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REVIEW

The Impact of Antimicrobial Resistance on Pediatric Oral Health Outcomes

El impacto de la resistencia a los antimicrobianos en los resultados de la salud bucodental pediátrica

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ABSTRACT

According to predictions, antimicrobial resistance (AMR) may overtake all other causes of death globally by 2050, posing a serious danger to public health globally. This review examines the prevalence, mechanisms, and management of antibiotic resistance in pediatric oral infections. The oral cavity harbors diverse microbial communities, and inappropriate antibiotic use in dental practice contributes to the selection of resistant bacteria. Common oral pathogens, including *Streptococci* and anaerobes, have demonstrated varying levels of resistance to frequently prescribed antibiotics like amoxicillin, penicillin, and metronidazole. The review outlines foundational principles for antibiotic usage in pediatric dentistry, emphasizing prevention, adjunctive therapy, proper selection, and dosing. Specific clinical scenarios, such as pulpal infections, facial swelling, dental trauma, and periodontal disease, are discussed, providing guidance on appropriate antibiotic management. The challenges of managing antibiotic-resistant oral infections are addressed, highlighting the need for improved surveillance, responsible prescribing practices, and development of new antimicrobial agents. Emerging trends in antibiotic management, including the potential of metal nanoparticles and artificial intelligence, are explored. The review concludes by stressing the importance of judicious antibiotic use in pediatric dentistry, balancing effective treatment with broader public health implications. Continuous professional education and adaptation to emerging evidence are crucial for optimal care delivery and contribution to antibiotic stewardship initiatives.

Keywords: Antimicrobial Resistance; Pediatric Dentistry; Oral Infections; Antibiotic Stewardship; Antibiotics.

RESUMEN

Según las predicciones, la resistencia a los antimicrobianos (RAM) puede superar a todas las demás causas de muerte en el mundo en 2050, lo que supone un grave peligro para la salud pública mundial. Esta revisión examina la prevalencia, los mecanismos y el tratamiento de la resistencia a los antibióticos en las infecciones orales pediátricas. La cavidad oral alberga diversas comunidades microbianas, y el uso inadecuado de antibióticos en la práctica odontológica contribuye a la selección de bacterias resistentes. Los patógenos orales comunes, incluidos los estreptococos y los anaerobios, han demostrado distintos niveles de resistencia a los antibióticos prescritos con frecuencia, como la amoxicilina, la penicilina y el metronidazol. La revisión esboza los principios fundamentales para el uso de antibióticos en odontología pediátrica, haciendo hincapié en la prevención, el tratamiento complementario, la selección adecuada y la dosificación. Se discuten escenarios clínicos específicos, como las infecciones pulpares, la inflamación facial, los traumatismos

dentales y la enfermedad periodontal, proporcionando orientación sobre el tratamiento antibiótico adecuado. Se abordan los retos de la gestión de las infecciones orales resistentes a los antibióticos, destacando la necesidad de mejorar la vigilancia, las prácticas de prescripción responsables y el desarrollo de nuevos agentes antimicrobianos. Se exploran las nuevas tendencias en la gestión de los antibióticos, incluido el potencial de las nanopartículas metálicas y la inteligencia artificial. La revisión concluye subrayando la importancia de un uso juicioso de los antibióticos en odontopediatría, equilibrando el tratamiento eficaz con implicaciones más amplias para la salud pública. La formación profesional continuada y la adaptación a las nuevas evidencias son cruciales para ofrecer una atención óptima y contribuir a las iniciativas de administración de antibióticos.

Palabras clave: Resistencia Antimicrobiana; Odontología Pediátrica; Infecciones Orales; Administración de Antibióticos; Antibióticos.

INTRODUCTION

Antimicrobial resistance (AMR) has emerged as a formidable global public health challenge in the 21st century.[1,2,3] This phenomenon, characterized by the evolution of microorganisms to resist antimicrobial medications, poses a significant threat to human health.[1,2,3,4,5,6] The primary cause of the widespread occurrence of antimicrobial resistance (AMR) is the overuse or misuse of antibiotics in a variety of industries, including agriculture, animal husbandry, healthcare, and the food industry.[7,8,9,10] AMR, often referred to as the "Silent Pandemic," requires prompt and extensive treatments in order to stop it from spreading and developing into a serious worldwide health emergency.[11] Projections show that, in the absence of adequate preventive efforts, AMR may overtake all other causes of death globally by 2050.[12] Global estimates suggest tha direct fatalities associated with AMR exceeded 1,2 million in 2019, with projections indicating a potential increase to approximately 10 million deaths annually by 2050 if AMR is not adequately addressed.[4,13]

