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Antibiotic Prophylaxis in Dentistry against Infective Endocarditis

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Received: July 29, 2021; **Published:** September 23, 2021

Abstract

Introduction: Bacteria that may be found in tooth plaque may multiply in tremendous amounts such that they can cause gingivitis (gum infection and bleeding). When gums bleed, there are probabilities that bacteria can enter the bloodstream and infect other body parts. Endocarditis affects the inner lining of the heart. Antibiotic prophylaxis against infective endocarditis is recommended in dental procedures to ensure that dental infections are not implicated in infections in other parts of the body, especially the heart. Dental professionals are conversant with the application of antibiotic prophylaxis as a potent remedy in the control of dental disorders, especially those that cause bleeding in the mouth (Kobayashi, 2019). However, it is vital to note some dentists get confused regarding the nature of and indications for antibiotic prophylaxis. Certain situations require expert opinion to prevent the occurrence of harmful effects when an infection occurs [1]. The onset of microbial endocarditis, the pathogenesis, symptoms and outcomes, epidemiological analyses, and recommendations on the treatment using different antimicrobial agents are pertinent facts to this paper. Moreover, the implementation of antimicrobial treatment against infective endocarditis is a process that requires attentive care because of the side-effect profiles of certain antibiotics on patients [2].

Objective: To examine carefully the prophylactic antibiotics to prevent endocarditis associated with dental procedures.

Methods: Different papers are analyzed.

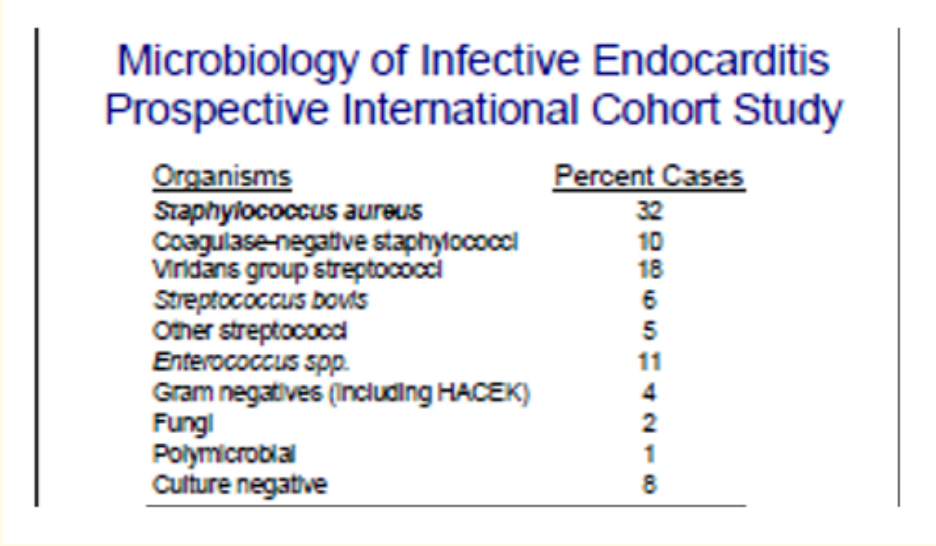
Conclusion: Engage weaker antimicrobial agents before using the stronger ones. That ensures that the problem of resistance to antibiotics is eliminated.

Keywords: *Clinical Attachment Level; Gingival Bleeding Index; Plaque Index; Probing Pocket Depth; Periodontal Health*

Introduction

Infective endocarditis refers to the infection of the endocardial surface of the heart that affects one or more valves of the heart. The disease is characterized by effects that may negatively impact the mural endocardium and the septa of the heart. In dentistry, infections from bacteria result in infective endocarditis. That is because when a patient is suffering from a bacterial gingivitis, bleeding may take place in the gums of the patient [3]. The bleeding may, in turn, lead to the transfer of the bacteria to heart tissue through inclusion into the systemic circulation [4]. The disease affects both adults and children. Epidemiological studies [5] on infective endocarditis have unraveled that the disease is rare in occurrence and that this finding pertains to general populations Infections of the endocardium can be life-threatening and target the valves of the heart. Infective endocarditis has shown significant morbidity implicated in heart surgery for half of the patients that have suffered from infective endocarditis. It has been established that infective endocarditis emanates from bacteria

that invade the mucosal cells of the buccal cavity [6]. According to Sunnerhagen, aerococci are one of the virulent bacteria known to cause infective endocarditis (Appendix 1 and 2) adapted from Brouqui and Raoult [7].



