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Antibiotic prophylaxis for the prevention of infective endocarditis cardiac disease in patients undergoing invasive dental procedures. A narrative review.

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Abstract

Introduction: The use of antibiotic prophylaxis (AP) for prevention of infective endocarditis (IE) has been a topic of debate for a long time. In recent times, recommendations for cardiologists and dentists have suggested that the use of AP be limited to high-risk populations or be prohibited entirely.

Objective: Purpose of this review was to evaluate the evidence supporting the use of AP to prevent bacteraemia or IE in patients undergoing dental procedures.

Methods: We conducted electronic searches in Pubmed, Web of science and Scopus databases. Two reviewers independently determined the eligibility of studies, assessed the methodology of included studies and extracted the data.

Results: A total of 834 publications were initially retrieved in this investigation and data was extracted from 41 selected articles.

Conclusion: Although using antibiotic prophylaxis for infective endocarditis may be pragmatic and justifed for high-risk patients undergoing invasive dental procedures, the evidence is inconclusive because post-procedural bacteraemia may not be a good surrogate marker for IE. Moreover, trials investigating the direct association between AP and IE are lacking due to low disease prevalence and high-cost challenges.

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Keywords- Infective endocarditis, Antibiotic prophylaxis, bacteremia, invasive dental procedures.

Introduction

Infective endocarditis (IE) is a cardiac condition characterised by infection of the endocardial surface of the heart, which may involve the mural endocardium, one or more heart valves, or a septal defect [1].Despite its modest prevalence, this disease is associated with significant mortality and morbidity. The prevalence of IE in the general populace varies from one to five cases per one hundred thousand individuals [1]. While rare, a considerable number of people with predisposing cardiac conditions have an elevated risk of developing IE. Researchers postulated a causal relationship between invasive dental procedures (IDPs) and the 30–40% of cases attributed to oral bacteria.In 1955, the American Heart Association (AHA) recommend antibiotic prophylaxis (AP) to prevent IE in individuals enduring IDPs due to this correlation[2]. Severe valvular insufficiency results in intractable congestive heart failure (HF) and myocardial abscesses, among other intracardiac complications [3]. While bacteraemia is the primary causative agent of IE, the presence of fungi and other pathogens in the bloodstream may also contribute to the condition. Bacteria are typically unable to adhere to the smooth endocardial lining unless it is compromised. Such harm may arise in the presence of specific congenital or acquired structural heart diseases, valve surgery, or other such conditions. The harm induces the discharge of various substances, which consist of tissue factors [4].

Oral microflora and infective endocarditis link

Since decades ago, oral microorganisms have been linked to IE, which causes cardiologists, patients, and dentists concern. Despite its extraordinary diversity, the oral microbiota is not distributed uniformly throughout the oral cavity. The bacterial plaque contains the highest concentration, which is estimated to be between 1011 and 1012 microorganisms per gram of moist weight. However, it is worth noting that the back of the tongue, cheek, and palatal mucosa may also exhibit elevated concentrations.A total of 700 bacterial species have been identified in the buccal cavity; however, twenty species are typically responsible for pathogenicity. Among

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these, streptococci of the viridans group, streptococcus mutans and streptococcus sanguis, are the most prevalent.90% of instances of IE are attributed to streptococci as the causative agent [5].The internal body environment is exposed to a high concentration of bacteria found in the oral cavity when the oral mucosa barrier is compromised [6]. This results in bacteraemia and IE, which is typically characterized by systemic symptoms of infection, embolic phenomenon, or endocardial vegetation.[4] Prevalently investigated as the source of bacteraemia in 88% to 96.2% of patients undergoing the procedure is tooth extraction. Nonetheless, bacteraemia is typically temporary due to the inherent immune system's ability to eliminate the bacteria from the bloodstream within minutes. However, certain patients may experience a prolonged duration of several hours. In variable populations, routine activities such as eating, chewing gum, brushing teeth, or using a toothpick may also induce low-level bacteraemia detectable via blood cultures.