In 1998, the Standing Medical Advisory Committee (SMAC) published the report "The Path of Least Resistance," which revealed that dentists accounted for 7 % of all community prescriptions of antimicrobials. Although this percentage may appear relatively small, it translates to a significant number of antibiotic prescriptions. Dentists issued 3,3 million antibiotic prescriptions in 1993, which increased to 3,5 million by 1996.[14] With around 22 000 general dentistry practitioners in the UK, this data shows that each practitioner might be prescribing an average of 159 antibiotic courses year, or roughly three prescriptions per week. This indicates a higher rate of antibiotic usage by dentists than previously recognized. The impact of AMR is projected to be substantial in the Western Pacific region between 2020 and 2030. Antimicrobial-resistant infections are predicted to cause an extra 172 million hospital days for patients, and drug-resistant bacterial infections are predicted to be the cause of 5,2 million fatalities in the region.[15]

Children constitute a substantial demographic in antimicrobial consumption and exhibit elevated rates of antimicrobial resistance (AMR). They are more susceptible to infectious diseases such as meningitis and pneumonia because of their undeveloped immune systems, demanding regular antibiotic treatment. The concern of antibiotic overuse and misuse in pediatric infections has increased due to a paucity of data specifically focused on pediatric illnesses and an inadequate comprehension of resistance mechanisms in prevalent pediatric diseases. Pediatric patients have considerable hurdles due to the presence of *Bordetella pertussis* and *Streptococcus pneumoniae*, which are resistant to both macrolides and clindamycin, in some countries like China. Furthermore, it has been noted that children have a greater detection rate of carbapenem-resistant *Enterobacteriaceae* than adults. Determining age-appropriate dosages is made more difficult by the fact that children have various growth and developmental stages, which lead to vastly varied pharmacokinetic (PK) and pharmacodynamic (PD) properties. Antibiotic overuse in children is further exacerbated by the lack of pediatric-specific data, which may result in treatment failure and heightened antibiotic resistance.

Global dynamics of antimicrobial resistance

Recent academic literature has significantly enhanced our comprehension of antimicrobial resistance (AMR) patterns in pediatric populations across diverse geographical regions and pathogenic organisms. A systematic examination of recent investigations reveals several noteworthy contributions to the field. In the context of pneumococcal research, an investigation conducted in Urumqi, China, evaluated the temporal changes in serotype distribution and antimicrobial resistance patterns of pneumococcal isolates. This study specifically examined the impact of two significant factors: the implementation of the PCV13 vaccination program and the introduction of COVID-19 mitigation strategies.[16] *Staphylococcus aureus* infections in pediatric skin and soft tissue infections were the subject of a ten-year, multicenter study carried out in China, which examined the clonal distribution and patterns of antibiotic sensitivity of the isolates.[17] This study was enhanced by additional data from the 2016–2021 Infectious Disease Surveillance of Pediatrics (ISPED) program, which highlighted the

antibiotic resistance features of methicillin-resistant *S. aureus* strains in pediatric populations.[18] In the domain of enteric pathogens, researchers conducted a detailed genetic analysis of azithromycin-resistant *Salmonella enterica* isolates obtained from pediatric patients in Shenzhen, China. This investigation focused on characterizing resistance genes and plasmid profiles.[19] Similarly, Japanese researchers assessed the prevalence of extended-spectrum ß-lactamase-producing and carbapenem-resistant *Enterobacterales* in neonatal cohorts. This study focused on fecal carriage rates during routine four-month health checks in a rural community.[20] The antibiotic susceptibility patterns of Escherichia coli isolates taken from newborns in critical care units were assessed in a statewide Chinese investigation conducted between 2015 and 2020.[21] Researchers looked on the clinical effects of macrolide resistance in juvenile respiratory disorders caused by Mycoplasma pneumoniae infections during the COVID-19 pandemic.[22] An additional significant contribution to the field examined the complex interactions between respiratory viruses in pediatric populations. By measuring the rate of coinfection, this study examined viral exclusion patterns and affinity interactions during the 2022 influenza and respiratory syncytial virus (RSV) outbreak.[23] The collective findings from these diverse investigations provide crucial insights into the current status of antimicrobial resistance in pediatric populations. These studies underscore the critical importance of sustained surveillance efforts and ongoing research initiatives in this domain. The varied methodologies and focal points of these investigations contribute to a more comprehensive understanding of the challenges posed by antimicrobial resistance in pediatric medicine.