Appendix 1: *Microbiology of infective endocarditis (Adapted from Fowler., et al. 2005) [8].*

Appendix 2: *Risk factors for specific pathogens that cause infective endocarditis (Adapted from Brouqui and Raoult, 2001) [7].*

Methodology

Search strategy

Several electronic databases were searched for relevant literature. These databases include Medline, Google Scholar, Journal of Clinical Medicine, and Joanna Briggs Institute. Vast search was conducted within the websites to ensure that appropriate journals were located. Keywords used included Antibiotic prophylaxis against Infective Endocarditis, Invasive Dental Procedures that lead to Infective Endocarditis and the Challenges of Antibiotic Prophylaxis. The search terms that were used to locate the items were applied singularly instead of in groups to be more specific in the search [9]. Additional limits were also put on the search especially the limit of time in which the articles were published to ensure that most recent literature are used. Concerning this, literatures that are mainly ten years old were considered in the search to ensure that that there were only contemporary literatures. More than twenty five sources were used in this study. Narrowing down on the sources was done by isolating sources that address the specific parts of this study like epidemiology of infective endocarditis and prophylaxis.

Epidemiology of infective endocarditis

Evidences of occurrence of infective endocarditis show that the disease is a rare one and that the incidences of its occurrence is between two to three episodes in a population of 150,000 inhabitants per year in the United Kingdom as shown in appendix 3 [10]. The incidences of the disease is higher in elderly people because the group of elderly people is often affected by comorbidities such as the high rate of the overall population ageing, the increased survival rate of patients with congenital and valvular heart disease, and increased use of prosthetic devices which leads to a higher incidence of infective endocarditis [12]. A third of the patients with infective endocarditis acquire the disease out in a nosocomial sense (in a health-care environment) such as in a hospital. In the United Kingdom, mortality from infective endocarditis is relatively low because of the adaptation of health guidelines. According to Shah., *et al*. [13] mortality in the UK is one per year. The diagnosis of the disease is done based on both minor criteria and major criteria [14]. Detection of incidents of infective endocarditis varies because of the varying series for diagnosis such as echocardiography and the oscillating mass [15]. The history of infective endocarditis can be investigated in children and young adults to predict incidences of occurrence of the disease. It has been shown that chronic rheumatic heart disease is implicated in the incidences of infective endocarditis [16,17].

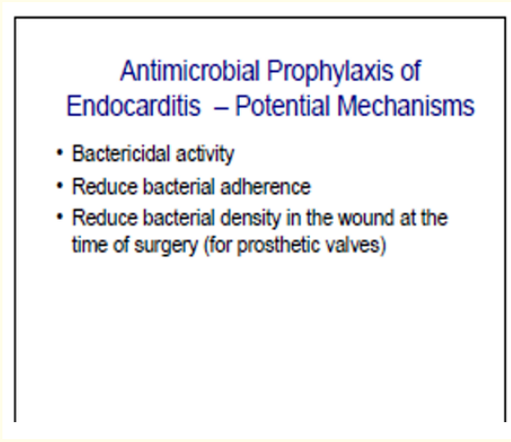
Historical Perspective
Osler's Gulstonian lectures provided the 1st comprehensive overview of the disease •
Lewis and Grant (1923) were the first to link a transient bacteremia with deformed heart valves as themain risk factors for infection
• The introduction of penicillin in 1948 marked the first successful therapy for this otherwise fatal

Appendix 3: *Adapted from Lowy., et al. 2004 [11].*

Antibiotic prophylaxis of infective endocarditis

In this case, prophylaxis involves the use of antimicrobial agents to thwart incidental occurrences of infective endocarditis [18]. However, it is important to consider certain factors that are vital in the administration of antimicrobial agents against infective endocarditis [19,20]. These factors are based on identification of patients who are at risk of suffering infective endocarditis. Firstly, individuals who have acquired a disease of the valve of the heart characterized with regurgitation coupled with stenosis. Secondly, those who have acquired cardiomyopathy in hypertrophic levels [21]. Thirdly, individuals who have had infective endocarditis in their medical history even if the condition had been corrected using surgical procedures [22]. Fourthly, individuals who have suffered from congenital heart disorders. Lastly, individuals who have suffered from a replacement of the valves of the heart owing to infective endocarditis [23].

Prophylaxis against infective endocarditis should, therefore, be carried out using some guidelines that ensure that the outcomes of prevention are favorable (See appendix 4). The first consideration is that antibiotics have potent side-effect profiles that can be deleterious to the recipients of the drug [24]. Owing to this, it is of vital importance to ensure that the individual who receives the drug cannot develop lethal conditions owing to the drug. Secondly, the administration of antibiotics should be done with considerations to the development of resistance to the drug by a certain strain or species of bacteria. That consideration is important in prophylaxis because the drug of a particular regimen should be outlined clearly. Then alternatives to the drugs against which resistance has been developed will become feasible. Thirdly, antibiotic prophylaxis should be done in consideration of the underlying conditions of a patient. For example, a patient who is pregnant may not be given certain antibiotics because some antibiotics are so toxic that they can be implicated in abortion. Therefore, healthcare professionals should come up with reasonable alternatives that can cater for some complications during prophylaxis [25].



