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Current Approaches to Antibiotic Prophylaxis for Infective Endocarditis in Pediatric Dentistry: A Review

Pediatrik Diş Hekimliğinde Enfektif Endokardit Profilaksisine Güncel Yaklaşımlar: Bir İnceleme

ABSTRACT

Infective endocarditis (IE) is a serious and potentially life-threatening bacterial infection of the cardiac epithelium, with a mortality rate of approximately 5% in children. The most common risk factor for IE in this population is congenital heart disease. The American Academy of Pediatric Dentistry acknowledges that certain medical conditions increase susceptibility to infections resulting from bacteremia. Antibiotic prophylaxis is recommended for high-risk patients prior to procedures that could induce bacteremia, with the goal of reducing or preventing transient bacteremia caused by invasive dental treatments. However, the effectiveness of prophylaxis in preventing or mitigating the frequency and severity of bacteremia associated with dental procedures remains controversial. This review explores current approaches to antibiotic prophylaxis in pediatric dentistry for the prevention of IE. While some studies suggest that preoperative antibiotics reduce these risks, others report no significant benefit. Given these uncertainties, maintaining good oral hygiene and promptly treating dental diseases are essential strategies to reduce the risk of bacteremia from routine daily activities. Historically, patients with most forms of congenital heart disease were prescribed antibiotics prior to dental procedures in line with American Heart Association guidelines. Today, however, antibiotics before dental procedures are recommended only for patients with cardiac conditions that pose a high risk for infective endocarditis. The overall health of vulnerable pediatric patients can be improved by reducing the risk of infective endocarditis through interdisciplinary collaboration, particularly between pediatric cardiologists and dentists.

Keywords: Antibiotic prophylaxis, pediatric dentistry, infective endocarditis

ÖZET

Enfektif endokardit (EE), kalbin endokardiyal yüzeylerinin bakteriyel enfeksiyonundan kaynaklanan ciddi, yaşamı tehdit eden bir durumdur. EE nadir görülen bir durum olmakla birlikte çocuklarda mortalite oranı %5'tir. Çocuklarda EE için en sık görülen risk faktörü konjenital kalp hastalığıdır. Amerikan Pediatrik Diş Hekimliği Akademisi, bazı tıbbi durumların hastaları bakteriyeminin neden olduğu enfeksiyonlara karşı daha duyarlı hale getirdiğini kabul etmektedir. Savunmasız bir hastanın ne zaman enfekte olabileceği önceden tahmin edilemediğinden, bakteriyemiye neden olabilecek işlemlerden önce uygun hastalara profilaktik antibiyotikler önerilir. Antibiyotik profilaksisinin amacı, invaziv diş tedavilerinden kaynaklanan geçici bakteriyemiyi en aza indirmek veya önlemektir. Diş operasyonuyla ilişkili bakteriyeminin sıklığını, yoğunluğunu veya süresini önlemede veya en aza indirmede antibiyotik profilaksisinin etkinliği tartışmalıdır. Bu derlemenin amacı pediatrik diş hekimliğinde enfektif endokarditi önlemek için antibiyotik profilaksisine yönelik en son yaklaşımları tartışmaktır. Bazı çalışmalar ameliyat öncesi antibiyotiklerin bu faktörleri azalttığını öne sürerken, bazı çalışmalar ise azalma olmadığını bildirmiştir. Bu belirsizlikler göz önüne alındığında, iyi ağız hijyeninin sağlanması ve diş hastalıklarının tedavi edilmesi, günlük aktivitelerden kaynaklanan bakteriyemi riskinin azaltılması açısından çok önemlidir. Geçmişte, çoğu konjenital kalp hastalığı türüne sahip hastalara, diş prosedürlerinden önce Amerikan Kalp Derneği tavsiyelerine uygun olarak antibiyotik reçete ediliyordu. Ancak günümüzde diş operasyonlarından önce antibiyotikler yalnızca yüksek enfektif endokardit riski taşıyan kalp rahatsızlığı olan hastalar için önerilmektedir. Pediatrik kardiyologlar ve diş hekimleri arasındaki iş birliği, enfektif endokardit riskinin azaltılması ve özellikle kalp hastalığı olan çocuklarda ağız sağlığının ve genel sağlığının iyileştirilmesi açısından önemlidir. EE geçirme açısından riskli olan pediatrik hastaların genel sağlığı, disiplinler arası iş birliği ve önleyici stratejiler yoluyla iyileştirilebilir.