Antimicrobial resistance patterns in pediatric oral infections

The human oral cavity represents an extraordinarily complex microbial ecosystem, second only to the intestinal tract in terms of bacterial diversity. Research has elucidated the presence of over 700 distinct bacterial species that colonize various oral surfaces, including the keratinized gingival tissue, mucosa of the cheeks, lingual surface, dentition, hard palate, palatal folds, and tonsillar regions.[24,25] The establishment of this oral microbiome in children occurs through a multifaceted process influenced by several factors during early development, encompassing genetic predisposition, birthing method, and feeding practices, whether through maternal lactation or formula supplementation. This microbial colonization initiates during prenatal development and undergoes significant diversification postnatally, with the initial years of life representing a critical period for microbial expansion. By approximately 24 months of age, the oral biofilm achieves a complexity of more than 32 distinct species-level taxonomic units.[24,25]

Children frequently encounter bacterial infections in the orofacial region that parallel those observed in adult populations.[26,27] Dental pathologies predominantly underlie these infections, with dental caries and its sequelae—including pulpal inflammation, necrosis, apical periodontitis, and periapical abscesses—representing the most frequently encountered conditions.[28] Antimicrobial therapy is frequently employed in managing both odontogenic and non-odontogenic infections, whether acute or chronic. Furthermore, antibiotic prophylaxis is prescribed for patients at elevated risk of focal infections, particularly those with systemic conditions such as endocarditis or congenital cardiac anomalies, as well as for individuals undergoing dental procedures or oral surgical interventions.[29] Despite existing clinical guidelines, the prescription of antibiotics in pediatric dentistry remains extensive, with data from England suggesting that antibacterial medications constitute 66,4 % of dental prescriptions.[30] This practice has raised significant concerns regarding inappropriate antibiotic utilization, including prescription for non-indicated conditions, utilization of broad-spectrum antibiotics when narrow-spectrum alternatives would suffice, extended duration of antibiotic courses, and inappropriate dosing protocols. These practices potentially expose pediatric patients to numerous adverse effects.[31,32] While general medical practitioners account for the majority of community antibiotic prescriptions, significantly impacting resistant bacterial selection in oral flora, the contribution of dental prescribing practices to antimicrobial resistance has received insufficient attention.[33,34] An estimated three million antibiotic-resistant illnesses are reported in the US each year, with over 35 000 deaths as a result. This highlights the need for healthcare providers to exercise prudent antibiotic stewardship.[33,34,35]

Research has demonstrated that 80 % of antibiotic prophylaxis prescriptions preceding dental procedures were unnecessary, as patients lacked relevant risk factors.[36] While certain patients undergoing invasive dental procedures do require antibiotic prophylaxis, emphasis should be placed on establishing consistent dental care, implementing preventive measures, maintaining optimal oral hygiene practices, and ensuring regular dental examinations.[37,38] Antibiotic administration can result in various adverse events, including allergic reactions, *Clostridioides difficile* infections, drug interactions, and various side effects.[33,39] These antibiotic-related adverse events frequently necessitate emergency department visits for pediatric patients, with studies indicating that amoxicillin predominantly affects children under nine years, while sulfamethoxazole-trimethoprim is more commonly implicated in adverse events among children aged 9-17.[38,39,40,41,42,43,44,45,46,47]

In the context of antibiotic selection, amoxicillin remains the primary choice for dental infections in children without penicillin allergy, owing to its efficacy against diverse gram-positive bacteria, enhanced gram-negative coverage compared to penicillin, demonstrated effectiveness against oral microbiota, superior gastrointestinal

absorption, sustained elevated serum concentrations, and limited adverse effect profile.[38,41,42] It is noteworthy that the American Heart Association has withdrawn its recommendation for clindamycin in infective endocarditis prophylaxis due to its association with severe reactions, particularly community-acquired *C. difficile* infections.[38] Recent evidence suggests that short-term doxycycline use does not cause dental discoloration in children below eight years, making it a viable alternative for patients with allergies to penicillins, cephalosporins, and macrolides.[44,45,46,47] Azithromycin presents a relatively safe option for penicillin-allergic patients, though cardiac complications, including cardiotoxicity, remain a concern. This risk appears elevated in patients with pre-existing cardiovascular conditions, while pediatric patients primarily face the risk of QT interval prolongation at higher dosages.[47,48]

Prevalence and mechanisms of antibiotic resistance in oral bacteria

The widespread use of antibiotics in dental practice, particularly amoxicillin, penicillin, and metronidazole, has the potential to exert selective pressure on the oral commensal flora, potentially facilitating the emergence of resistant bacterial strains.[49] Aminopenicillins, among the most frequently prescribed antibiotics in dentistry,[50] have shown variable efficacy against oral microorganisms. Research has identified both high susceptibility rates among anaerobes isolated from deeper oral sites and the presence of ß-lactamase production, notably in *Prevotella* species.[51,52] Resistance to aminopenicillins has been observed in various oral bacteria. For example, *Veillonella spp.* and *Prevotella denticola* isolated from root canals have demonstrated amoxicillin resistance. Conversely, a study reported that all 34 strains of facultative anaerobic bacteria and 96 % of obligate anaerobes isolated from root canals were sensitive to amoxicillin.[51] While ß-lactamase-producing *Prevotella* strains were found in 39,4 % of periodontal pockets and 53,2 % of patients, Fosse et al. reported Gram-negative bacilli, including *Prevotella*, are susceptible to amoxicillin when coupled with clavulanic acid.[52]