Appendix 4: *(Adapted from NICE, 2016) [23].*

Concerning infective endocarditis, several considerations must be made in prophylaxis. Patients that have suffered from cardiac lesions and are at the risk of developing infective endocarditis should be excluded from antibiotic prophylaxis. The rationale behind this is that even though they stand a high chance of developing infective endocarditis, they only become intoxicated because they have not been diagnosed with the infection. Antibiotic remedies are vital in treating active infections caused by microbes [23,26,27].

There are some outstanding guidelines based on recommendations in the administration of prophylaxis against infective endocarditis. Firstly, the identification of cardiac risk factors should be made. Risk factors predispose the heart tissue to infective endocarditis based on different factors [28]. Such factors include the likelihood of heart valve replacement, acquired disease of the heart valve that may increase the risk of invasion by bacteria, possession of congenital heart disease and history of endocarditis. A history of heart problems is an indication of risk to disease development because it may produce an inclination towards the development of infective endocarditis because traces of infective bacteria may have remained in the patient's system after treatment [10,15].

During prophylaxis, patient advice should be given to ensure that they can accept the antibiotic regimen for favorable outcomes. There are four pieces of advice that a patient should be given. Firstly, the benefits and risks of antibiotic therapy should be made articulate to the patient. The patient should know the risks because that will ensure that they can bear up with the important outcomes of the therapy much as they benefit from the antibiotics. Secondly, the healthcare professional should be emphatic about the importance of excellent oral health. That is because infective endocarditis is caused by bacteria that originate from the buccal cavity and invade the tissues of the heart through systemic circulation [29]. The latter occurs during dental procedures or during oral health practices such as brushing one's teeth. Thirdly, the patients should be made to know the symptoms that indicate infective endocarditis to identify them when they show up.

One of the most important factors which can control the infection is to seek medical advice as soon as possible, yet it has been found according to many researchers such as [5,30] that a high rate of infective endocarditis cases are diagnoses within the late stages of infection which might increase the mortality rate [10]. Lastly, healthcare providers should explain to the patients the risks associated with invasive procedures in medical interventions [23].

Prophylaxis for patients who are at risk of developing infective endocarditis should be done under some circumstances. Firstly, patients undergoing dental procedures stand risks of developing infective endocarditis and should, therefore, be put on prophylaxis. That is because most dental problems emanate from infections by bacteria. Antibiotics should be administered to ensure that chances of developing infective endocarditis are reduced [16,17]. Secondly, incidences of infection should be diagnosed and treated promptly to minimize the risk of developing endocarditis. Thirdly, individuals who have undergone surgical procedures in other body systems such as the genitourinary tract should receive antibiotic treatment promptly because bacteria that cause endocarditis can enter through surgical wounds and create disease development.

Results

Tables of results (See appendix 5) indicate that there is a wide variety of microbes that cause infective endocarditis which were the same findings reported by Ghosh., *et al* [31]. Some of the common pathogens that cause infective endocarditis are streptococcus, aerococci, and staphylococcus. Of note is that specific antibiotics that are used in the treatment of infective endocarditis are shown in the table which is adopted from Tafreshi., *et al* [32]. These are the penicillins (amoxicillin) and cephalosporins (cephalexin). The clearance of bacteria from the tissues of the heart is expected when antibiotics are administered to the patient as antibiotics inhibit microbial cell growth and multiplication.

Procedure	Common pathogens	Drug of choice	Adult dose	Penicillin hypersensitivity drug of choice	Adult dose
Dental	Viridans group streptococci	Amoxicillin Amoxicillin/ampicillin **Second line** Cephalexin Cefazolin/ceftriaxone	2 gr p.o. 2 gr i.m./i.v. 2 gr p.o. 1 gr i.m./i.v.	Clindamycin	600 mg
Implantable cardiac electronic device insertion	Staphylococci (methicillin-sensitive) Staphylococci (methicillin-resistant)	Cefazolin Vancomycin*	1 gr i.v. 1-1.5 gr	Vancomycin*	1.5 gr
Procedure in infected/ colonized tissue					
Respiratory	Staphylococci	Cefazolin	1 gr i.v.	Clindamycin Vancomycin*	600 mg 1-1.5 gr
Genitourinary or gastrointestinal	Enterococci	Amoxicillin/ampicillin	2 gr i.m./i.v.	Vancomycin*	1-1.5 gr
Skin	Staphylococci Beta-hemolytic streptococcus Staphylococci (methicillin-resistant)	Amoxicillin Cephalexin Cefazolin/ceftriaxone Vancomycin*	2 gr i.m./i.v./p.o. 2 gr p.o. 1 gr i.m./i.v. 1-1.5 gr	Clindamycin Vancomycin*	600 mg 1-1.5 gr

Appendix 5: *Showing results of antibiotic prophylaxis against infective endocarditis.*
** Vancomycin should be given as a slow infusion 1 gr/hr dose. Initiate infusion 60 - 90 minutes before the procedure (Adapted from Tafreshi., et al. 2007) [32].*

The graphs (Figure 1-3 adapted from Levison and Levison 2009 [33]) indicate the relationships in the interactions of microbes and antibiotics (Appendix 5). The first graph shows the relationship between the concentration of antibiotic at the site of infection and the number of bacterial cells. The effectiveness of the antibiotic is directly proportional to a lower number of bacterial cells at the site of infection. The second graph shows the concentration of antibiotics in blood plasma per hour. The latter relationship is vital because it is an indication of whether or not there will be a sufficient concentration of antibiotics in systemic circulation to clear the bacteria responsible for the infection. The last paragraph shows the rapid distribution phase of the antibiotic and its clearance from the system.