Invasive dental procedures

Procedures were categorized according to the American Dental Association (ADA) (Centers for Disease Control and Prevention (CDC), 2019): (i) Invasive dental procedures (IDPs)—procedures that necessitate perforation of the oral mucosa or manipulation of gingival tissue or the periapical region of the teeth, such as scaling, endodontic procedures, dental extractions, and oral surgical procedures. (ii) Intermediate dental procedures—procedures, such as the majority of restorative dental procedures, that may necessitate AP when gingival manipulation is necessary to complete the procedure, but not otherwise—are included. (iii) Non-identical diagnostic procedures—adjustment processes such as routine dental examinations, radiographs, or the implantation of removable orthodontic or prosthodontic appliances—do not recommend AP. Each visit was assigned the most invasive procedure, and in cases where a treatment required multiple visits, each visit was assessed individually in terms of the procedures carried out and AP coverage. Additionally, classifications particular to dental extractions, oral surgery procedures, scaling, and endodontics were employed to sub-analyze IDPs [7].

Recent AHA recommendation limited AP to patients enduring IDPs who posed the greatest risk of adverse drug reactions (AE) due to the absence of efficacy data, concerns regarding antibiotic resistance, and the lack of efficacy data [8]. The European Society of Cardiology (ESC) introduced comparable recommendations in 2009 [9].

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Materials and Method

Bibliographic databases such as PubMed, Scopus, Web of Science were searched for relevant studies in english language. Searching through databases was done with different keywords: infective endocarditis, antibiotic prophylaxis, invasive dental procedures.Searching in each database was adapted to databases characteristics and additionally Medical Subject Headings (MeSH) in searching through PubMed was considered. The last version of searching in mentioned databases carried out in the first week of January 2024.

Results

A total of 834 publications were initially retrieved in this investigation. A screening process was used to determine the relevance of article titles to the issue of interest, and only those deemed pertinent were selected for inclusion. After removing 312 duplicate articles and excluding irrelevant ones, the researchers included a total of 107 papers based on an assessment of their summaries. After due consideration data was extracted from 41 articles.

Discussion

Assessing the actual risk of bacterial-induced femoritus (IE) associated with dental procedures and correlating this potential health hazard with the present oral condition, oral hygiene practices, and the nature of the dental procedure constitutes the most critical element. By practicing proper infection control and maintaining good oral hygiene, the incidence of IE in patients at moderate risk can be reduced, thereby eliminating the need for AP of IE. Disagreement exists regarding the oral health disparities between healthy individuals and those afflicted with congenital cardiac diseases. Several studies have demonstrated that oral streptococci, which are the primary causative and cariogenic organisms of IE, proliferate more in the oral cavity of cardiac patients [10]. Dental caries, pericoronitis, and subacute IE are all caused by Viridans streptococci. S. sanguinis is the viridans Streptococcus most commonly isolated from patients with IE (31.9%), followed by S. oralis (29.8%) [11]. Additionally, they account for 40–60% of IE cases. Patients with cardiovascular conditions are more susceptible to