Streptococci, particularly α-haemolytic species, have exhibited varying degrees of resistance to penicillins. Streptococci that produce ß-lactamase were found in the subgingival plaque of periodontitis patients as early as 1986.[53] However, most *Streptococci* do not produce ß-lactamase; instead, resistance is usually mediated by changes to penicillin-binding proteins.[54] Research on the susceptibility of different types of *Streptococci* has produced inconsistent results. While *Streptococcus mutans* has generally demonstrated universal susceptibility to penicillin and other antimicrobials,[55,56,57,58,59] other species such as *Streptococcus oralis* and *Streptococcus mitis* have exhibited higher levels of resistance.[48,60] *S. salivarius* strains accounted for 8 %, *S. mitis* strains for 20 %, and *S. oralis* strains for 35 % of the high-level penicillin resistance (MIC > 4 mg/L).[30] Research has indicated that the minimum inhibitory concentrations of benzylpenicillin for *S. oralis* and *S. mitis* vary between 32 and 64 mg/L.[48,60] The transfer of resistance determinants between *Streptococcal* species, particularly from *Streptococcus pneumoniae* to other α-haemolytic *Streptococci,* is a matter of concern.[57,58,59,60] TMosaic genes are involved in this interspecies transmission; they consist of sections that are resistant to penicillin and sections that have nucleotide sequences comparable to those of strains susceptible to the antibiotic.[48,49]

Anaerobic bacteria commonly isolated from oral infections, such as *Porphyromonas gingivalis*, *Prevotella intermedia*, and *Prevotella nigrescens*, have demonstrated varying levels of resistance to penicillins. *P. gingivalis* isolates generating ß-lactamase have rarely been identified from periodontal pockets,[33,34] penicillin resistance is more consistently observed in *Prevotella* species.[34] Other oral anaerobes implicated in infections, penicillin resistance has also been linked to species including *Fusobacterium* and *Veillonella*.[28,48] Metronidazole, frequently prescribed by dental practitioners,[22] has generally shown effectiveness against anaerobic bacteria. However, resistance mechanisms have been identified, including mutations affecting drug activation, cellular uptake, and efflux.[23] While most studies have found high susceptibility rates among anaerobes,[44,51] there have been reports of reduced susceptibility in some species, such as *Prevotella loescheii*.[45,46] Cephalosporin resistance has been observed in α-haemolytic *Streptococci*, with MICs as high as 128 mg/L reported for cefotaxime.[48] *Enterococcus* species isolated from root canal exudates have expressed high-level resistance to cephalosporins.[50] *Staphylococci* from the oral cavity have generally shown susceptibility to cephalosporins,[47] although methicillin-resistant *Staphylococcus aureus* has been reported in the oral cavity.[31]

The oral flora is largely resistant to tetracycline due to a variety of tet genes, 27 of which have been identified.[31,32] This resistance is often associated with resistance to other antibiotics, particularly penicillins and erythromycin.[39,40] The presence of both tet(Q) and erm(F) genes is common in oral anaerobes.[5] Macrolide resistance, most commonly due to erm genes, has been observed in oral α-haemolytic *Streptococci* and anaerobes.[37,38,39,40] Studies have demonstrated the persistence of resistant populations following macrolide treatment and the co-occurrence of macrolide and tetracycline resistance.[32,37,40] Ioannidou et al. found that 38,5 % of oral α-haemolytic *Streptococcal* isolates from healthy Greek children were resistant to erythromycin.[13]

Chlorhexidine, widely used as an antibacterial agent in dentistry, has shown varying results in resistance studies. While some in vitro studies have suggested potential resistance development in *S. aureus* and *Streptococcus sanguis*,[16,17] others have found low MICs against common oral bacteria such as *S. mutans* and *Streptococcus sobrinus*.[15,24] The prevalence and degree of antibiotic resistance in the oral flora remain unclear

and require further investigation. The potential for high-level resistance transfer, particularly to *S. pneumoniae*, underscores the importance of accurate determination of resistance prevalence in the oral microbiome. Continued surveillance and judicious use of antibiotics in dental practice are crucial to mitigate the spread of antibiotic resistance among oral bacteria.