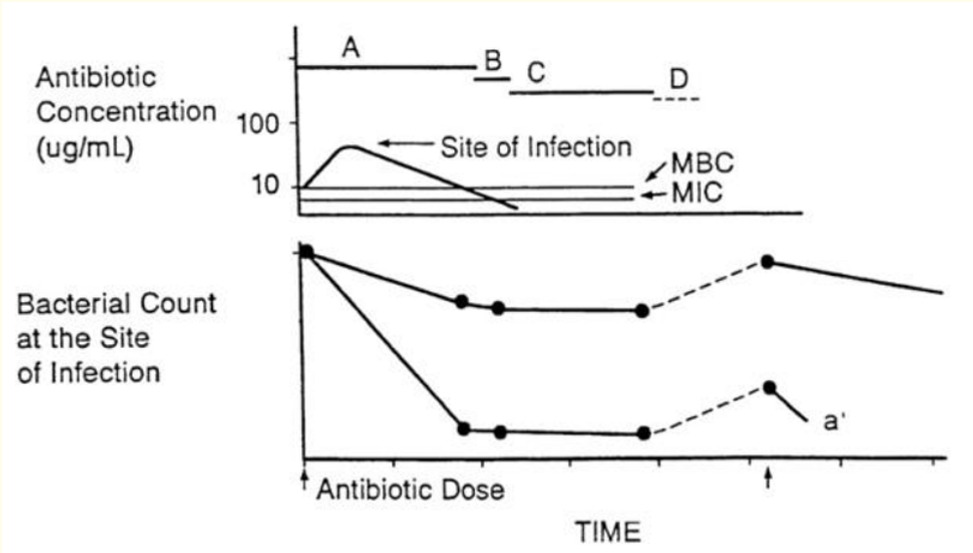


Figure 1: *A graph showing the relationship between antibiotic concentration and bacterial count at the site of infection depending on the dose of the antibiotic. Adapted from Levison and Levison 2009) [33].*

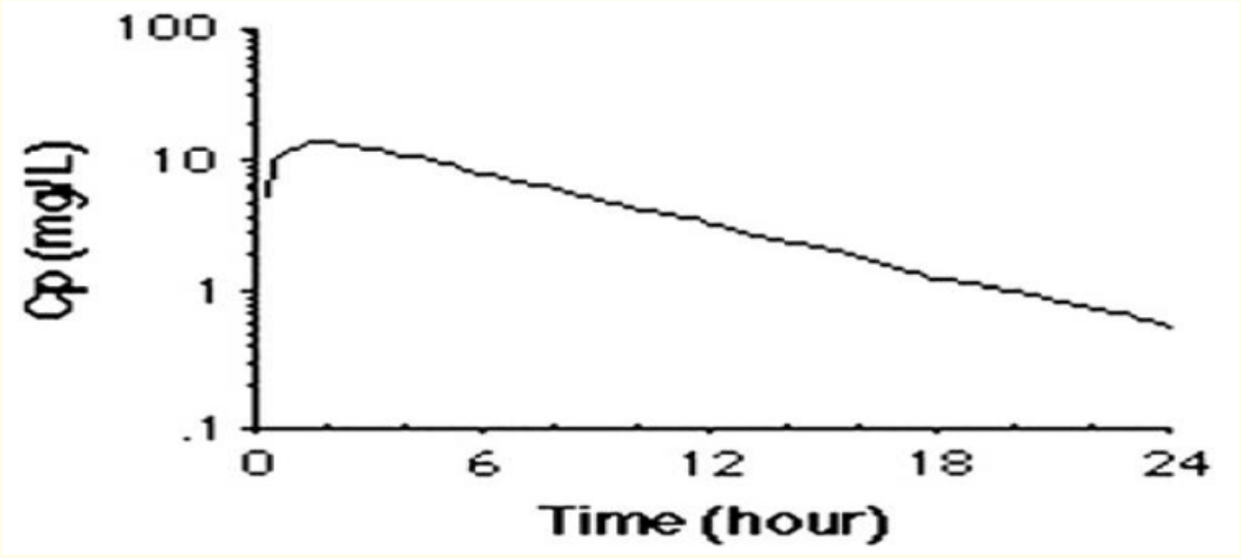


Figure 2: *A graph showing the concentration of antibiotics (in mg/L) in blood plasma per hour (Adapted from Levison and Levison 2009) [33].*

