recruited from the Outpatient section of the Department of Oral and Maxillofacial Surgery, Dr. D.Y. Patil Dental College & Hospital, Dr. D.Y. Patil Vidyapeeth, Pune, India. The study design was approved by the Institution's Scientific and Ethical Committee and Review Boards. Written informed consent was obtained from those subjects who agreed to participate voluntarily.

Study group comprised of subjects over 18 years of age, having tooth indicated for extraction under local anaesthesia were included foe the study. Patient received antibiotics or analgesic therapy in the previous 6 months, history of allergy or intolerance to Amoxicillin and Moxifloxacin, pregnant or lactating woman, subjects with known systemic diseases or Acquired immune deficiency were excluded from the study.

Study Design: A detailed case medical and dental history was obtained. The study samples (n=30) were randomly divided by a computer generated list into 3 groups (n= 10 each): group 1: controls (subjects receiving no antibiotics), group 2: subjects receiving cap. Amoxicillin (AMX), group 3: subjects receiving tab. Moxifloxacin (MXF).

Prescription:

Cap. Amoxicillin 2g

Tab. Moxifloxacin 600mg

To determine the prevalence of bacteremia following tooth extraction, a peripheral venous blood sample (6 ml) was drawn from each patient at the baseline (before the dental extraction), 30 seconds and 1 hour after extraction. For the collection of blood for culture, a large-bore (18- to 22-gauge) angiocath needle was placed in a puncture site in the antecubital fossa, after the site was scrubbed in the usual manner with alcohol and then with povidone-iodine. The angiocath needle and line were flushed with 3 ml of saline after each blood drawn, and 2 ml of blood was drawn and discarded just before each blood sample was drawn. Each blood sample was placed into bottles containing Brain-Heart Infusion Broth media for transportation.

***Microbiological Analysis*:** Blood sample collected then was incubated for 24 hours at 95°F (35°C). This sample was then plated on Mackonkey's and blood agar media for gram staining and microscopic examination and culture sensitivity and kept for overnight incubation. First sample was taken for gram staining for microscopic examination. Another sample was taken and was treated with specific chemical reagents and was kept overnight in an incubator for biochemical reactions. Antibiotic disc containing Amoxicillin and Moxifloxacin was mounted on the media plate and plating was done with sample and was incubated.

III. Results

Characteristics of study group: The study group was made up of 30 patients, including 17 (57%) males and 13 (43%) females, with a average age of males 40.64 years (age range, 20 to 72 years) and of females were 35.53 (age ranges from 22-62). The median number of teeth extracted per patient was 1.13. No significant differences were found between the different study groups with regard to age, sex, or number of teeth extracted.

Prevalence of bacteremia: At the baseline, the percentages of positive blood cultures detected were 40% in the control group, 40% in the AMX group, and 30% in the MXF group. The prevalence of bacteremia immediately after completion of the tooth extraction was 80% in the control group. In comparison with the control group, this percentage was significantly lower in the AMX group (70%; $P< 0.001$) and in the MXF group (60%; $P< 0.001$). The prevalence of bacteremia at 1 hour after completion of the final dental extraction was 70% in the control group. In comparison with the control group, this percentage was significantly lower in the AMX group (50%; $P \leq 0.01$) and in the MXF group (30%; $P< 0.05$).

Characteristics and identification of bacterial isolates (table 1): Significant differences were observed in the percentages of positive blood cultures between the control group and the AMX and MXF groups (63.33% versus 53.33% and 40%, respectively). The bacteria that were the most frequently isolated from all the study groups were the aerobic bacteria, the percentages of aerobes varied between 26.66% in the control group, 40% in the AMX group and 16.66% in the MXF group; the percentages of facultative anaerobes varied between 36.66% in the control group, 10% in the AMX group and 26.66% in the Moxifloxacin. Gram-negative were the most frequently observed bacteria in all the study groups i.e. 87.22%. Gram-positive were 12.78%.
Culture sensitivity: Isolated bacteria's sensitive to Amoxicillin were 36.17% and that were resistant were 63.83%.Isolated bacteria's sensitive to Moxifloxacin were 76.59 % and that were resistant were 23.41%.