Anahtar Kelimeler: Antibiyotik profilaksisi, çocuk diş hekimliği, enfektif endokardit

REVIEW
DERLEME

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Infective endocarditis (IE) is a serious and potentially life-threatening bacterial infection of the cardiac epithelium. Despite advances in diagnostic methods and treatment strategies in recent years, pediatric IE remains a complex condition.[1] It is associated with a high risk of mortality.[2] The annual prevalence of infective endocarditis among hospitalized children is estimated to range between 0.05 and 0.12 cases per 1,000, with an associated mortality rate of approximately 5%.[3,4] Historically, rheumatic heart disease was the leading cause of pediatric IE and continues to pose a significant public health challenge in developing countries.[5] In recent years, improved survival rates among patients with congenital heart disease (CHD) have made CHD the most common cause of pediatric IE.[6] Approximately 50–70% of pediatric infective endocarditis cases occur in patients with CHD,[7] making it the primary predisposing factor. The specific type of CHD influences the risk of developing IE. Cyanotic and complex CHD, along with left-sided defects and endocardial cushion defects, are most commonly associated with an increased risk. Recent reconstructive cardiac surgery (within the last six months) in patients with CHD is a significant risk factor for IE. Additionally, patients with shunts or residual heart defects following corrective surgery, those who have undergone prosthetic valve implantation (whether surgical or transcatheter), and individuals with prosthetic materials are at increased risk.[8] IE has also been reported in children with structurally normal hearts, often in association with immunocompromised conditions or the presence of a surgically inserted central venous catheter.[9]

The American Academy of Pediatric Dentistry (AAPD) acknowledges that certain medical conditions increase a patient's vulnerability to infections resulting from bacteremia. Because it is unpredictable when an at-risk patient may become infected, prophylactic antibiotics are recommended for these patients prior to procedures that could lead to bacteremia. The primary goal of antibiotic prophylaxis in dentistry is to reduce or prevent transient bacteremia that may occur following invasive dental treatments.[10] This review aims to summarize current approaches to antibiotic prophylaxis, emphasizing the link between pediatric dentistry and infective endocarditis.

Oral Microbiome in Children

The oral microbiome, second in size only to the gut microbiome, consists of over 700 different bacterial species and plays a crucial role in both oral health and overall well-being.[11] It begins to develop shortly after birth, with its maturation influenced by factors such as the mode of birth and infant feeding practices.[12] Breast milk is considered the optimal source of nutrition for infants, enhancing infection resistance and providing essential nutrients. It also contains approximately 10^6 bacterial cells per milliliter, which help inoculate newborns, particularly with species from the dominant genus *Streptococcus*,[13] including *Streptococcus salivarius*, a common inhabitant of the infant oral cavity.[14] Metabolic by-products produced by *Streptococcus* species, in conjunction with dietary oligosaccharides found in breast milk, may promote the growth and adherence of other microorganisms in the oral cavity. During early childhood, the oral microbiota exhibits high variability but typically stabilizes into an adult-like composition by around two years of age.[15]

ABBREVIATIONS

AAE	Antibiotic adverse effect
AAOS	American Academy of Orthopaedic Surgeons
AAPD	American Academy of Pediatric Dentistry
ADA	American Dental Association
ADR	Adverse drug reaction
AHA	American Heart Association
BAV	Bicuspid aortic valve
CDI	Clostridium difficile infection
CHD	Congenital heart disease
CIED	Cardiac implantable electronic device
HACEK	*Haemophilus parainfluenzae, Aggregatibacter spp. (A. actinomycetemcomitans, A. aphrophilus, A. paraphrophilus, A. segnis), Cardiobacterium hominis and valvarum, Eikenella corrodens, Kingella kingae*
IE	Infective endocarditis
PDA	Patent ductus arteriosus
PJI	Prosthetic joint infection
PVR	Pulmonary valve replacement
SRP	Scaling and root planing
VGS	Viridans group streptococci
VSD	Ventricular septal defect