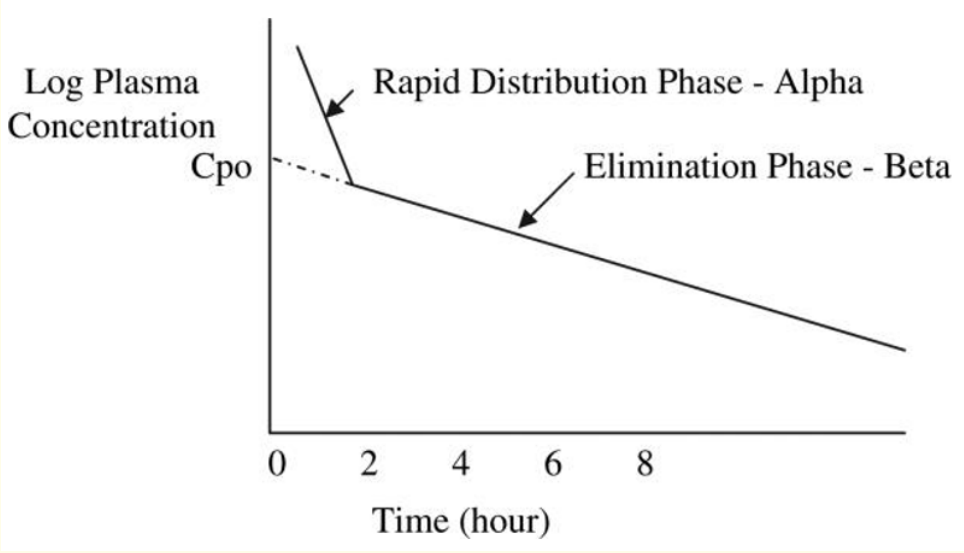


Figure 3: *A graph showing the relationship between plasma concentration of antibiotics administered against infective endocarditis against time. The graph shows the elimination phase of the antibiotic and the rapid distribution phase (Adapted from Levison and Levison 2009) [33].*

Discussion

Incidences of antibiotic resistance in developing countries are a significant cause of prevention to the development of strategies in prophylaxis that can be applied globally in individuals who have suffered from infective endocarditis [12]. Therefore, the use of antibiotics to prevent the occurrence of infective endocarditis cannot be universally achievable. Additionally, continued use of antibiotics in different places on the globe has been found to result in resistance expressed by microbes against the particular drugs that have been applied [26,27]. The latter is related to infective endocarditis because the disease is caused by bacteria that enter the circulatory system in the case that invasive dental procedures that lead to bleeding causing infective bacteria to enter into the systemic circulation. Consequently, the bacteria can invade the tissues of the valves and septa of the heart, causing infection [33].

The search criteria employed in this report are appropriate because the two approaches are used to ensure that proper literature is searched. Firstly, relevant keywords are used in the electronic databases to give commendable results. Albeit, the keywords are used, there is also the element of narrowing down on the search to provide the articles most appropriate for the search [34]. That ensures that the search done is not bereft of that which pertains to antibiotic prophylaxis issues. The search gave data in tabular form as well as in graphical form. The data has been used in the results and appendices section of this report.

The results comprise tables and graphical data which show the relationship between parameters such as time and concentration of antibiotics and their potent effects in preventing the growth of bacterial vegetation on the tissues of the heart as a mechanism for prevention. The results give a totalitarian measure of the bacteria that have been implicated explicitly in the causation of infective endocarditis and even mention them. The most common species is the Staphylococci. Epidemiological studies on infective endocarditis have shown that the disease is much prevalent among the elderly than the young, especially in the United Kingdom and Europe [12]. The reason why the disease is common among the elderly is that they are more predisposed to risk factors than children and young adults. The primary

risk factors for infective endocarditis are dental procedures such as invasive dental surgery and brushing of teeth in individuals who have contracted dental diseases such as gingivitis [35]. Mortality incidences are low in developed countries with annual data of a single death in the UK.

Critical analysis

Antibiotic prophylaxis against infective endocarditis is instrumental in the elimination of virulent microbes that cause infective endocarditis from the body. When using antibiotics, there are specific parameters that are vital to ensuring that the outcomes are favorable in eliminating the bacteria from the invaded tissue. Firstly, the concentration of the antibiotic in blood plasma per unit time is indicative of the bioavailability of the drug to the infected tissues. When the antibiotic is available to the infected tissues, their activity against microbes will be made manifest, unlike when the drug is unavailable. According to Loyola., *et al*. [36] the bioavailability of drugs used in the prevention of infective endocarditis through prophylaxis is an essential consideration because it ensures antimicrobial action can easily be mounted. In the last graph, two aspects of the antibiotic prophylaxis are addressed. Firstly, the distribution of the drugs in blood plasma and body tissues is addressed. When the antibiotic is adequately distributed in the blood and body tissues, the drugs can easily be absorbed into the tissues that have been affected by the virulent microbe. Secondly, the clearance of the drug from the body system is addressed. The removal of drugs from body tissues is essential because it prevents the building up of the drugs to toxic levels. The toxicity of drugs should be checked during prophylaxis and is a crucial element of drug pharmacokinetics [37]. Breakdown of antibiotics in the liver is a step that the body carries out to ensure that toxicity is eliminated because of the detrimental effects it has on the body tissues [33]. Therefore, in this study, these parameters of pharmacodynamics and pharmacokinetics of drugs are considered.

