

Antibiotic Therapy and Pediatric Dentistry

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Abstract

Antibiotics are widely used in dentistry for prophylactic as well as for therapeutic purposes. They have either a bacteriostatic or a bactericidal effect and can be effective against a small group of bacteria (narrow-spectrum) or a wide range of pathogens (broad-spectrum). They have an important role in dental antibiotic prophylaxis where their use may prevent bacteremia and consequent infective endocarditis. Very often antibiotics are used in undue situations, which may give rise to resistant bacterial

strains, consequently, good knowledge about the indications of antibiotics is the need of the hour in prescribing antibiotics for dental conditions. The purpose of this review article is to discuss about the legitimate use of antibiotics in pediatric practice for control of oral infection, antibiotic prophylaxis in case of systemic conditions and the overuse and misuse of antibiotics.

Keywords: Antibiotics, Infection, Children, Prophylaxis, Resistance

Introduction

The word antibiotic originated from the word “antibiosis”, a term coined in 1889 by *Louis Pasteur* which means an antagonistic association between two micro-organisms in which one is adversely affected. The term antibiotic was first used in 1942 by *Selman Waksman* and his colleagues in articles to describe any substance produced by a micro-organism that is antagonistic to the growth of other microorganisms in high dilution.^[1] Antibiotics prevent the infection either by killing or inhibiting the growth of bacteria at a very low concentration.^[2] Antibiotics are among the most continually prescribed medication for the treatment as well as prevention of bacterial infection in modern medicine.

Infection remains an extensive problem in medical practice in which the microorganisms such as bacteria, viruses, fungi or other organisms invade the body, attach to cells, and get multiply, and their circumspect treatment with drugs is of prime importance. The similar process is also seen in the oral cavity. Oral infections are polymicrobial and mixed; they arise when normal flora changes from commensal to opportunistic due to an imbalance with the host in certain circumstances. The oral microbial flora starts to grow in the new born’s mouth just after the eight hours of birth and furthermore it is followed by a continuous change in its composition from the time the child is edentulous until the eruption of teeth in the oral cavity.^[3]

Antibiotics are typically prescribed in dental practice for some of the following scenario: (a) as treatment for acute odontogenic infections; (b) non-odontogenic infections; (c) prophylaxis against focal infection in patients at risk (endocarditis and joint prostheses); and (d) prophylaxis against local infection and systemic spread in oral surgery. Therapeutic and prophylactic antibiotic prescribing practices are usually followed by dental surgeon.

Nevertheless antibiotics are not an alternative to dental intervention; they are adjunct.

Choice of an Antibiotic

We have so many therapeutically effective antimicrobials available; it is necessary to lay down certain guiding principles for tailoring a rational therapeutic regimen for an individual patient. The choice of an antibiotic depends on the following factors:^[4]

- Host related factors: Age, Renal and hepatic function, Local factors
- Pathogen related factors: Nature and seriousness of the infection
- Drug factors: Spectrum of activity, Type of activity, Compliance by the patient, Cost consideration, drug’s possible side effects, possibility of allergies or other serious reactions to the drug

A series of differential characteristics must be taken into consideration while prescribing an antibiotic in children^[5]:

- Young children tend to lack medical antecedents advancing towards the possibility of drug allergies or adverse reactions.
- The increased amount of water in the tissues of children, and their increased bone sponginess facilitate faster diffusion of infection. Hence they need appropriate dose adjustment of the prescribed medication.
- The deficient oral hygiene found in most children and the consumption of sugar-rich foods contribute to increase the presence of microorganisms in the mouth and thereby increasing the risk of bacteraemia following oral treatments.

Antibiotic Selection

Oral antibiotics that are effective against the odontogenic infections, Streptococci and oral anaerobes comprise of penicillin, clindamycin, erythromycin, cefadroxil, metronidazole, and the tetracyclines. For the prophylaxis

of endocarditis associated with dental treatments, amoxicillin is the antibiotic of choice. Amoxicillin with clavulanic acid offers the advantage of preserving activity against the betalactamases commonly produced by microorganisms associated with odontogenic infections. Clindamycin is an alternative for the patients who are allergic to penicillins. The drug is bacteriostatic, although bactericidal action is clinically achieved with the generally recommended dosage. The latest generation macrolides, clarithromycin, and azithromycin can also be used if a child is allergic to penicillin. Cephalosporin and cefadroxil are additional options with the broader spectrum of action if required. Metronidazole is usually used against anaerobes, and is characteristically reserved for situations in which only anaerobe bacteria are suspected. Tetracyclines are of very limited use in dental practice, as these drugs can cause alterations in tooth color, they must not be administered to children below the eight years of age, or pregnant or nursing women.