Foundational principles of antibiotic usage

The utilization of antibiotics in pediatric dentistry constitutes a critical domain of clinical practice that necessitates meticulous consideration and judicious implementation. Dental professionals are confronted with the challenge of balancing efficacious treatment protocols with the escalating concern of antimicrobial resistance. This discourse aims to elucidate the fundamental principles, clinical applications, and salient considerations pertaining to antibiotic usage in pediatric dental care, drawing upon contemporary research findings and established guidelines to provide a comprehensive analysis of this significant topic. The foundation of antibiotic utilization in pediatric dentistry is predicated upon a set of core principles that should inform practitioners' clinical decision-making processes. Paramount among these is the emphasis on prophylaxis.[54,55] By prioritizing preventive measures to mitigate the incidence of dental pathologies, the necessity for antibiotic intervention can be substantially reduced. This proactive approach not only confers benefits to individual patients but also contributes to the broader objective of antimicrobial stewardship.

In instances where antibiotic administration is deemed clinically necessary, it is crucial to conceptualize their role as adjunctive therapy rather than a primary therapeutic modality. Primary dental interventions such pulp therapy, extractions, and periodontal therapies should not be replaced by antibiotics; rather, they should only be recommended in cases of verified bacterial infections.[54,55] This principle underscores the importance of addressing the etiological factors of infection through appropriate dental procedures. The selection of an appropriate antibiotic agent is a nuanced decision that must take into account multiple factors. Practitioners must consider the pharmacological properties of the antibiotic, including its spectrum of activity and safety profile. Additionally, the patient's history of antibiotic use plays a crucial role in this decision, as do their individual medical history, any drug allergies, current medications, and factors affecting ease of administration.[54,55] This patient-centered approach ensures that the chosen antibiotic is not only effective against the targeted pathogens but also safe and suitable for the individual child.

Accurate dosing is another critical aspect of antibiotic therapy in pediatric dentistry. Prescribing the correct pediatric dose is essential for achieving therapeutic efficacy while minimizing the risk of adverse effects. Practitioners must remain cognizant of current dosing guidelines and be prepared to adjust dosages based on the child's age, weight, and specific clinical presentation. The route of administration is yet another factor that requires careful consideration. While oral antibiotics are often the most practical choice in outpatient settings, there are situations where intravenous or intramuscular administration may be necessary, particularly in cases of severe infections or when rapid systemic distribution of the antibiotic is required.[55,56]

In circumstances where a patient is currently receiving parenteral antimicrobial therapy for an existing infection, it is generally advisable to continue with the same antibiotic, provided it demonstrates efficacy against the dental pathogens in question. This approach helps maintain continuity of care and reduces the risk of drug interactions or adverse effects from multiple antibiotics. Given the complex nature of some dental infections and the omnipresent concern of antibiotic resistance, collaboration with other medical professionals is sometimes warranted. In cases where there is suspicion of resistant infections, consultation with an infectious disease specialist is recommended.[54,55] This interdisciplinary approach ensures that patients receive the most appropriate and effective treatment. The judicious use of antibiotics in pediatric dentistry requires a comprehensive understanding of microbiology, pharmacology, and patient-specific factors. By adhering to evidence-based principles and guidelines, dental practitioners can optimize treatment outcomes while contributing to the global effort to combat antimicrobial resistance.

Optimizing antibiotic therapy in pediatric endodontic infections

In pediatric dentistry, the standard protocol for antibiotic therapy is five days after significant improvement in clinical condition.[19,20] This strategy generally results in a five to seven-day duration of medication, depending on the antibiotic chosen. However, the escalating threat of antibiotic resistance has necessitated a reevaluation of this practice. Current recommendations advocate for a more adaptive approach to the duration of antibiotic therapy. Practitioners are now urged to consider terminating antibiotics upon confirmation of possibly ineffectiveness and cure, potentially before finishing which had been deemed a full course of medication.[10,11] This shift in practice requires close monitoring of the patient's response to treatment and a willingness to adjust the treatment plan based on clinical outcomes. In cases where an infection does not respond as expected to the initial antibiotic selection, further investigation is warranted. Culture and sensitivity tests from the infection site, or in certain situations, blood microbiology, may be necessary.[20] These diagnostic tools can provide valuable information about the specific pathogens involved and their susceptibility to various

antibiotics, allowing for more targeted and effective treatment. The importance of proper documentation cannot be overstated. All antibiotic prescriptions must be meticulously documented in the patient's oral health records.[53] This practice not only ensures continuity of care but also provides a valuable resource for tracking antibiotic usage patterns and evaluating treatment efficacy over time. Antibiotic allergies present a particular challenge in pediatric dentistry. Given the potential severity of allergic reactions, it is crucial to accurately identify true antibiotic allergies. Patients believed of exhibiting an antibiotic intolerance should be tested to confirm or disprove an existence of a serious allergy. This approach helps prevent unnecessary avoidance of effective antibiotics while ensuring patient safety.