The oral mucosa and teeth of children host a wide variety of both pathogenic and non-pathogenic bacteria, encompassing hundreds of aerobic and anaerobic strains. The oral flora of children, whether healthy or diseased, is less diverse than that of adults but gradually becomes more similar with age. This transition includes increased proportions of viridans group streptococci (VGS, α-hemolytic streptococci), *Actinomyces*, and *Prevotella* species.[16,17] In healthy children, the oral microbiota typically includes *VGS*, *Neisseria*, *Haemophilus*, and *Staphylococcus* species. As children grow older, they may also harbor periodontal disease-associated bacteria such as *Capnocytophaga*, as well as species linked to infective endocarditis, including *Aggregatibacter actinomycetemcomitans*.[18]

The oral cavity also hosts a range of other microorganisms, including protozoa such as *Entamoeba gingivalis* and *Trichomonas tenax*, as well as fungi, primarily *Candida* species. Sharma et al.[19] identified 85 fungal genera in the oral cavities of 20 healthy individuals, with the most common being *Candida*, *Cladosporium*, *Aureobasidium*, *Aspergillus*, and *Fusarium*. Microbial diversity in the oral cavity increases with tooth eruption and continues to develop as children transition from primary to permanent dentition.[12] Additionally, high sugar consumption and inadequate oral hygiene significantly influence the composition of the oral microbiome in children.[20,21]

Research shows that children with CHD often exhibit poor oral health, with a higher prevalence of dental caries, gingivitis, and increased plaque accumulation compared to healthy children.[22-24] Since the first teeth typically erupt between 6 and 12 months of age,[25] and parents of children with CHD often have limited awareness of the importance of oral hygiene, dental care may be neglected. This is particularly concerning, as many children with CHD undergo corrective surgery within their first year of life, further increasing health risks.[26] Diuretics, which are commonly prescribed as adjunct therapy for pediatric patients with cardiomyopathies,[27]

are known to affect salivary flow rates.[28] One study found no significant differences in *Streptococcus mutans* or *Lactobacillus spp*. counts between healthy children and those with CHD receiving angiotensin-converting enzyme (ACE) inhibitors or diuretics; however, total viable bacterial counts were higher in the control group.[29] Another study found elevated levels of *Streptococcus mutans* serotype k in the saliva of patients with CHD; this serotype was also more commonly detected in heart valve specimens from individuals with subacute IE.[30] Notably, *Streptococcus mutans* serotype k was found exclusively in CHD cases.[31]

The primary pathogens responsible for IE in children are gram-positive cocci, particularly α-hemolytic streptococci, staphylococci, and enterococci. HACEK organisms (*Haemophilus parainfluenzae*, *Aggregatibacter spp*., *Cardiobacterium hominis* and *valvarum*, *Eikenella corrodens*, and *Kingella kingae*) account for approximately 1.4% of cases.[32] One study found no significant differences in salivary composition between children with CHD and healthy controls, although CHD patients had higher colony-forming unit counts.[33]

Relationship Between Invasive Dental Procedures, Infective Endocarditis, and Antibiotic Prophylaxis

According to guidelines established by the European Society of Cardiology and the American Heart Association (AHA), invasive dental procedures are defined as any dental intervention involving manipulation of the gingival tissue, the periapical region of the teeth, or perforation of the oral mucosa. This broad definition encompasses a variety of dental procedures, including but not limited to tooth extractions and oral surgeries such as periodontal surgery, implant placement, and oral biopsies. Additionally, the guidelines classify scaling and root canal therapy as invasive due to their potential impact on the gingival and periapical tissues. Restorative and orthodontic treatments that involve manipulation of the gingival tissues, cause bleeding, or result in perforation of the oral mucosa are also included in this category. This comprehensive definition underscores the importance of recognizing dental procedures that may pose an increased risk to patients with certain health conditions.[34,35]