β -lactam antibiotics are useful and frequently prescribed antimicrobial agents that share a common structure and mechanism of action of inhibiting the synthesis of the bacterial peptidoglycan cell wall. β -lactam antibiotics include Penicillins and Cephalosporins.^[6]

Amoxicillin

Amoxicillin is a broad spectrum Penicillin group of antibiotics. It became first available in 1972 and one of the most frequently prescribed antibiotics in children. It is on the World Health Organization's list of Essential Medicines, the most important medication needed in a basic health system.^[7] Amoxicillin is active against many gram positive and gram negative bacteria e.g. Streptococcus, Bacillus subtilis, Enterococcus, Haemophilus, Helicobacter, and Moraxella etc, whereas Citrobacter, Klebsiella, and Pseudomonas aeruginosa are resistant to it. Some E.coli and most clinical isolates of

Staphylococcus aureus have developed resistance to Amoxicillin.

Indications: Dental prophylaxis in patients at risk of endocarditis, treatment of pulpal, periapical and periodontal infection, upper respiratory tract infection, infection of skin and soft tissues due to streptococci and susceptible staphylococci.

Contraindication: Penicillin allergy, hypersensitivity reaction (anaphylaxis or Steven Johnson syndrome), kidney disease, phenylketonuria, intestinal colitis Pediatric

Dosage^[8]: 25-50mg/kg/day q 8-12 hr oral, Adult dose: 250-500 mg q 6-8 hr

Maximum dosage for Children: 2 g/day

Available as: Caps 250 and 500 mg, DT 125 mg, 250 mg, syrup 125 mg/ 5 ml and 250 mg/5ml; drops 100 mg per ml (*AMOXIL, AMOCLOX, NOVAMOX, AMOXYBID, COMOXYL, CIDOMEX*)

Cephalosporins

Cephalosporins were discovered in 1945 and indicated for the prophylaxis and treatment of infections for children who are allergic to penicillin group of drugs. First generation cephalosporins are active predominantly against gram positive bacteria, and further generations have increased activity against gram negative bacteria.^[9]

Cephalexin

Dosage^[8]: 25-100 mg/kg/ day q 6-8 hrs oral; **Adult dose:** 250-500 mg every 6 hours (maximum 4g/day)

Available forms: Tablet 125mg, 250 mg and 500mg (*SPORIDEX DT, CEFF KID TAB*), Capsule 250 mg, 500 mg (*CEPHAXIN, SEPEXIN, CEFF, SPORIDEX, MONACEF, SOLEXIN*), Oral Suspension 125 mg/5ml and 250 mg/5ml.

Cefadroxil

Dosage^[8]: 30-50 mg/kg/day q 12 hr oral; **Adult dosage:** 1-2 g/day q 12-24 hr

Available forms: Tablet 500mg, 1g (CEDADROX, ODOXIL), Capsule 500 mg (IYDROXIL), Oral suspension 125MG/5ML, 250 mg/5 ml and 500 mg/5 ml (DROXYL, IYDROXIL)

Cefixime

Dosage^[8]: 8 mg/kg/day oral once or twice a day; **Adult dose:** 200-400 mg daily q 12-24 hr

Available forms: Tablet 50 mg, 100mg, 200mg, 400 mg, and syrup 100 mg/5 ml, 200 mg/5 ml and 500 mg/5 ml.

Doxycycline Hyclate

Dosage^[8]: 2-5 mg/kg/day q 12 hr oral; **Adult dose:** 200 mg on day 1, then 100 mg daily (Avoid in children below 8 years of age due to risk of staining of teeth and growth retardation, pregnancy and lactation)

Available forms: 50 mg, 100 mg, 200 mg tabs and syrup 25mg/5ml, 50 mg/5ml (CEDOX DT, REVIDOX, VIVOCYCLINE, DOX-T, MINICYCLINEN, TETRADOX, VIBAZINE DT, SOLOMYCIN ; MINOCYCLINE SYRUP)

Metronidazole

Metronidazole was introduced in 1959 and is one of the mainstay drugs for the treatment of anaerobic and certain parasitic infection. It is a potent inhibitor of obligate anaerobic bacteria and protozoa.^[10]

Indications: Acute necrotizing ulcerative gingivitis (Vincent's Stomatitis), Pericoronitis and pericoronal abscess, Chronic aggressive periodontitis, Periapical and periodontal abscess, Dentalveolar abscess, Cellulitis and Space infections, Osteomyelitis, Infected sockets, Surgical prophylaxis