Specific Clinical Scenarios

Pulpal Infections - Antibiotic treatment is typically neither necessary nor beneficial in situations of acute pulpitis, where the infection is limited to the pulpal tissue or the subsequent surroundings.[12] The appropriate treatment in these instances focuses on addressing the underlying cause of the infection through dental procedures such as pulpotomy, pulpectomy, or extraction. This approach emphasizes the importance of accurate diagnosis and targeted treatment in the management of dental infections.

Non-Odontogenic Bacterial Infections - Pediatric dentists can encounter patients with advanced non-odontogenic bacterial diseases such oral syphilis, gonococcal stomatitis, staphylococcal mucositis, and tuberculosis, albeit these are less common. In these instances, the use of antibiotics requires careful consideration. Due to the specific character of many infections, a final diagnosis and treatment planning may require referral for microbiological evaluation, sensitivity and culture examination, biopsy, and other investigations in the lab.

Acute Facial Swelling of Dental Origin - The management of facial swelling or cellulitis secondary to odontogenic infection necessitates prompt and decisive action. The patient's age, degree of cooperation, ability to receive sufficient anesthesia, the severity of the infection, the patient's health, and pertinent social difficulties are just a few of the variables that must be taken into account while designing the treatment plan.[19,20] When patients exhibit non-localized, progressive swelling along with systemic symptoms like fever or respiratory distress, it is advised to proceed with immediate surgical intervention and intravenous antibiotic therapy.[45,46,47,48,49,50,51,52] This aggressive approach is essential to rapidly control the infection and prevent potentially life-threatening complications.

Systemic involvement and septicemia signs, comprising fatigue, fever, abnormalities of the face, lymphadenopathy, trismus, tachycardia, dysphagia, severe respiratory distress, require immediate medical attention.[51,52] In severe cases, a multidisciplinary approach involving dental and medical professionals is often necessary to manage both the local infection and its systemic effects. Additional diagnostic tools such as radiographs, ultrasound, or computed tomography scans may be employed. Additionally, a number of laboratory tests, such as sensitivity testing, bacterial culture, C-reactive protein measurements, and complete blood counts, might offer important information to help with treatment choices.[11,12]

Penicillin derivatives continue to be the empirical choice when it comes to antibiotic selection for oral infections because of its potency against prevalent oral bacteria. However, in cases where anaerobic bacterial involvement is suspected, consideration should be given to adjunctive antimicrobial therapy such as metronidazole.[53] Cephalosporins should be investigated as an alternative for controlling odontogenic infections in young children with a history of penicillin usage or are allergic to it.[26]

Dental Trauma - In cases of dental trauma, particularly avulsed permanent incisors, systemic antibiotics are recommended as adjunctive therapy, regardless of whether the tooth has an open or closed apex.[15] Amoxicillin or penicillin are commonly used in these conditions due to their efficacy against oral bacteria and low prevalence of side effects. Doxycycline's antibacterial, anti-inflammatory, and antiresorptive qualities make it an intriguing substitute in dental trauma situations.[11,19] However, the use of tetracyclines in young children should be approached with caution due to the risk of dental staining. Topical antibiotics such as minocycline or doxycycline have been shown in animal experiments to enhance periodontal regeneration and pulpal revascularization in young non-vital traumatized teeth. However, its efficacy in human studies remains unproven and controversial. The International Association of Dental Traumatology has not recommended this practice, and further randomized clinical trials are needed to establish its efficacy and safety.[41]

Periodontal Disease -Distinct variations of periodontal disease are identified in juvenile patients: necrotizing periodontitis, which includes the previously recognized aggressive or chronic forms, and periodontitis as a symptom of systemic disease.[37] Antibiotic therapy may need to be administered differently for each of these forms. Supplementary antimicrobial care may be necessary in addition to targeted treatment in situations of advanced periodontal disease.[22,23,24] Based on the degree of progression of the health issues, the patient's general health, and the outcome of the initial periodontal therapy, systemic antibiotics should be used in these circumstances. Particular difficulties arise from periodontal disorders linked to systemic problems, such as leukocyte adhesion deficit, Papillon-Lefèvre syndrome, or severe congenital neutropenia. In certain

circumstances, the immune system may be unable to effectively regulate the spread of periodontal infections. Treatment may include administration of antibiotics or prophylactic antibiotics.[25] Culture and susceptibility screening of specimens from the regions of interest can be very helpful in guiding the choice of the most suitable antibiotic. It's important to note that in severe and refractory cases of periodontal disease, particularly those associated with systemic conditions, extraction of the affected teeth may be indicated.[22] This decision should be made carefully, considering both the long-term oral health of the patient and their overall medical condition.

