

## Antibiotic Prophylaxis: New Concepts and Paradigm Shifts

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### Abstract

The concept that invasive dental procedures may cause infective endocarditis was first suggested in 1923. With the advent of antibiotics, the idea that antibiotic prophylaxis can be used before invasive dental procedures to reduce the risk of infective endocarditis. The decision to use preoperative prophylactic antibiotics is controversial. Some researchers have written that this decision is based on the assumption that the patient does not have large medical risk factors that could affect the patient's defense mechanisms. Various risk factors include poorly controlled diabetes, renal disease, severe alcoholism, immunosuppressive diseases (e.g. leukemia, lymphoma, or advanced malignancy), and the use of chemotherapeutic agents or other immunosuppressive drugs. The objective of the present literature review is to evaluate the current practice in cases in which antibiotic prophylaxis is necessary and essential. Antibiotics have played a key role, and have undoubtedly revolutionized many aspects of health care. However, its use and overuse has resulted in several public health problems. In addition, its risks and side effects have inadvertently, and negatively impact on the quality of life of patients. We conclude that the way antibiotic prophylaxis is used nowadays is much more precautionary than effective in protecting bacterial invasion. Randomized clinical trials are needed to see if prophylaxis assists and protects the patient or is only a medication with inadequate efficacy.

**Keywords:** Antibiotic prophylaxis; Focal infection; Dental; Endocarditis; Bacterial

### Introduction

In 1955, the American Heart Association (AHA) published its first recommendations for the prevention of infective endocarditis (IE). These guidelines have been modified over the last decades by AHA and American College Cardiology (ACC). Updates of available guidelines, from 1955 to 2007, have taken a number of factors into consideration, such as: drug resistant microorganisms, risk stratification of the patient population, etiology of bacteremia, and the complexity of prophylaxis.

The 1997 guidelines were the first to recognize that IE is often not associated with invasive procedures, but more often caused by random bacteremia from routine activities. The rationale for these guidelines was largely based on expert opinion, which seemed prudent practice to avoid life-threatening infection. In 2007, the guidelines were developed based on publications and data questioning the efficacy of antibiotic therapy in the prevention of infective endocarditis, and in an attempt to reduce the complexity of previous guidelines. These new guidelines significantly reduced the use of antibiotic prophylaxis to prevent IE. Pathogenic microorganisms can gain access to the bloodstream through the multiplicity of mechanisms and portals. Perhaps the most obvious and common pathway is trauma-induced procedures such as, dental extractions, periodontal probing, scaling and other instruments resulting in an exposure of the vascular bed to the biofilm bacteria spill. Although this trauma is often attributed to invasive dental procedures, other activities, such as chewing, brushing and flossing, fall into this category of inducing bacteremia.

Bacteremia can be quantified based on two general parameters. The first is the degree of inflammation present at the site, which demonstrates the type of microbiota found in the biofilm. The second is the extent of trauma or tissue damage that has occurred due to exposure of the bloodstream to the biofilm.

Guidelines that recommend antibiotic prophylaxis for IE prevention are primarily based on three main observations: (1) bacteremia has been recognized as a cause of IE, (2) group *S. viridans* can result in critical bacteremia, and (3) these organisms are susceptible to common

antibiotics. In general, the risk of adverse effects from a single dose of antibiotics is lower. The risk of fatal anaphylaxis reaction was reported at 15 to 25 people per million. Antibiotic resistance is less likely to occur due to a single dose of antibiotics. However, with continued use, resistance becomes a worrisome factor. Shedding of antibiotics and other drugs in drinking water has captured the attention of the global community and has resulted in several health-related concerns [1].

The decision to use preoperative prophylactic antibiotics is controversial. Some researchers have written that this decision is based on the assumption that the patient does not have large medical risk factors that could affect the patient's defense mechanisms. Various risk factors include poorly controlled diabetes, renal disease, severe alcoholism, immunosuppressive diseases (e.g. leukemia, lymphoma, or advanced malignancy), and the use of chemotherapeutic agents or other immunosuppressive drugs. In these patients, the health professional should be concerned with the prevention of initial contamination and the possibility of reinfection during the postoperative period [2]. To evaluate the current practice in cases in which antibiotic prophylaxis is necessary and essential, the indiscriminate use of antibiotics without adequate scientific foundation harms everyone and it is our duty to be attentive to the slightest changes in this area.