Contraindications: Hypersensitivity to metronidazole and alcohol consumption

Dosage^[11]: 30 mg/kg/day in 3 divided doses; Age 1 – 3 years: 150 mg in three divided doses, Age 3 – 7 years: 200 mg in three divided doses, Age 7 - 10 years: 300 mg in three divided doses; **Maximum dosage for Children:** 2 g/day ; **Adult dose:** 200-400 mg q 8 hr

Available forms: Tablet 200 mg, 400 mg, Infusion solution 500 mg/100ml, Oral suspension 200 mg/5 ml (FLAGYL, ARISTOXYL, METROXYL, ROXYL)

Antibiotic Combinations

Antibiotic combinations used to enhance antibacterial activity against manifold potential pathogens for initial empirical treatment. Antimicrobial agents acting at different targets may enhance or impair the overall antimicrobial activity. A combination of drugs also may have additive or super additive toxicities. However, selection of an appropriate combination requires an understanding of the potential for interaction between the antimicrobial agents.

Amoxicillin with clavulanic acid:

Amoxicillin/Clavulanic acid combination was introduced in United States in 1984 as an antimicrobial agent that would increase the activity of Amoxicillin by the addition of the beta-lactamase inhibitor Clavulanic acid.

Indication: Wide spectrum activity with coverage of beta-lactamase producing strains of S. pneumonia, S.aureus, H.influenza

Contraindications: jaundice, penicillin allergy, hepatic dysfunction

Dosage^[11]: For Severe infections 45mg/kg/day every 12 hours Or 40 mg/kg/day every 8 hours, For less severe infections 25 mg/kg/day every 12 hours Or 20 mg/kg/day every 8 hours, 50-100 mg/kg/day (amoxicillin base) q 6-8 hr IV; **Adult dose:** 250-500 mg of amoxicillin p.o. 3 times a day, 1.2 g q 6-8 hr IV infusion; **Maximum dosage:** For children < 40 kg, 1000 - 2800 mg Amoxicillin/ 143 - 400 mg

Available forms: AUGEMNTIN, ADVENT, MOXCLAV, MOXKIND-CV, MEGACLAV, CLAVAM Tablets 375 mg (AMOXYCILLIN 250 mg+ 125 mg clavulanate), 625 mg(AMOXYCILLIN 500mg+ 125 mg clavulanate) and 1000mg(AMOXYCILLIN 875 mg+ 125 mg

clavulanate), syrup 156mg/5ml (125 mg amoxicillin +31.5 mg clavulanate); Augmentin duo, Moxclav.d. Andaugpen HS syrup (200mg amoxicillin +28.5 mg clav/5ml); AUGPEN, AUGMENTIN DDS, MOXCLAV DS

Antibiotic Combinations in Pediatric Restorative Dentistry

Pediatric restorative dentistry has emerged over the years and the search for an ideal restorative material has led the researchers for the development of numerous restorative materials each surpassing the other with their innumerable advantages over one another. The addition of antibiotics to Glass ionomer cement (GIC) has recently been recommended for the treatment of carious lesions and to preserve the pulp vitality of the tooth. A combination of antibiotics i.e. Ciprofloxacin, Metronidazole and Minocycline has been shown to be successful in sterilizing carious lesion.^[12] But staining of dentin has been observed due to the use of Minocycline in the triple antibiotic mixture. Therefore, a change from the original triple antibiotic mixture has been suggested, whereby Minocycline was left out of the combination and Bi antibiotic paste containing only Metronidazole and Ciprofloxacin has been suggested.

Recommendations

Dental practitioners should be practicing the following general guidelines while prescribing antibiotics for the child patient.^[13]

- **Pulpitis/apical periodontitis/draining sinus tract/localized intra-oral swelling:** Antibiotic therapy usually is not indicated and nor effective if the dental infection is confined within the pulpal tissue or the immediate surrounding tissue. Therefore, the use of antibiotics should be considered in cases of advanced non-odontogenic bacterial infections such as staphylococcal mucositis, tuberculosis, gonococcal stomatitis, and oral syphilis and in the presence of

systemic signs of an infection i.e., fever and facial swelling.