Viral Conditions - It is imperative that healthcare professionals understand that viral illnesses, such acute primary herpetic gingivostomatitis, are not appropriate to be treated with antibiotics.[16] Antibiotic resistance is a result of inefficient utilization of antibiotics in viral illnesses, where they are ineffective against the virus. Rather, the goal of treatment ought to be to promote the patient's immunological response while regulating symptoms.

Salivary Gland Disorders - Salivary gland disorders in pediatric patients can present significant diagnostic and treatment challenges. Antibiotic therapy is encouraged for the treatment of acute bacterial salivary gland swellings. The most prevalent pathogens in bacterial infections of the salivary glands arising from oral flora are streptococcal and staphylococcal species, which are covered by amoxicillin/clavulanate, which is frequently the empirical choice for these illnesses.[17] Invasive procedures including incision and drainage are occasionally necessary if the patient does not respond after 24 to 48 hours of antibiotic medication alone.[5] Juvenile recurrent parotitis (JRP) is the most prevalent inflammatory salivary gland disorder in the United States, with symptoms appearing between the ages of three and six years and lasting until puberty. The duration of symptoms may be reduced with ß-lactam antibiotics, even though JRP is self limiting.[28] Antibiotic medication is part of the treatment plan for both acute bacterial and chronic recurring submandibular sialadenitis.[35] However, it's important to note that antibiotic therapy alone may not be sufficient, and additional interventions such as hydration, sialogogues, or in some cases, surgical management may be necessary.

Challenges and strategies for managing antibiotic-resistant oral infections

Due to their extensive use in medical procedures and the financial aspects of raising animals for food, antimicrobial usage is not expected to decline.[51] As an initial line of defense against bacterial infections, clinicians usually choose to administer empiric antibiotics rather than expedient point-of-care diagnostics. Comparably, modern farming practices depend on routine antibiotic treatment to prevent animal diseases and promote growth. Despite greater awareness of the risks associated with antibiotic abuse, antimicrobial stewardship initiatives in healthcare and amended animal husbandry regulations remain inadequate. The continual evolution of multidrug resistant microbes exacerbates these issues, as the pipeline for developing antibiotic drugs cannot keep up with the pace of advancement.

International cooperation on AMR surveillance and stewardship standards is fragmented, despite organizations such as the United Nations (UN), World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) and recognizing its transnational concerns. Disparities in access to quality diagnostics and antibiotic supervision between nations enhance the local genesis and global dissemination of new resistance mechanisms. Inadequate management techniques in some areas could persistently impede regional advancement. Antibiotic resistance is a unique 'tragedy of the commons' that requires equitable, integrated global response and mutual accountability. However, geopolitical constraints continue to hamper agreement on linking international policies and financial frameworks vital for promoting antimicrobial stewardship and inventiveness globally.[58] The impact of AMR extends across borders, affecting populations all across the world. Previously treatable infections have become major health threats. The scarcity of effective antimicrobial drugs heightens the dangers associated with common medical treatments including surgery, chemotherapy, and organ transplants. AMR creates significant economic issues for healthcare systems, governments, and society in addition to human health concerns.[49,50] The financial burden of managing resistant infections is much higher due to more prolonged hospitalizations, supplementary healthcare consultations, and the need for expensive last-line treatments.

Mitigating AMR requires a comprehensive, multi-sectoral strategy involving various stakeholders. The development and implementation of enhanced surveillance systems are vital for successfully monitoring and tracking the emergence and transmission of resistant diseases.[10] The careful and conservative use of antimicrobials must be stressed in order to limit the negative selection that triggers resistance generation. Antimicrobial surveillance initiatives inside healthcare institutions, as well as the enforcement of legislation solving antibiotic usage in farming and animal healthcare, may significantly decrease excessive drug consumption.[45,46,47,48,49,50] These efforts, combined with continued research and development of new antimicrobial agents and alternative therapies, form the foundation of a comprehensive approach to combating the global threat of AMR.

Emerging trends in antibiotic management for pediatric oral infections

The global challenge of antimicrobial resistance (AMR) necessitates a multifaceted approach to research

and development, encompassing a wide range of disciplines and strategies. Action-oriented research forms the cornerstone of developing and implementing effective strategies against AMR. A comprehensive research agenda must investigate the complex interplay of factors contributing to resistance development. The prescription of antibiotics, agricultural usage trends, comprehending the role of horizontal gene transfer in the spread of resistance, and examining sociocultural variables influencing the use of antibiotics are important research issues.[23,29,30,31,32,33,34] Furthermore, understanding microbial ecosystem interactions, encompassing the resistome and environmental impacts, is critical for designing comprehensive methods to combat AMR.