Van der Meer et al. evaluated the efficacy of prophylaxis for bacterial endocarditis in valves with a national case-control study in the Netherlands. Of a total of 438 patients with endocarditis diagnosed for

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**Received:** February 15, 2017; **Accepted:** February 28, 2017; **Published:** March 05, 2017

**Citation:** Roman-Torres CVG, Mendonça MA, Abbott MLE, Duran APG, Reyes RMD, et al. (2017) Antibiotic Prophylaxis: New Concepts and Paradigm Shifts. Oral health case Rep 3: 132. doi:10.4172/2471-8726.1000132

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2 years, 48 were eligible for the study. The results suggested that strict adherence to commonly accepted recommendations for prophylaxis could do little to decrease the total number of patients with endocarditis in the community [3].

Lacassin et al. evaluated the relative risk of infective endocarditis associated with various procedures and the protective efficacy of antibiotic prophylaxis by means of a case-control study. The protective efficacy of 46% of antibiotic prophylaxis was not significant. They concluded that the procedures increase the risk of infective endocarditis. From the efficacy rate of antibiotic prophylaxis, it can be estimated that the overall incidence of infective endocarditis can be reduced by 5% to 10% in France through the appropriate use of antibiotic prophylaxis in cardiac patients [4]. Dental treatment does not appear to be a risk factor for infective endocarditis, even in patients with valvular abnormalities, but cardiac valve abnormalities are strong risk factors. Few cases of infective endocarditis could be avoided with antibiotic prophylaxis, even with 100% assumed effectiveness. Current prophylaxis policies should be reconsidered [5].

A 2006 study to evaluate the usefulness of antibiotic prophylaxis showed that the incidence of IE from a dental procedure without the use of antibiotics was estimated at 1 in 46,000, concluded that a large number of doses of antibiotic prophylaxis would be required for avoiding a very small number of potential EI cases. Due to the high amount of medication necessary to treat effectively if it prevents cardiac damage, there is a greater concern with the adverse effects and complications associated with the use of antibiotics [6].

Antibiotic prophylaxis given prior to invasive dental procedures in patients at risk of developing IE has historically been the focus of IE prevention. Recent changes in the guidelines for antibiotic prophylaxis in the US and Europe have substantially reduced the number of patients for whom antibiotic prophylaxis is recommended. In the United Kingdom, guidelines from the national institute for health and clinical excellence (NICE) recommend complete cessation of antibiotic prophylaxis for prevention of infective endocarditis since March 2008. Although the data do not allow a causal relationship to be established, prescriptions for antibiotic prophylaxis have fallen substantially and the incidence of infective endocarditis has increased significantly in England since the introduction of the new NICE guidelines in 2008 [7,8].

No significant effect of prophylaxis with penicillin on the incidence of endocarditis can be verified. A study conducted in 2013 concluded that there is no longer any evidence that antibiotic prophylaxis is effective or ineffective against bacterial endocarditis in people at risk who are about to undergo an invasive dental procedure [9]. It is imperative that antibiotics are prescribed only when they are likely to result in clinical benefit to a patient. Clinical guidelines have been produced to assist dentists in the proper use of antimicrobials. Despite these guidelines, there is evidence that antibiotics are still widely used and poorly used in the management of acute dental conditions [10].

Since 2008, the UK has been at odds with the rest of the world, where antibiotic prophylaxis is recommended for high-risk patients undergoing invasive dental procedures. Recent evidence has identified an increase in the incidence of endocarditis, necessitating a review and guidance by the NICE and the European Society of Cardiology (ESC)-which provides guidance for the whole of Europe. The conflict of opinions and guidelines is confusing and presents difficulties for dentists, cardiologists and their patients. Recent changes in the law on consent, however, may provide a patient-centered and pragmatic solution to these problems [11].