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developing periodontitis, caries, and various other dental infections. Dental infections contribute to an elevated risk. Approximately 8 to 10 percent of IE is attributed to oral infections for which there is no treatment. Blood prostaglandins and the permeability of the epithelium encircling the tooth-gingival tissue interface increase the number of leukocytes and fibrinogen, respectively, which contribute to this. There is a reduction in blood flow, which may allow pathogens to enter [9]. Gingivitis and dental caries are significantly more prevalent in children with congenital cardiac disease compared to healthy children [7]. Endocarditis is additionally a risk factor for periodontal disease in patients with congenital cardiac conditions. Inadequate oral hygiene, concurrent systemic diseases, and the use of multiple medications are all risk factors for periodontal disease in patients with heart disease. Certain research studies have indicated that there may be an inverse relationship between congenital cardiovascular complications and periodontal disease [10]. Patients with cardiac conditions who are at an increased risk for caries and periodontitis have a heightened incidence of IE due to the presence of potentially hazardous bacterial species and the increased frequency of dental procedures. Additionally, the function of dental hygiene as a potential cause of bacteraemia in cardiac patients is unclear. While regular flossing and brushing may temporarily elevate the risk of oral streptococcal bacteraemia, it may concurrently reduce the long-term risk of invasive plaque. The existing body of literature offers inconclusive findings regarding the correlation between periodontal or gingival disease and the likelihood of bacteraemia following tooth extraction. A direct correlation has been identified by Lockhart et al. [11] between gingival inflammation parameters, dental plaque, and viridans streptococcal bacteraemia. Conversely, Duval et al. observed no disparities between cases and controls in terms of gingival inflammation or calculus score. This finding implies that the heightened susceptibility to IE-associated bacteraemia among patients who maintain inadequate oral hygiene may not be substantial enough to trigger endocarditis [12]. Patients should be reminded that regular visits to the dentist and optimal oral health and hygiene can reduce the incidence of bacteraemia caused by activities such as chewing food, cleansing teeth, and engaging in daily activities; therefore, these practices are crucial for preventing IE. In order to reduce the risk of IE, optimal oral hygiene and health maintenance are more crucial than prophylactic antibiotic use [13]. According to epidemiological studies, between 14 and 20 percent of IE cases are attributable to improper oral hygiene [14]. Bacteraemia may result from oral hygiene practices including brushing, flossing, using toothpicks, or gnawing during non-

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exposure periods. Bacteraemia is induced in comparable proportions by the microtrauma induced by these routine activities and invasive oral procedures, for which AP is advised. The significantly lengthier cumulative non-exposure periods compared to the exposure periods provide strong evidence that the majority of cases of IE are caused by bacteraemia that occurs in daily life [15]. Consistent scientific evidence supports the notion that twice-daily tooth hygiene for children results in a 154,000-fold increased risk of bacteraemia in comparison to a single tooth extraction. Furthermore, research suggests that the risk of contracting bacteraemia from toothbrushing is approximately 5 times greater than the risk associated with a single dental tooth extraction [16]. The incidence of bacteraemia varies between 18% and 85% during tooth extraction, 60% to 90% during periodontal surgery, and 7% to 50% during toothbrushing or irrigation. Analogous daily tasks that are not directly linked to a dental procedure also carry an equivalent risk of bacteraemia [17]. These are more frequent and shorter-lasting activities than dental procedures. Furthermore, considering that the majority of individuals visit the dentist a maximum of once or twice yearly, their exposure to bacteraemia associated with dental hygienist or dentist procedures is infrequent. Conversely, they are frequently subjected to transient bacteraemia resulting from their daily activities. Although these daily transient bacteraemias are brief in duration and of low grade, their incidence is quite high. A mere fraction of IE is attributable to dental procedures; rather, it is associated with oral hygiene practices. Bacteraemia incidence varies between 20% and 68% when flossing and brushing teeth, 20% to 40% when using wooden toothpicks, 7% to 50% when using water irrigation devices, and 7% to 51% when consuming food [18]. Clearly, prophylactic treatment against these sporadic daily physiological bacteraemias is not feasible. Therefore, even IE prophylaxis were to be administered annually or biannually prior to a dental procedure, its effectiveness would be minimal, preventing an extremely small percentage of cases of IE [19]. 5.3% of cases might have been preventable, according to estimates, had antibiotic therapy been 100 percent efficacious and administered to all patients at risk during dental treatment [20]. Moreover, it has been noted that the development of endocarditis frequently transpired several months subsequent to the procedure, or that the etiological agent did not belong to a species of bacteria commonly found in the buccal cavity [21]. There is variation in the incidence and severity of bacteraemia across distinct surgical procedures. The oral cavity serves as a repository for more than 700 distinct bacterial species. Hence, any procedure that has the potential to breach the oral mucosal barrier exposes the