Tooth extractions are associated with the highest rates of bacteremia, occurring in 62% to 66% of cases, followed by scaling and root planing (SRP) at 36% to 44%, and oral health procedures such as dental prophylaxis and probing without SRP at 27% to 28%. Furthermore, everyday activities, including flossing and chewing, can result in bacteraemia in approximately 16% of cases, while toothbrushing has been associated with bacteraemia rates ranging from 8% to 26%.[36] Although these daily activities generally produce low levels of bacteraemia, their frequency may result in a cumulative risk that surpasses that of individual dental procedures.[37]

The effectiveness of antibiotic prophylaxis in reducing bacteremia associated with dental procedures is controversial. A meta-analysis of 36 studies found that while antibiotic prophylaxis did reduce the incidence of bacteremia, it did not significantly lower the risk of IE in case-control studies.[38] However, recent findings suggest that prophylaxis in high-risk individuals can significantly reduce IE rates following invasive dental procedures, particularly extractions and oral surgeries.[39,40]

Prevention of Infective Endocarditis

Historically, antibiotics were prescribed for patients with most types of CHD prior to dental procedures, in accordance with AHA guidelines.[41] Currently, antibiotic prophylaxis is recommended for patients with a history of IE, surgically implanted prosthetic valves, and transcatheter pulmonary or aortic valve prostheses. It is also advised for individuals undergoing transcatheter mitral or tricuspid valve repair, as well as for those with untreated cyanotic CHD or postoperative palliative shunts and prosthetic devices. Following surgical repair, prophylaxis is recommended only for the first six months, provided there are no residual defects or prosthetic valves.[35]

Preventing IE involves more than just antibiotic prophylaxis. Individuals at risk should be educated on the importance of maintaining good oral and skin hygiene, recognizing signs of infection, and notifying their physician if they develop an unexplained fever. In such cases, clinicians should consider screening for IE before initiating antibiotic therapy.[35]

Specific Subpopulations and Infective Endocarditis

Not all patients face the same level of risk for developing IE. The incidence of IE varies depending on the type of heart lesion, and factors such as the repair status of the heart lesion and the method of valve replacement (surgical or transcatheter) must also be considered.

Bicuspid Aortic Valve (BAV)

Patients with a bicuspid aortic valve are at significantly increased risk for developing IE of the native valve, with a 12-fold higher risk and an incidence rate of 48.13 cases per 10,000 patient-years.[42] These patients also show a higher prevalence of IE caused by viridans group streptococci, with many cases likely originating from odontogenic sources.[43]

The use of antibiotic prophylaxis to prevent IE in patients with BAV is an area of active discussion. Although international guidelines no longer universally recommend antibiotic prophylaxis, some studies suggest that it may be beneficial due to the increased risk of IE in this population.[42,44] Nevertheless, additional high-quality prospective studies are needed to accurately assess the incidence of IE, the relative risk, and the potential benefits of antibiotic prophylaxis in patients with BAV.[42]

Ventricular Septal Defect (VSD)

Patients with VSD are at increased risk of IE. A Danish cohort study reported hazard ratios of 28.0 for unrepaired VSD and 82.7 for surgically closed defects.[45] However, an individual's lifetime risk may vary depending on the severity of the defect and the presence of additional risk factors.[46]

Eisenmenger Syndrome

Patients with Eisenmenger syndrome have a significantly elevated risk of IE and require antibiotic prophylaxis. The presence of a right-to-left shunt can facilitate the formation of abscesses in systemic organs such as the spleen and brain.[47]

Patent Ductus Arteriosus (PDA)

Patent ductus arteriosus may contribute to the development of right-sided IE due to bacterial adhesion promoted by the left-to-right shunt.[48] The incidence of IE in patients with PDA has declined

significantly in recent decades, likely due to the widespread use of antibiotics and advancements in surgical and catheter-based closure techniques.[49] However, IE can still occur, particularly if the ductus remains patent or recanalizes after closure.[50]

Tetralogy of Fallot (ToF)

Patients with ToF are at high risk for IE. In a study involving 1,164 patients with ToF, the incidence of IE was 22.4 cases per 10,000 person-years, compared to just 0.1 in the control group. Those who underwent pulmonary valve replacement (PVR) had an even higher incidence, 46.7 per 10,000 person-years, compared to 2.8 in those who did not undergo the procedure.[51] This study highlights the significantly increased risk of IE in patients with ToF, particularly in those who have received PVR. As a result, heightened awareness, preventive strategies, and close monitoring are essential for this patient population.