IV. Discussion:

The oral cavity is one of the areas of human body with the greatest microbial population and variety. Different ecosystems can be found in the mouth, where over 200 different aerobic and anaerobic bacterial species live. Oral bacteria (dental or commensal pathogens) and their products (toxins) may move from this primary location to other neighbouring or distant locations. Invasive dental procedures and oral surgery favour bacterial dissemination, especially into the bloodstream, causing transient bacteremia. Transient bacteremia is unavoidable, but its severity (bacterial load), duration (time in which bacteria remain in the bloodstream), type of bacteria in the blood (aerobic, anaerobic or mixed) and the patient's predisposition (underlying diseases, susceptible site of infection, etc.), all play a significant role in the onset of possible complications.[28]
Traditionally prophylaxis has been defined as pre- and peri-operative administration of antibiotics in order to prevent local and/or systemic post-operative infection. In Altemeier's classification, oral surgery is often graded as class II (clean-contaminated surgery), with a rate of local infection of 5 to 15% without antibiotics and <7% with antibiotics.[20] In oral surgical prophylaxis, the target microbiota differ, depending on whether the intention is to prevent local complications (abscess) or distant infections (endocardial infections, bone prostheses, joint replacements) in high risk patients who require prophylaxis because of their underlying condition.[29]

Penicillin G (parenteral), or phenoxymethyl penicillin (oral), continues to be one of the drugs of choice in dentistry and oral surgery because the majority of oral aerobic and anaerobic bacteria are sensitive to it. However, there are an increasing number of oral anaerobic bacteria that produce inactivant enzymes (ß-lactamases), making them resistant to penicillin, and leading to treatment failure.[30, 31]

To date, most of the studies on the prevalence of post-dental manipulation bacteremia have confirmed that most of the bacteria isolated in the blood cultures are sensitive to the antibiotics recommended in the prophylaxis protocols by the Expert Committees. However, increasing resistance to the beta-lactams, macrolides, and lincosamides has recently been found in oral bacteria and this could restrict their use for BE prophylaxis. Recently, new antibiotics, such as the fluoroquinolones, have been shown to be successful in the prophylaxis of bacteremia following tooth extractions in humans, and to prevent endocarditis in animal models.[20,21]

In our setting, Moxifloxacin seemed as an alternative to Amoxicillin for the prevention of bacteremia in patients who are "at risk" of BE. In contrast, we would question the effectiveness of prophylaxis with Amoxicillin for the prevention of bacteremia following dental extraction in patients "at risk" of BE. Moxifloxacin might represent a safe prophylactic alternative for the prevention of bacteremia following dental extraction in when beta-lactams are contraindicated or in infection of bacteria resistant to Amoxicillin.

It has been shown that the inefficacy of some antibiotic prophylactic regimens for the prevention of post-dental manipulation bacteremia does not necessarily imply that these cannot prevent the development of bacterial endocarditis. However, more scientific evidence of the effect of antibiotic prophylaxis on the prevalence and duration of bacteremia following dental procedures is needed, with analysis of the influence of the increasing prevalence of bacterial resistance in the oral ecosystem. Prophylactic alternative such as oral antiseptics (*i.e.*, chlorhexidine) and peptides that can interfere with bacterial adhesion should also be explored.

V. Conclusion:

In our study the efficacy of Moxifloxacin for the prevention of bacteremia following tooth extraction was found clinically satisfactory. However, the efficacy of Amoxicillin for the prevention of bacteremia after dental manipulations was found clinically unsatisfactory concluding that over-prescribing and improper dosage continues to contribute to the emergence of resistant organisms to Amoxicillin.