The incidence of infections in the oral cavity decreased with the use of antibiotic prophylaxis in patients submitted to tooth extraction. However, for implant surgery and endodontic surgery antibiotic prophylaxis showed no differences compared to *placebo*.

No neck or chest infection has been reported. It is necessary to evaluate antibiotic prophylaxis in high-risk patients [2]. Dental surgeons should consider greater engagement in this dialogue and play an active role in improving the quality of life of their patients through the education of their colleagues and other health professionals on the impact of oral health on IE and IPA and other outcomes clinical relationship [12].

## Methodology

The authors reviewed the medical and dental literature for scientific evidence regarding the use of antibiotics to prevent local and systemic infections associated with dental treatment. Situations commonly considered by dentists for potential use of prophylactic antibiotics were reviewed to determine current evidence with regard to use of antimicrobial agents. This included prevention of distant spread of oral organisms to susceptible sites elsewhere in the body and the reduction of local infections associated with oral procedures.

This study had as methodology the active search for information in the databases of the Latin American and Caribbean Center for Health Sciences Information (BIREME), MEDLINE, LILACS and SciELO virtual library. It was sought to carry out the bibliographic research on the two central themes of this work: antibiotic prophylaxis, antibiotic prophylaxis in dentistry, antibiotic prophylaxis in dental practice, antimicrobial prophylaxis, prophylactic antibiotics. Selected articles were published in English between 1980 and 2016.

The selection was based on the conformity of the boundaries of the subjects with the objectives of this work, disregarding those that, although appearing in the search result, did not approach the subject from the point of view of the antibiotic prophylaxis.

## Discussion

The concept that invasive dental procedures may cause infective endocarditis was first suggested in 1923. With the advent of antibiotics, the idea that antibiotic prophylaxis may be used before invasive dental procedures to reduce the risk of infective endocarditis in susceptible individuals was developed [11].

According to NICE clinical guidelines since 2008 "Antibiotic prophylaxis against infective endocarditis is not recommended for people undergoing dental procedures." This has put UK counseling at odds with orientation in the rest of the world where antibiotic prophylaxis is recommended for patients at high risk for IE undergoing invasive dental procedures [13]. Several expert groups including, but not limited to, AAOS, ADA, AHA and NICE have shown that the use of prophylactic antibiotics for the purpose of IE prevention is not supported.

An incorrect dose of antibiotic prophylaxis may reduce the ability of the drug to decrease the occurrence and duration of bacteremia following dental procedures. Being that the continuation of drug therapy after dental procedures is not rational because these antibiotics have no effect on the incidence of postoperative infections after oral surgery and are not recommended to prevent infective endocarditis. Drada et al. reported that the use of a prophylactic antibiotic, especially amoxicillin, has been shown to favor a decrease in bacteremia, similar to other studies confirming the efficacy of amoxicillin in preventing bacteremia after dental manipulation [14].

The prudent use of antibiotics plays an important role in minimizing the impact of antimicrobial resistance on collective health [15]. Antibiotic prophylaxis prior to invasive procedures has been a key strategy in favor of decreasing bacteremia like IE for several decades, and remains so in many parts of the world [7,9]. Dental procedures as a source of bacteremia and the effectiveness of antibiotics to prevent IE from such bacteremia remains nebulous. Due to the high number needed to treat, there is a greater concern with the adverse effects and complications associated with the use of antibiotics<sup>6</sup>. The judicious use of antibiotics in conjunction with surgical therapy is the most appropriate method to treat odontogenic infections being made in susceptible individuals [16].

The use of antibiotics can lead to several unfavorable consequences for patients, such as ineffective drug therapy, avoidable adverse effects, harmful drug interactions and unnecessary costs. At sub-therapeutic doses, antibiotics do not reach adequate inhibitory concentrations in the blood, contributing to the emergence of resistance to antibiotics<sup>1</sup>. Its use and overuse results in several public health problems. In addition, its risks and side effects inadvertently, and negatively impacted on patients' quality of life [1]. The indiscriminate use of antibiotics is one of the main contributors to the appearance of bacterial strains resistant to antibiotics due to the large number of doses of prophylaxis to avoid a very small number of cases of IE. It is therefore imperative that antibiotics be prescribed only when they are likely to result in clinical benefit to a patient [1,6,10].