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internal body environment to the exceedingly contaminated oral cavity, thereby facilitating the penetration of potentially hazardous microorganisms into the systemic circulation. A considerably greater incidence of bacteraemia is observed during all surgical dental procedures in comparison to non-surgical procedures. An estimated 58–100% of bacteraemia cases occur during adult dental extractions, while 10–62% of bacteraemia cases occur during third molar extractions [22]. A greater incidence of bacteraemia is observed during the extraction of impacted or partially erupted third molars compared to more aggressive maxillofacial surgical procedures. The risk of bacteraemia associated with suture removal (10 percent), abscess incision and drainage (12 percent), and osteosynthesis plate removal (8 percent) is extremely low [23]. In implants, the potential for bacteraemia is negligible. The assessed risk is 7%. The utilization of a mucoperiosteal flap for implant implantation does not pose a substantial risk of bacteraemia in comparison to the initial percentage. The periodontal space remains unaffected throughout the implant placement procedure, despite being the critical region through which oral bacteria infiltrate the bloodstream. The prevalence of bacteraemia following non-surgical dental interventions is comparable following conservative dental procedures and other orthodontic procedures, but it is reduced following root canal treatment (0–42%). [24]. An estimated 73% of bacteraemia cases are attributed to the administration of local anesthesia. It is common for periodontal surgery, periodontal prophylaxis, scaling, and root planning to be associated with an increased risk of bacteraemia. Bacteraemia is associated with periodontal treatment in a range of 13 to 80.9%, periodontal probing in 20 to 43%, and periodontal surgery in 60%. A total of 46% of patients who undergo non-surgical periodontal therapy have positive bacteraemia [25]. It is accompanied by a distinct bacterial community that inhabits the periodontal cavity. A total of 700 bacterial species have been identied in the oral cavity to date, with 400 of those being discovered in the periodontal pocket contiguous to the teeth. Streptococci constitute a substantial proportion of the dental flora, particularly in the supragingival plaque, and they are commonly linked to IE. Due to the high incidence of bacteremia in periodontitis, AP should be administered to patients at risk for IE [26]. The slightest likelihood of bacteraemia induction is attributed to the relatively non-invasive and atraumatic nature of orthodontic treatment. Amidst the orthodontic treatment procedures that were considered, including alginate impression, separator placement, band cementation, and arch wire change, the incidence of bacteraemia was found to be highest during separator placement. Birlutiu et al. described the case of a female patient who,

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devoid of preexisting cardiac pathology, developed IE due to Streptococcus viridans colonization of the mitral valve in conjunction with a fixed orthodontic appliance. A case of IE induced by Abiotrophia defectiva in a patient undergoing treatment with a fixed orthodontic appliance was documented by the same authors [27]. Endocarditis of the aortic valve has also been documented as an adverse effect of tongue piercing [24]. When evaluating the bacteraemia during IE development, it is crucial to take into account not only the extent of the bacteraemia but also its duration and any other modifying factors. After two minutes have passed since tooth extraction or an invasive dental procedure, bacteremia reaches its maximum and then gradually decreases. Blood cultures have detected oral pathogens, however, between one and forty-five minutes following tooth extraction. The investigation assessed the bacterial presence in peripheral blood prior to, immediately following, and 30 minutes subsequent to scaling and root planning. The incidence decreased by 25% 30 minutes after treatment, from its peak immediately following treatment (70%). [28]. Bacteraemia decreases within minutes following dental instrumentation as a result of the host's immune system's ability to expeditiously eliminate microorganisms from the blood. Variability in a patient's capacity to neutralize blood microorganisms may constitute an additional risk factor for the development of IE [28]. The majority of pathogenic bacterial species are eliminated within the initial thirty minutes of the procedure. Nonetheless, without the use of an antibiotic, certain pathogenic species can persist for at least sixty minutes following brushing and extraction [29]. The bacteria that are most persistent in the blood are anaerobic. Several studies indicate that the occurrence of bacteraemia exhibits a comparable decline over time in all three groups, peaking 30 minutes after the procedure, and then declining further at 60 minutes and 90 minutes. This phenomenon can be explained by the bacteria being eliminated by the reticuloendothelial system after being transferred from the bloodstream to tissues under physiological conditions. Dental extraction and supragingival debridement are associated with an equivalent incidence of bacteraemia in groups that receive prophylactic antibiotic therapy versus those that do not, according to molecular analysis. There are no statistically significant differences in the occurrence or severity of bacteraemia between the two cohorts of patients five or thirty minutes following the evaluation of each procedure, according to the identical analysis. However, blood culture reveals that viable cultivable bacteria in the circulation are diminished following tooth extraction due to antibiotic therapy [30]. An examination of the relationship between surgery duration and bacteraemia revealed that the incidence of post-extraction