References:

[1]. Lake R. Aural Bacteremia, with Illustrative Cases: (Abstract). *Proc R Soc Med.* 1918; 11:47-53.
[2]. Kuppermann N. Occult bacteremia in young febrile children. *Pediatr Clin North Am*. 1999; 46(6):1073-109.
[3]. Manford M, MatharuJ, Farrington K. Infective endocarditis in a district general hospital. *J R Soc Med* 1992; 85:262-266.
[4]. Bouza E, Menasalvas A, Muñoz P, Vasallo FJ, del Mar Moreno M, García Fernandez MA. Infective endocarditis—a prospective study at the end of the twentieth century: new predisposing conditions, new etiologic agents, and still a high mortality. *Medicine (Baltimore)* 2001; 80:298-307.
[5]. Cecchi E, Forno D, Imazio M, Migliardi A, Gnavi R, Dal Conte I, et al.. New trends in the epidemiological and clinical features ofinfective endocarditis: results of a multicenter prospective study. *Ital Heart J* 2004; 5:249-256.
[6]. Heiro M, Helenius H, Mäkilä S, Hohenthal U, Savunen T, Engblom E, et al. Infective endocarditis in a Finnish teaching hospital: a study on326 episodes treated during 1980-2004. *Heart* 2006; 92:1457-1462.
[7]. Fiehn NE, Gutschik E, Larsen T, Bangsborg JM. Identity of streptococcal blood isolates and oral isolates from two patients with infective endocarditis. *J Clin Microbiol* 1995; 33:1399-1401.
[8]. Heiro M, Helenius H, Mäkilä S, Hohenthal U, Savunen T, Engblom E, et al. Infective endocarditis in a Finnish teaching hospital: a study on326 episodes treated during 1980-2004. *Heart* 2006; 92:1457-1462.
[9]. Horacio Casabé J, Deschle H, Cortés C, Stutzbach P, Hershson A, Nagel C, et al. Predictors of hospital mortality in 186 cases of active infective endocarditis treated in a tertiary medical center (1992-2001). *Rev Esp Cardiol* 2003; 56:578-585.
[10]. Hoen B, Alla F, Selton-Suty C, Béguinot I, Bouvet A, Briançon S, et al. Changing profile of infective endocarditis: results of a 1-yearsurvey in France. *J Am Med Assoc* 2002; 288:75-81.
[11]. Suzuki J, Komatsuzawa H, Sugai M, Suzuki T, Kozai K, Miyake Y, et al. A long-term survey of methicillin-resistant Staphylococcus aureus in the oral cavities of children. *Microbiol Immunol* 1997; 41:681-686.
[12]. Murdoch FE, Sammons RL, Chapple ILC .Isolation and characterization of subgingival staphylococci from periodontitis patients and controls.Oral Dis 2004; 10:155-162.
[13]. Tomás I, Diz P, Limeres J, Gónzalez A, Martínez C, Castro A . An update on infective endocarditis of dental origin. *J Dent* 2002; 30:37-40.
[14]. Garvey GJ, Neu HC. Infective endocarditis-an evolving disease.A review of endocarditis at the Columbia Presbyterian Medical Center 1968-1973. *Medicine (Baltimore)* 1978; 57:105-127.
[15]. Lepori M, Bochud PY, Owlya R, Broccard A, Schaller MD Endocarditis due to HACEK bacteria. A case report of endocarditis due to Kingella kingae. *Rev Med Suisse Romande* 2001; 121:47-50.
[16]. Paturel L, Casalta JP, Habib G, Nezri M, Raoult D. Actinobacillus actinomycetemcomitans endocarditis. *Clin Microbiol Infect* 2004; 10:98-118.
[17]. Brook I .Endocarditis due to anaerobic bacteria. *Cardiology* 2002; 98:1-5.
[18]. Garvey GJ, Neu HC. Infective endocarditis-an evolving disease. A review of endocarditis at the Columbia Presbyterian Medical Center, 1968-1973. *Medicine (Baltimore)* 1978; 57:105-127.
[19]. Bisharat N, Goldstein L, Raz R, Elias M. Gram-negative anaerobic endocarditis: two case reports and review of the literature. *Eur J Clin Microbiol Infect Dis* 2001; 20:651-654.