Cardiac Implantable Electronic Devices (CIEDs)

IE associated with CIED is a serious and potentially life-threatening complication, accounting for approximately 10% of all endocarditis cases.[52] The criteria for CIED implantation are expanding for both adults and children. Pacing for congenital heart block now includes indications such as a mean heart rate below 50 and the presence of complex ventricular arrhythmias. Currently, there are approximately 4.5 million active cardiac implantable electronic devices, with over 1 million new implants performed each year.[53] In pediatric cardiac surgery patients, the incidence of heart block requiring a permanent pacemaker or defibrillator is approximately 1%.[54]

Patients at Risk of Infection Related to Prosthetic Joint Implants

Patients with prosthetic joints are considered at higher risk for developing prosthetic joint infections (PJI) following dental procedures. In 2012, the American Dental Association (ADA) and the American Academy of Orthopaedic Surgeons (AAOS) concluded that routine prophylactic antibiotics are not necessary for patients with knee or hip joint implants undergoing dental procedures. Instead, these patients should focus on maintaining good oral hygiene.[55]

The 2015 guidelines stated that administering antibiotics prior to dental procedures does not prevent PJI. Furthermore, it emphasized that for most patients, the potential risks—such as antibiotic resistance, anaphylaxis, and opportunistic infections like *Clostridium difficile*—outweigh the benefits of prophylactic antibiotic use. The decision to prescribe prophylactic antibiotics before dental procedures should be based on the individual patient's medical condition and personal preferences.[56] In 2017, the AAOS and ADA reaffirmed the recommendations made in 2015.[57]

Immunocompromised Patients

Non-cardiac patients with compromised immune systems may be at increased risk of bacteremia and perioperative infection following invasive dental procedures. Current evidence does not support the routine use of antibiotic prophylaxis;[58] instead, it should be reserved for those who are immunocompromised or considered high risk. Consultation with the child's healthcare provider is recommended to determine the need for prophylaxis. High-risk patients for whom prophylaxis may be considered include those with:[59]

1. Immune system suppression due to:
    a. Human immunodeficiency virus;
    b. Neutropenia;
    c. Severe combined immunodeficiency;
    d. Hematopoietic stem cell or solid organ transplantation; or
    e. Cancer chemotherapy.
2. History of radiotherapy to the head and neck.
3. Asplenia or status post-splenectomy.
4. Sickle cell anemia.[60]
5. Autoimmune disease.
6. Hemodialysis.
7. Chronic high-dose steroid use.
8. Drug-induced osteonecrosis of the jaw.[61]
9. Uncontrolled diabetes mellitus.

Patients with Shunts, Medical Devices, or Indwelling Vascular Catheters

Recent reconstructive cardiac surgery performed within the last six months in patients with congenital heart disease significantly increases the risk of IE. Additionally, patients with shunts or residual heart defects following corrective surgery, those undergoing prosthetic valve implantation (either surgical or transcatheter), and those with prosthetic materials are also at increased risk.[8] The rising incidence of IE is likely attributed to the increased use of diagnostic tools for its detection. Echocardiography is now more frequently used in patients with positive blood cultures for *Enterococcus faecalis*, *Staphylococcus aureus*, or streptococci, due to the known association of these pathogens with a higher risk of IE.[62] Moreover, the adoption of computed tomography and nuclear imaging techniques has led to an increase in confirmed cases of infective endocarditis, particularly in patients with prosthetic valves and implanted cardiac devices.[63]

Ventriculovenous, ventriculocardiac, or ventriculoatrial shunts used in the management of hydrocephalus are susceptible to infections caused by bacteremia due to their vascular access. In contrast, ventriculoperitoneal shunts do not involve vascular structures and therefore do not require antibiotic prophylaxis.[64] It is advisable to consult the child's healthcare provider when managing patients with vascular shunts.