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bacteraemia is 96% when the operation lasts longer than 100 minutes, compared to 67% when the operation lasts shorter. The incidence of bacteraemia is greater during operations lasting longer than 65 minutes as opposed to those lasting less than 65 minutes [31].

Assessment of the effectiveness and safety of antibiotic prophylaxis

Currently, all prophylactic antibiotic recommendations should be accompanied by a comprehensive evaluation of the potential benefits and adverse effects of the drug. In addition to causing bacterial death, AP also hinders bacterial adhesion. Antibiotics used for the prevention of IE exclusively target streptococci [32]. Reducing antibiotic use, particularly in patients with a low to moderate risk of IE, is motivated, in part, by an unfavorable balance between drug-related adverse effects and effective antibacterial activity. All antibiotics that are prescribed for the protection of at-risk patients are effective against the most prevalent bacterial species that cause IE and are therefore widely recommended. Nevertheless, their regular and extensive application gives rise to bacterial strains that are resistant to drugs, including viridans group streptococci (VGS). The incidence of VGS that is resistant to multiple drugs has increased substantially over the last 25–30 years. As a consequence, the number of efficacious antibiotics accessible for the prevention of IE has decreased. Prolonged amoxicillin use induces the development of antibiotic-resistant strains, and repeated amoxicillin use can increase the proportion of resistant strains in the oral microbiota as a whole [33]. The utilization of antibiotics in dentistry is projected to account for as much as 10% of the overall antibiotic usage, and this figure must be adjusted to account for the possibility of bacterial resistance developing. Despite the potential rarity of amoxicillin-resistant strains in the population and the fact that invasive dental procedures can introduce oral bacteria into the bloodstream, a study reported a median detection rate of 10.9% for such strains in healthy subjects who had taken amoxicillin within the previous three months [31]. This rate was found to be higher than the rate observed in subjects who had not taken amoxicillin (2.4%). Furthermore, current studies indicate that patients who are at risk of developing IE may have a higher prevalence of amoxicillin-resistant strains than healthy individuals. Aside from the development of resistant bacterial species, the use of antibiotics is also associated with a significant risk of severe adverse reactions. A single dose of amoxicillin or ampicillin administered before dental procedures is generally considered safe for patients without a history of type I hypersensitivity reaction to penicillin. However, 2.9% of patients have reported experiencing antibiotic-related adverse effects after using amoxicillin. Anaphylactic