The AHA recommendation as the standard protocol is that a single oral dose of 2 g of amoxicillin or for patients allergic to penicillin an oral dose 600 mg of clindamycin. For patients, unable to be remembered orally, 2 g of ampicillin or 1 g of cefazolin is recommended for patients allergic to penicillin and administered intramuscularly or intravenously. They are used as antibiotic prophylaxis for 30 to 60 minutes before an invasive dental procedure to prevent infective endocarditis in high-risk patients [7,11,16]. Antibiotic prophylaxis should only be considered for dental procedures that require gingival manipulation (including extractions and scaling) or periapical region of the teeth (including root canal procedures) or perforation of the oral mucosa. Being for dental procedures, which cause bleeding in the oral cavity [11,16].

Although AHA and ESC changed their guidelines, they did not recommend complete cessation of antibiotic prophylaxis. Both continued to recommend antibiotic prophylaxis for patients with cardiac valve prostheses undergoing invasive dental procedures, patients with valves repaired using prosthetic material, and patients with significant congenital heart lesions, heart transplantation with valve lesions, or a history of endocarditis [7]. The recommendation that antibiotic prophylaxis be made in those individuals considered to be at high risk for infective endocarditis such as those with previous history of infective endocarditis, any type of cardiac valve prosthesis (including a transcatheter valve), those in which prosthetic material was used for repair of the heart valve with any type of congenital cyanotic heart disease with any type of congenital heart disease repaired with prosthetic material if surgically placed or by percutaneous techniques during the first 6 months after the procedure or throughout life if a shunt or valvar residual remains regurgitation. However, it is recommended to stop for those individuals with moderate risk such as those patients with a history of rheumatic fever, anti-rheumatic valve disease for example, mitral valve prolapse or unrepaired valve for congenital heart anomaly [17].

In USA, dentists prescribed 24.5 million courses of antibiotics in 2013, a prescribing rate of 77.5 prescriptions per 1,000 people.

Penicillin's were the most commonly prescribed antibiotic category. Dentists prescribed most antibiotics for adults older than 19 years. The Northeast census region had the highest prescribing rate per 1,000 people. The District of Columbia had the highest prescribing rate of 99.5 per 1,000 people, and Delaware had the lowest prescribing rate of 50.7 per 1,000 people [16]. In England, antibiotic prophylaxis was even more cost-effective in patients at high risk of IE. Only a marginal reduction in annual IE rates (1.44 cases in high-risk and 33 cases in all at-risk patients) would be required for AP to be considered cost-effective at £20 000 (\$26 600) per quality-adjusted life-year. Annual cost savings of £5.5 to £8.2 million (\$7.3 to \$10.9 million) and health gains >2600 quality-adjusted life-years could be achieved from reinstating AP in England [17,18].

Despite a substantial decrease in the prescription of antibiotic prophylaxis since the introduction of NICE in 2008 there was no significant increase in the number of cases of infective endocarditis above the long-term baseline trend, there was no significant increase in the rate of related deaths with infective endocarditis nor a significant increase in the number of cases related to *Streptococci* of possible oral origin [19-25].

## Conclusion

We conclude that the way antibiotic prophylaxis is used today is much more precautionary than effective in protecting bacterial invasion, and further clinical trials should determine whether antibiotic prophylaxis still plays a role in protecting some patients at risk particularly high.

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**Citation:** Roman-Torres CVG, Mendonça MA, Abbott MLE, Duran APG, Reyes RMD, et al. (2017) Antibiotic Prophylaxis: New Concepts and Paradigm Shifts. Oral health case Rep 3: 132. doi:[10.4172/2471-8726.1000132](https://doi.org/10.4172/2471-8726.1000132)

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