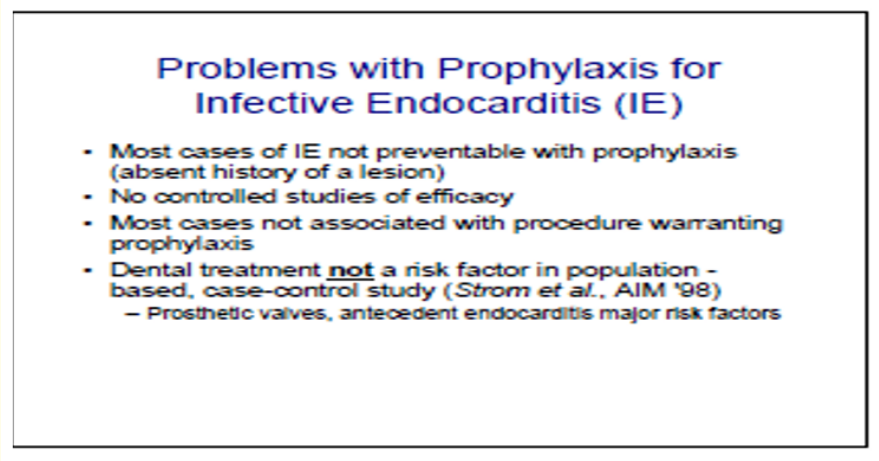
Since the year 2010, the World Health Organization has led tremendous ways of ensuring that global response against infective endocarditis is mounted through antibiotic prophylaxis. International collaboration spearheaded by WHO to bring the disease to an end has been proven to be utterly vital through recognition of interdependence among states to end incidences of the disease. Currently, the consumption of antibiotics is well established across the UK [38]. Albeit, there are impediments in the collection of evidence that highlights feasible prevention strategies that can be applied globally. According to Ayukekbong (2017), there is the threat of antimicrobial resistance in developing countries which determines why the latter is infeasible.

Conclusion

The infection is characterized by effects that may negatively impact the mural endocardium and the septa of the heart. Besides, in dentistry, infections from bacteria as the causative agents have been implicated in the causation of infective endocarditis. That is because when a patient is suffering from a bacterial infection such as gingivitis, bleeding may take place in the gums of the patient. The bleeding may, in turn, lead to the transfer of the bacteria to heart tissue through inclusion into the systemic circulation [39]. The disease affects both adults and children. Epidemiological studies on infective endocarditis have unraveled that the disease is rare in occurrence and that this finding pertains to general populations. Infections of the endocardium can be life-threatening and target the valves of the heart [40]. Infective endocarditis results from cases of invasion of the heart tissues, especially the septa and valves by bacteria that enter systemic circulation from the mouth during dental procedures that cause bleeding of gums. Conventional methods of offering health to the mouth, especially teeth cleaning by brushing is also implicated in the causation of infective endocarditis (See appendix 2). Antibiotics are drugs that eliminate virulent bacteria from the body of an individual who has suffered an infection. Antibiotics are used depending on their strength to inhibit the development of a particular pathogenic microbe, especially bacteria. When carrying out antibiotic prophylaxis against bacteria that are involved in the causation of infective endocarditis, it is noteworthy to engage weaker antimicrobial agents before using the stronger ones. That ensures that the problem of resistance to antibiotics is eliminated [23].

Prophylaxis is preventive against disease occurrence, especially when risk factors have been implicated and antibiotics have a side-effect profile that should be made known to patients who use them [41].

Several recommendations are crucial to dealing with infective endocarditis. Future research should be centered on these recommendations. Besides, it is recommendable that more research is required in the field of epidemiology of microbes that cause infective endocarditis. That is because there are still two things that healthcare professionals have not discovered about infective endocarditis. Firstly, the risk implicated in developing infective endocarditis in individuals suffering from diseases of the valve and congenital diseases of the heart is unknown. Secondly, the level of bacteremia emanating from non-oral activities in day-to-day activities, and their frequency is unknown. The last recommendation is that individuals who used chlorhexidine mouth wash should not be given antibiotic prophylaxis against infective endocarditis (See appendix 6).