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reactions, cutaneous reactions, gastrointestinal disorders, liver problems, and haematological complications are among these adverse effects associated with the drug. Anaphylaxis or hypersensitivity reactions to penicillin transpire in a relatively low incidence rate of 0.04% to 0.11% during penicillin therapy. This adverse effect occurs more frequently when administered intravenously as opposed to orally [23]. It is important to note that anaphylactic reactions to antibiotics may account for five to ten times more fatalities than IE. The second-choice prophylactic agent, clindamycin, is linked to a significant incidence of adverse drug reactions (ADR), with 149 non-fatal ADR reports per million prescriptions and 13 fatal ADR reports [28]. Indiscriminate use of antibiotics may increase the risk of adverse reactions beyond that of IE, according to these findings. While certain clinical trials have demonstrated the efficacy of AP in decreasing the occurrence of bacteraemia, this may not necessarily translate into a statistically significant preventive effect against IE in patients with a low disease risk. The majority of studies evaluate the efficacy of the AP solely in terms of its ability to decrease bacteraemia, and not IE. Bacteremia merely represents the preliminary stage in the progression of IE. Infectious endocarditis is a disease influenced by numerous factors, all of which must be taken into account when developing a strategy to prevent the infection [34]. The aforementioned promoting factors consist of the patient's oral sanitation, orodental health, the composition of oral flora, and their own defense mechanisms. The majority of conducted randomized clinical trials disregard these promoting factors in favor of examining the efficacy of AP in mitigating bacteraemia. Moreover, the potential negative consequences of AP might surpass its advantages. In global strategies for the prevention of IE, additional considerations should be given to the practicality, cost-effectiveness, and health hazards associated with the routine use of AP. Both amoxicillin and clindamycin AP are associated with improved health outcomes and reduced costs for high-risk and all-at-risk populations when compared to the absence of AP [27]. Considering the relatively low costs associated with AP and the severe consequences and high costs associated with IE, these results indicate that AP is a cost-effective preventive measure against IE, especially for those at high risk, even when the number of cases prevented is extremely low [29].

As a result of restrictions on the use of antibiotics in patients at moderate and low risk, new prevention and management strategies for IE have been developed. They incorporate novel suggestions pertaining to dental care. These prioritize the maintenance of proper oral hygiene

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and the control of infections [35]. Consensus among international organizations is that judicious antimicrobial usage is preferred over the indiscriminate application of AP in dental procedures. The emergence of amoxicillin-resistant bacterial strains has prompted consideration of the potential substitution of quinolone antibiotics for amoxicillin in order to prevent IE. In accordance with the tenets of rational AP, dental procedures ought to be executed in order to minimize the frequency of antibiotic usage. If multiple prophylactic episodes are necessary, they should occur at least every two weeks. It is advisable to discontinue treatment for a duration of three to four days when the patient is concurrently using other antibiotics [36]. Following this, it is advised that the buccal cavity be disinfected prior to any dental procedure. This approach may be substituted for AP and is particularly recommended for patients in the moderate-to-low-risk categories. The incidence of bacteraemia following tooth extraction can be decreased, according to Sendi et al., by cleansing the mouth with 0.2% chlorhexidine prior to the intervention [37]. The degree of risk mitigation achieved is analogous to the systemic administration of AP. Iodine compounds and attenuated oxygenated water are two additional efficacious antiseptics. Basilio et al. establish that chlorhexidine and povidone-iodine are the most effective antiseptics [38]. Certain scholars propose that an ultrasonic scaler may eliminate a portion of the bacteria associated with periodontal non-surgical treatment-related bacteraemia through the cleansing action of the water irrigation. However, an opposing viewpoint is that this may result in increased tissue trauma. The variety of prescribed procedures—ultrasonic scaling of the entire mouth, scaling with hand instruments, and root planning for ten minutes—impedes the ability to compare results [39]. Opting for non-surgical dental treatments in lieu of the most invasive dental procedures is an additional suggested course of action. Furthermore, certain studies do not recommend dental treatment prior to surgical valve approaches as a preventive measure against IE. De Souza et al. stated that dental preparation prior to cardiac surgery has no effect on the incidence of IE. Patients who have developed IE have an equivalent need for dental treatment as those who have not, and both groups necessitate an equivalent number of visits to finalize the dental treatment prior to undergoing cardiac valve surgery [40]. The current recommendation for antibiotic prophylaxis in individuals at risk of IE is to take 2 grams of Amoxycillin orally one hour prior to the procedure. Clindamycin 600 g is advised to be taken by individuals with a penicillin allergy sixty minutes prior to the procedure [41].

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Conclusion:

Although using antibiotic prophylaxis for infective endocarditis may be pragmatic and justified for high-risk patients undergoing invasive dental procedures, the evidence is inconclusive because post-procedural bacteraemia may not be a good surrogate marker for IE. Moreover, trials investigating the direct association between AP and IE are lacking due to low disease prevalence and high-cost challenges.

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