Fostering interdisciplinary collaboration is critical for improving our understanding of antimicrobial resistance. Policymakers, epidemiologists, microbiologists, pharmacologists, and social scientists should all be included in this collaborative effort. By combining diverse expertise, researchers can develop more comprehensive and effective approaches to tackle the multifaceted challenges posed by AMR. The discovery of new antimicrobial medications and complementary therapies is an important step toward combating antibiotic resistance. This endeavor should augment current monitoring and diagnostic investigations. Drug development is focused on discovering new molecular targets, improving existing antibiotics, and researching non-traditional therapeutic approaches such as antibacterial bacteriophage therapy and autoimmune regulation. Integrative research is crucial for expediting the adoption of new interventions by connecting laboratory discoveries to clinical applications. Collaboration among academics, pharmaceutical companies, and regulatory bodies is crucial for speeding the development, appraisal, and approval of innovative antimicrobial drugs.[57]

Collaboration between governments, pharmaceutical corporations, and research organizations is necessary to stimulate innovation in antimicrobial development by streamlining the development process and offering incentives. Several promising strategies have emerged in recent years. Metal nanoparticles represent a potential therapeutic approach to address AMR.[36,37,38,39] Artificial intelligence shows promise in tackling high rates of AMR by enabling more efficient drug discovery and optimizing treatment strategies.[40] Another innovative approach involves the concurrent use of antibiotics and antivirulence drugs, which has been proposed as a means to enhance the management of pathogenic microorganisms while minimizing AMR development.[41] In addition to developing new antimicrobial agents, resources must be allocated towards advancing vaccines and diagnostics. These approaches aim to lessen dependency on antibacterial drugs and permit greater accuracy in therapeutic interventions.[39] By preventing infections through vaccination and improving diagnostic accuracy, the overall use of antibiotics can be reduced, thereby slowing the development of resistance.

The multifaceted nature of AMR requires a comprehensive approach to research and development. This strategy should include not only the discovery of new pharmaceuticals, but also the enhancement of present-day therapies, the investigation of alternative treatment options, and the promotion of preventative measures. By pursuing these diverse avenues of research, the scientific community can work towards ensuring the continued efficacy of antimicrobial treatments in the future. Addressing the complex challenges posed by AMR requires a concerted effort from various stakeholders in the scientific, medical, and policy-making communities. Through interdisciplinary collaboration, innovative research, and the development of novel therapeutic approaches, we can hope to mitigate the impact of AMR and preserve the efficacy of antimicrobial treatments for future generations. The path forward demands sustained commitment, substantial resources, and a willingness to explore unconventional solutions in our ongoing battle against antimicrobial resistance.

CONCLUSION

The rapid evolution of antimicrobial resistance in microorganisms presents a formidable challenge to contemporary medicine, particularly in the realm of effective antimicrobial therapies. Unrestrained application of antibiotics in the medical field and in agriculture has resulted in significant selected evolutionary pressure, which has enabled pathogenic bacteria to evolve a variety of resistance mechanisms. This phenomenon, coupled with the deceleration of novel antibiotic discovery, has ushered in an extremely challenging post-antibiotic period. The implementation of comprehensive antimicrobial stewardship programs and the enhancement of infection control protocols constitute crucial initial interventions. Interestingly, the distinct ‘tragedy of the commons’ characteristic of AMR, which transcends geographical and sectoral boundaries, necessitates coordinated global action. The establishment of synchronized surveillance systems, equitable access policies, and conservation strategies is imperative to mitigate resistance transmission and preserve antimicrobial efficacy. Procrastination in addressing these issues risks a reversion to pre-antibiotic susceptibility patterns, potentially undermining decades of progress in infectious disease management and jeopardizing superior medical expertise and international health security.

In the specific context of pediatric dentistry, the judicious application of antibiotics demands a sophisticated understanding of microbiology, pharmacology, and clinical practice. Practitioners must strike a delicate balance between effectively treating dental infections and addressing the broader public health implications of antibiotic resistance. This necessitates continuous engagement with current guidelines, emerging research, and best practices in antibiotic stewardship. The principles and practices elucidated herein provide a

comprehensive framework for approaching antibiotic use across various clinical scenarios in pediatric dentistry. Nevertheless, it is paramount to recognize the unique circumstances presented by each patient, necessitating careful consideration of factors such as age, overall health status, infection severity, and antibiotic history in treatment decision-making.

As the understanding of oral microbiology and antibiotic resistance continues to advance, clinical practices must evolve concomitantly. Ongoing professional education and a willingness to adapt therapeutic approaches based on emerging evidence are essential for delivering optimal care to pediatric patients. The ultimate objective of antibiotic use in pediatric dentistry is to effectively manage infections while minimizing adverse effects and contributing to broader antibiotic stewardship initiatives. Through rigorous adherence to evidence-based principles, meticulous evaluation of individual clinical situations, and interdisciplinary collaboration when necessary, practitioners can achieve this equilibrium and ensure optimal outcomes for their young patients.

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