Appendix 6: *(Adapted from McDonald, 2009) [15].*

Recommendations

Future research on how infective endocarditis can be controlled requires that considerations centered on ways of managing the disease be pursued with prompt. Dental treatment involving invasive procedures is a causative factor in the occurrence of infective endocarditis. The first recommendation concerning antibiotic prophylaxis against infective endocarditis is that the effectiveness of an antibiotic regimen given before invasive dental procedures is not trustworthy. That is because the bacteria responsible for the causation of infective endocarditis can invade one's system only after the individual has had an invasive dental surgery [29]. The recent evidence is valid to a high probability. Still, it may not always be true except in cases whereby an individual has been infected with bacteria that can cause the disease. The second recommendation is that priority should be given to research based on the risk of development of infective endocarditis in patients who stand the greatest risk of cardiac conditions. The third recommendation is that medical practitioners should consider the levels of bacteremia caused by various dental procedures that are invasive as a tool for conducting antibiotic prophylaxis. Another recommendation is that activities such as brushing teeth every day can cause the emergence of certain levels of bacteremia and should, therefore, be used as a criterion for antibiotic prophylaxis against the disease [42]. Besides, it is recommendable that more research is required in the field of epidemiology of microbes that cause infective endocarditis. That is because there are still two things that healthcare professionals have not discovered about infective endocarditis. Firstly, the risk implicated in developing infective endocarditis in individuals suffering from diseases of the valve and congenital diseases of the heart is unknown. Secondly, the level of bacteremia emanating from non-oral activities in day-to-day activities, and their frequency is unknown. The last recommendation is that individuals who used chlorhexidine mouth wash should not be given antibiotic prophylaxis against infective endocarditis. Caution should, therefore, be taken to ensure that proper dental health is practiced. Dentists may not have the capacity to curb the occurrences of the infective endocarditis [43-54].

Bibliography

1. Jimenez A. "1-Expert Opinion: The need for Research and Evaluation skills for Exercise Professionals, a high-value challenge to be addressed [Alfonso Jimenez and Simona Pajaujiene]. The House of Sport Avenue des Arts 43–7ème étage 1040 Brussels, Belgium (2017).

2. Li X., *et al*. "Systemic diseases caused by oral infection" (2010).

3. Kumar D., *et al*. "Clinical effect of Manjisthadi Kwatha orally and Pippali Churna Pratisaran in the management of Gingivitis–A Case Study". *International Journal of AYUSH Case Reports* 3.1 (2019): 28-31.

4. Okaro U., *et al*. "Bartonella species, an emerging cause of blood-culture-negative endocarditis". *Clinical Microbiology Reviews* 30.3 (2017): 709-746.

5. Damasco PV., *et al*. "Epidemiological and clinical profile of infective endocarditis at a Brazilian tertiary care center" (2019).

6. Sunnerhagen T., *et al*. "Clinical and microbiological features of infective endocarditis caused by aerococci". *Infection* 44.2 (2016): 167-173.

7. Brouqui P and Raoult D. "Endocarditis due to rare and fastidious bacteria". *Clinical Microbiology Reviews* 14.1 (2001): 177-207.

8. Fowler VG., *et al*. "Staphylococcus aureus Endocarditis A Consequence of Medical Progress". *JAMA: The Journal of the American Medical Association* 293.24 (2005): 3012-3021.

9. Haidich AB. "Meta-analysis in medical research" (2010).

10. Holland TL., *et al*. "Infective endocarditis" (2016).

11. Lowy F., *et al*. "Guidelines For The Microbiology/Infectious Diseases Course" (2004).

12. Gregoratos G. "Infective endocarditis in the elderly: diagnosis and management" (2013).

13. Shah A., *et al*. "3325 Incidence, outcomes and microbiology in patients with infective endocarditis". *European Heart Journal* 40.1 (2019): 745-777.

14. Prendergast BD. "Diagnostic criteria and problems in infective endocarditis" (2004).

15. Mc Donald JR. "Acute Infective Endocarditis". *Infectious Disease Clinics of North America* 23.3 (2009).

16. Thornhill MH., *et al*. "A change in the NICE guidelines on antibiotic prophylaxis". *British Dental Journal* 221.3 (2016): 112.

17. Thornhill MH., *et al*. "The effect of antibiotic prophylaxis guidelines on incidence of infective endocarditis". *Canadian Journal of Cardiology* 32.12 (2016).

18. Kaya CT and Erol C. "How to achieve infective endocarditis prophylaxis" (2018).

19. Enzler MJ., *et al*. "Antimicrobial Prophylaxis in Adults" (2012).

20. Dayer MJ. "Indications for antibiotic prophylaxis to prevent infective endocarditis in adults" (2018).

21. Sollecito TP., *et al*. "The use of prophylactic antibiotics prior to dental procedures in patients with prosthetic joints: evidence-based clinical practice guideline for dental practitioners—a report of the American Dental Association Council on Scientific Affairs". *The Journal of the American Dental Association* 146.1 (2015): 11-16.

22. Liang F., *et al*. "Optimal timing for early surgery in infective endocarditis: a meta-analysis". *Interactive Cardiovascular and Thoracic Surgery* 22.3 (2015): 336-345.

23. National Institute for Health and Care Excellence. "Prophylaxis against infective endocarditis: antimicrobial prophylaxis against infective endocarditis in adults and children undergoing interventional procedures (NICE guidance) (2016).