Antibiotic Regimens for Dental Procedures

Prophylactic antibiotics should be administered as a single dose 30 to 60 minutes before the dental procedure. If the prophylactic dose is mistakenly not given prior to the procedure, it may still be administered within two hours afterward. Certain patients undergoing invasive surgery may have incidental endocarditis. The presence of fever or other symptoms indicative of a systemic infection should alert healthcare providers to the possibility of IE. Failure to recognize these signs may result in delayed diagnosis or treatment of IE.[65]

Table 1. Protocols for Dental Treatment

Condition	Drug	Adults	Children
Oral administration	Amoxicillin	2 g	50 mg/kg
Unable to take oral medication	Ampicillin OR	2 g IV or IM	50 mg/kg IV or IM
	Ceftriaxone or cefazolin	1g IV or IM	50 mg/kg IV or IM
Allergic to penicillins (oral route)	Cephalexin OR	2 g	50 mg/kg
	Clarithromycin or Azithromycin OR	500 mg	15 mg/kg
	Doxycycline	100 mg	< 45 kg: 2.2 mg/kg > 45 kg: 100 mg
Allergic to penicillins and unable to take oral medication	Ceftriaxone or Cefazolin	1 g IV or IM	50 mg/kg IV or IM

IM, Intramuscular; IV, Intravenous.

As illustrated in Table 1, amoxicillin is the drug of choice for oral prophylaxis due to its good gastrointestinal absorption and its ability to maintain high and prolonged serum concentrations. For patients allergic to penicillins, recommended alternatives include cephalexin or another first-generation oral cephalosporin, doxycycline, clarithromycin, or azithromycin. Although one study found cephalexin to be less effective against viridans group streptococci (VGS) compared to another first-generation oral cephalosporin, it remains a recommended option.[66] There is no conclusive evidence that one oral cephalosporin is superior to another in preventing IE. Cephalexin is widely available, easy to administer, and cost-effective. Due to the risk of cross-reactions, cephalosporins should be avoided in patients with a history of anaphylaxis, urticaria, or angioedema following any penicillin treatment, including ampicillin or amoxicillin. For patients who cannot tolerate oral antibiotics, intramuscular or intravenous administration of ampicillin, cefazolin, or ceftriaxone is a suitable alternative. Patients who are allergic to ampicillin and unable to take oral medications should be treated with cefazolin or ceftriaxone. Clindamycin is no longer recommended for antibiotic prophylaxis before dental procedures,[34] as it has been associated with more frequent and severe adverse reactions compared to other prophylactic antibiotics. Notably, antibiotics prescribed for dental procedures may contribute to approximately 15% of community-acquired *Clostridium difficile* infections.[67] Doxycycline may be used as an alternative in patients who are unable to tolerate penicillins, cephalosporins, or macrolides. Severe reactions to a single dose of doxycycline are extremely rare.[34]

Prophylaxis recommendations cannot account for every clinical scenario, so clinical judgement and collaboration with the patient are essential. For patients taking a short course (7–10 days) of oral antibiotics prior to dental procedures, it is advisable to use a different class of antibiotic and to delay any elective dental work for at least 10 days after completing treatment. If multiple dental appointments are required, a similar 10-day interval is recommended between procedures. For patients receiving parenteral antibiotics for active infections, the same antibiotic may be continued during dental procedures. To help prevent antibiotic resistance in patients requiring multiple procedures, it is recommended to alternate antibiotic regimens or allow at least a 4-week interval between treatments.[34]

Antibiotic Adverse Effect

Antibiotic adverse effects (AAE) are classified as adverse drug reactions (ADR) and refer to any unwanted effects caused by a medication. It is important to distinguish between an ADR and an allergy: an allergy is an immune-mediated response to a drug, such as anaphylaxis, whereas an ADR includes any undesired effect of a drug, such as sedation. In essence, while all allergies are ADRs, not all ADRs are allergies.[68]