[20]. C Hutto, TJ Pallasch, TW Gage, Dental aspects of endocarditis prophylaxis: new recommendations from a working group of the British Cardiac Society Clinical Practice Committee and Royal College of Physicians Clinical Effectiveness and Evaluation 2004.
[21]. Dajani AS, Taubert W, Wilson AF, Bolger A, Bayer P, Ferrieri MH. Prevention of bacterial endocarditis: recommendations by the American Heart Association. *JAMA* 1997; 277:1794-1801.
[22]. Horstkotte D, F Follath, E Gutschik, M Lengyel, A. Oto, A. Pavie, J. Task Force Members on Infective Endocarditis of the European Society of Cardiology; ESC Committee for Practice Guidelines (CPG); and Document Reviewers. Guidelines on prevention, diagnosis and treatment of infective endocarditis executive summary: the task force on infective endocarditis of the European Society of Cardiology. *Eur Heart J.* 2004; 25:267-276.
[23]. Limeres, J., I. Tomás, M. Álvarez, and P. Diz..Empirical antimicrobial therapy for odontogenic infections. *Oral Surg. Oral Med. Oral Pathol Oral Radiol Endod.* 2005; 100:263.
[24]. Milazzo, I., G. Blandino, R. Musumeci, G. Nicoletti, A. M. Lo Bue, and A. Speciale..Antibacterial activity of moxifloxacin against periodontal anaerobic pathogens involved in systemic infections. *Int J Antimicrob Agents* 2002; 20:451-456.
[25]. Sobottka, I., G. Cachovan, E. Sturenburg, M. O. Ahlers, R. Laufs, U. Platzer, and D. Mack.. In vitro activity of moxifloxacin against bacteria isolated from odontogenic abscesses. Antimicrob. *Agents Chemother.*2002; 46:4019-4021.
[26]. Tomás, I., M. Álvarez, J. Limeres, J. L. Otero, E. Saavedra, C. López-Meléndez, and P. Diz.. In vitro activity of moxifloxacin compared to other antimicrobials against streptococci isolated from iatrogenic oral bacteremia in Spain. *Oral Microbiol Immunol.* 2004; 19:331-335.
[27]. Limeres Posse J, E Vázquez García, M. Otumuro Rial, F. Caamaño Durán, I. Tomás Carmona, and P. Diz Dios.. Eficacia clínica del moxifloxacino en el tratamiento de abscesos odontogénicos submucosos. *Semergen* 2006; 32:58-62.
[28]. Okell CC, Elliott D. Bacteremia and oral sepsis with special reference to aetiology of bacterial endocarditis. *Lancet* 1935; 2:869-872.
[29]. Dajani AS, Taubert KA, Wilson W et al. Prevention of bacterial endocarditis: recommendations by the American Heart Association. *Clin Infect Dis.* 1997; 25:1448-1458.
[30]. Sixou JL, Magaud C, Jolivet-Gougeon A, Cormier M, Bonnaure-Mallet M. Microbiology of mandibular third molar pericoronitis: incidence of beta-lactamaseproducing bacteria. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003; 95:655-659.
[31]. Heimdahl A, Von Konow L, Nord CE. Isolation of betalactamase producing Bacteroides strains associated with clinical failures with penicillin treatment of human orofacial infections. *Arch Oral Biol* 1980; 25:689-692.

Table 1: Characteristics of Bacterial Species Isolated

Klebsiela pneumonia	Gram-negative and Facultative Anaerobic	11	12.22%
Pseudomonas aureginosa	Gram Negative and Facultative Anaerobic	6	6.66%
Citrobacter koseri	Gram-negative and Aerobic	1	1.11%
Proteus mirabilis	Gram-negative and Facultative Anaerobic	3	3.33%
Citrobacter freundi	Gram-negative and Aerobic	7	7.77%
Escherichia coli	Gram-negative and Aerobic	4	4.44%
Sporebeing bacilli	Gram-negative and Aerobic	5	5.55%
Serratia species	Gram-negative and Facultative Anaerobic	1	1.11%
Streptococci species	Gram-positive and Aerobic	6	6.66%
Acenitobacter	Gram-negative and Aerobic	2	2.22%
Enterobacter	Gram-negative and Facultative Anaerobic	1	1.11%
Total		47	52.22%