24. Lipkin G., *et al*. "Drugs Chapter". *Renal Disease in Pregnancy* (2018): 70.

25. Scottish Dental Clinical Effectiveness Programme -SDCEP. Antibiotic Prophylaxis Against Infective Endocarditis Implementation Advice (2018).

26. Chambers J., *et al*. "Antibiotic prophylaxis of endocarditis: the rest of the world and NICE" (2011).

27. Hepburn L. "Grown-up congenital heart disease" (2009).

28. Kuijpers JM., *et al*. "Incidence, risk factors, and predictors of infective endocarditis in adult congenital heart disease: focus on the use of prosthetic material". *European Heart Journal* 38.26 (2017): 2048-2056.

29. Nobbs A. "Getting to the heart of the matter: role of Streptococcus mutans adhesin Cnm in systemic disease". *Virulence* 8.1 (2017): 1-4.

30. Netzer RO., *et al*. "Infective endocarditis: determinants of long term outcome" (2012).

31. Ghosh S Ratnakar., *et al*. "A Study of Clinical, Microbiological, and Echocardiographic Profile of Patients of Infective Endocarditis" (2014).

32. Tafreshi MJ., *et al*. "Prevention of Infective Endocarditis: An Update" (2007).

33. Levison ME and Levison JH. "Pharmacokinetics and pharmacodynamics of antibacterial agents". *Infectious Disease Clinics* 23.4 (2009): 791-815.

34. Renada A. "Searching for harm or harming search? A look at the European Commission's antitrust investigation against Google" (2015).

35. Lockhart PB., *et al*. "Poor oral hygiene as a risk factor for infective endocarditis-related bacteremia (2009).

36. Loyola-Rodriguez JP., *et al*. "Prevention of infective endocarditis and bacterial resistance to antibiotics: A brief review". *Special Care in Dentistry* (2019).

37. Leekha S., *et al*. "General Principles of Antimicrobial Therapy" (2011).

38. Dayer MJ., *et al*. "Incidence of infective endocarditis in England, (2000–13): a secular trend, interrupted time-series analysis". *The Lancet* 385.9974 (2015): 1219-1228.

39. Nishimura RA., *et al*. "AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease". *Circulation* 129.3 (2014).

40. Donald C and Catherine M. "Intraoperative and Interventional Echocardiography (Second Edition) (2018).

41. Habib Gilbert., *et al*. "ESC guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European Society of Cardiology (ESC) endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM)". *European Heart Journal* 36.44 (2015): 3075-3128.

42. Nicholson LB. "The immune system". *Essays in Biochemistry* 60.3 (2016): 275-301.

43. Bentata Y. "Physiopathological approach to infective endocarditis in chronic hemodialysis patients: left heart versus right heart involvement". *Renal Failure* 39.1 (2017): 432-439.

44. Colomer-Winter C., *et al*. "Basal levels of (p) ppGpp differentially affect the pathogenesis of infective endocarditis in Enterococcus faecalis". *Microbiology* 164.10 (2018): 1254-1265.

45. Jei Lin C., *et al*. "Diabetes Mellitus: An Independent Risk Factor of In-Hospital Mortality in Patients with Infective Endocarditis in a New Era of Clinical Practice". *International Journal of Environmental Research and Public Health* 16.12 (2019): 2248.

46. Kaasch AJ and Seifert H. "Infections 23". Textbook of Stroke Medicine (2019): 395.

47. Kavanaugh JS., *et al*. "Identification of Extracellular DNA-Binding Proteins in the Biofilm Matrix". *mBio* 10.3 (2019): e01137-01119.

48. Liesman RM., *et al*. "Laboratory Diagnosis of Infective Endocarditis (2017).

49. Loos BG., *et al*. "Plausible mechanisms explaining the association of periodontitis with cardiovascular diseases". In Oral Infections and General Health Springer, Cham (2016): 19-33.

50. Svenningsen SL., *et al*. "Transfer RNA is highly unstable during early amino acid starvation in Escherichia coli". *Nucleic Acids Research* 45.2 (2016): 793-804.

51. Weiss JP. "Molecular determinants of bacterial sensitivity and resistance to mammalian Group IIA phospholipase A2". *Biochimicaet Biophysica Acta* 1848.11 (2015): 3072-3077.

52. Wojda TR., *et al*. "Septic Embolism: A Potentially Devastating 2 Complication of Infective Endocarditis 3". *Contemporary Challenges in Endocarditis* (2016): 143.

53. Yang QE and Walsh TR. "Toxin–antitoxin systems and their role in disseminating and maintaining antimicrobial resistance". *FEMS Microbiology Reviews* 41.3 (2017): 343-353.

54. Zea-Vera R., *et al*. "Surgical Management of Multiple Valve Endocarditis Associated with Dialysis Catheter". *Case Reports in Infectious Diseases* 206 (2016): 5.

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