Aside from anaphylactic reactions, the antibiotics most commonly used in dentistry today are generally well tolerated. The most prevalent ADR associated with antibiotics is gastrointestinal distress, including diarrhea, nausea, and vomiting. Approximately 2% to 10% of all antibiotics can cause diarrhea, with rates exceeding 25% for Augmentin (amoxicillin combined with clavulanic acid).[69] A more serious concern is the risk of developing opportunistic infections, such as *Clostridium difficile* or *Candida infections*, following antibiotic use. *Clostridium difficile* infection is most commonly linked to clindamycin use, although any antibiotic has the potential to cause it.[70]

A study examined a national database of adverse drug reactions voluntarily reported by medical professionals.[71] Among 11,061 cases of amoxicillin-associated anaphylaxis, 17 were attributed to prophylactic administration prior to dental procedures, while no cases were reported for clindamycin. A report from the UK, covering the period from 1972 to 2007, found no deaths related to amoxicillin-induced anaphylaxis when used for dental prophylaxis.[72] Between 1980 and 2014, approximately 2.9 million doses of 3 g amoxicillin were associated with 67 adverse reactions, including 16 anaphylaxis, none of which were fatal. In contrast, a study reported that about 1.2 million prescriptions of 600 mg clindamycin resulted in 193 adverse reactions, including 15 deaths, 12 of which were due to *Clostridium difficile* infection (CDI). While these events are considered rare, studies suggest they are likely underreported, with a median underreporting rate of approximately 94%.[73]

One study reviewing community-acquired CDIs reported that 8% of CDI cases were associated with antibiotic prophylaxis for dental procedures.[74] Another study focused on the inappropriate use of antibiotic prophylaxis prior to dental visits, revealing that 1.4% of 136,177 visits were associated with serious AAEs within 14 days. Most of these were emergency department visits (83%), while allergic reactions accounted for 16% of cases.

Severe AAEs, including anaphylaxis and CDI, were reported in 5 and 14 individuals, respectively.[75] Clindamycin was associated with a higher rate of AAEs compared to amoxicillin and accounted for the highest number of emergency department visits due to antibiotic-related effects. Even a single dose of clindamycin poses a greater risk for developing CDI and is also associated with allergic reactions during prophylaxis.[76] For these reasons, doxycycline is now recommended instead of clindamycin for antibiotic prophylaxis in patients with a penicillin allergy (Table 1).

Another potentially life-threatening drug interaction involves clarithromycin, erythromycin, and azithromycin when taken concurrently with digoxin.[77] These antibiotics inhibit the elimination of digoxin from the bloodstream, which can significantly increase digoxin levels and lead to digitalis toxicity.[78] Symptoms of digitalis toxicity commonly include vomiting, nausea, and an irregular heartbeat.[70]

The growing and emerging antibiotic resistance in oral streptococci is a cause for concern. Resistance rates to azithromycin and clarithromycin are notably higher than to penicillin.[79] One study found that infants with CHD and adults with a history of rheumatic fever had significantly more amoxicillin-resistant *Streptococcus* strains in their dental plaque compared to healthy controls. The authors suggested that this increased resistance may be linked to the prophylactic use of antibiotics in the study group, emphasizing the role of antibiotic exposure in resistance development.[80]

Conclusion

This review is essential for pediatric dentists and healthcare providers, as it consolidates current knowledge on antibiotic prophylaxis for the prevention of IE in pediatric patients with CHD who are at risk. By synthesizing recent advancements and clinical recommendations, it supports informed decision-making regarding prophylactic strategies and highlights the ongoing challenges associated with managing pediatric IE. Furthermore, the review explores the connection between oral health practices and systemic infections, emphasizing the need for greater awareness and proactive dental care in at-risk pediatric populations. It promotes a multifaceted approach to IE prevention that goes beyond antibiotic use, underscoring the importance of patient education on oral hygiene and early recognition of infection. Additionally, the review outlines the varying degrees of risk associated with specific congenital heart defects, helping clinicians tailor prophylactic approaches accordingly. Collaboration between pediatric cardiologists and dentists is vital to address the unique needs of children with heart conditions. By fostering interdisciplinary collaboration and implementing comprehensive preventive strategies, we can improve the overall health and reduce the risk of infective endocarditis in vulnerable pediatric patients.

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