- **Acute facial swelling of dental origin:** Any facial swelling or facial cellulitis secondary to an odontogenic infection with the signs of systemic involvement and septicemia (e.g., fever, malaise, asymmetry, facial swelling, lymphadenopathy, trismus, tachycardia, dysphagia, respiratory distress) warrant emergency treatment. Intravenous antibiotic therapy management is indicated. Penicillin derivatives remain the empirical choice for odontogenic infections; however, additional adjunctive antimicrobial therapy (i.e., metronidazole) can be given where there is anaerobic bacterial involvement. Cephalosporins could be considered as an alternative choice for odontogenic infections.
- **Dental trauma:** Systemic antibiotics should be recommended as adjunctive therapy for avulsed immature and mature permanent incisors. Tetracycline (doxycycline twice daily for seven days) is the drug of choice, but child's age must be taken into consideration before the systemic use of tetracycline owed to the risk of discoloration in the developing permanent dentition. Penicillin V or amoxicillin can be given as an alternative in patients under 12 years of age. The use of topical antibiotics (minocycline or doxycycline) to heighten pulpal revascularization and periodontal healing in immature non-vital traumatized teeth has exhibited some potential. Antibiotics are not indicated for the luxation injuries of primary dentition. Antibiotics can be used in cases of concomitant soft tissue injuries and when imposed by the patient's medical status.
- **Pediatric periodontal diseases:** Patients with aggressive periodontitis require adjunctive antimicrobial therapy in conjunction with localized

treatment. In pediatric periodontal diseases associated with systemic disease (e.g., severe congenital neutropenia, Papillon-Lefèvre syndrome, leukocyte adhesion deficiency), the immune system is unable to control the growth of periodontal pathogens and treatment may involve antibiotic therapy.

- **Endodontic Flare-ups:** Adverse reactions (flare-ups) during the endodontic treatment occur infrequently. Antibiotics are frequently administered to avert the adverse post treatment sequelae of root canal treatment and oral surgery.

Antibiotic Prophylaxis

Most orofacial infections are of odontogenic origin and mainly characterized by the spontaneous drainage. However, bacteremia is likely to occur in blood following invasive dental procedures. Infective endocarditis (IE) is an uncommon but a life threatening complication resulting from bacteremia.^[14] The boundless cases of IE caused by oral microflora can be the aftereffect from bacteremia associated with regular activities such as tooth brushing, flossing and chewing. Therefore, antibiotic prophylaxis is recommended with certain dental procedures.

Antibiotic prophylaxis is given prior to dental procedures in children who acquire some kind of cardiac conditions, compromised immunity, patients with shunts, indwelling vascular catheters, or medical device and prosthetic joints.^[15]

Table .1 Specific antibiotic regimen revised by the American Heart Association (AHA) in 2014.^[15] In 2017, the ADA reaffirmed the recommended regimen as follows.^[16]

Antibiotic Resistance

Antibiotic resistance is one of the biggest threats to global health, food security, and development today. A growing number of infections such as pneumonia and tuberculosis are becoming harder to treat as the antibiotics used to treat

them become less competent. Some of the complications associated with the use of antibiotics are drug toxicity, hypersensitivity reactions, antimicrobial drug resistance, superinfection, nutritional deficiencies, masking of an infection.^[17] Antibiotic resistance is accelerated by the misuse and overuse of antibiotics, as well as poor infection prevention and control.

According to Dr. Thomas J. Pallasch, antibiotic misuse in dentistry mainly involves prescribing them in 'inappropriate situations' or for too long, which includes,^[18]

- Giving an antibiotic after a dental procedure in an otherwise healthy patient to 'prevent' infection which in all likelihood will not occur.
- Using antibiotics as analgesics, particularly in endodontics - employing antibiotics for prophylaxis in patients not at risk for metastatic bacteremia
- Using antimicrobials to treat chronic adult periodontitis, which is almost totally responsive to mechanical treatment
- Using antibiotics instead of surgical incision and drainage of infections
- Using antibiotics to prevent claims of negligence.

A global action plan on antimicrobial resistance, including antibiotic resistance, was endorsed at the World Health Assembly in May 2015 with an aim to ensure prevention and treatment of infectious diseases with safe and effective medicines.

The "Global action plan on antimicrobial resistance" has 5 strategic objectives^[19]:

- To improve awareness and understanding of antimicrobial resistance.
- To strengthen surveillance and research.
- To reduce the incidence of infection.
- To optimize the use of antimicrobial medicines.

- To ensure sustainable investment in countering antimicrobial resistance.

Conclusion

Appropriate and precise use of antibiotics is imperative to ensure that effective and safe treatment is available. Practices that may augment microbial resistance should be avoided.

“Microbes will leave us alone; if we leave them alone”

Use of antimicrobials have to be reduced to the level where they are necessary for our survival & not merely for Doctor & patient comfort.

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