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Review Article

Antibiotic usage in pediatric dentistry: A review

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ABSTRACT

Antibiotics play a major role in the treatment of numerous diseases in the oro-dental region. Dentists need to keep their knowledge updated regarding the pharmacology of antibiotics and there use in the treatment of dental infections for children with a better understanding of action to provide better treatment and also to reduce misuse and over prescription of drugs to inhibit bacterial resistance. This review article is scripted with a motive to provide essential information of the antibiotics used in pediatric dentistry so as to render healthy information to parents and children.

1. Introduction

The term anti, means "against" and bios, means "life". According to the literature antibiotic denotes "opposing life" of the bacteria that causes infections.[1] Antibiotics are the chemical substances obtained from microorganisms that kill or suppress growth of other microorganisms at a very low concentration.[2] The effect of an antibiotic on different microorganism species is defined by its spectrum activity. Narrow spectrum agents are medications that target only one type of pathogen and do not cause resistance in other infections as a result of selection pressure.[3] Broad-spectrum antibiotics are the use of one or more antimicrobial agents with the specific intent of broadening the range of potential pathogens covered, to ensure adequate antimicrobial coverage.[4] Bacteriostatic and bactericidal antibacterial agents are the two types of antibacterial agents. Bacteriostatic medications stop bacterial growth and multiplication, limiting the spread of illness. The immune system is then able to assault, paralyse, and kill the infections. Bactericidal medications kill cells without relying on the immune system of the host. Following appropriate medication exposure, the bacterium will eventually die.[5]

2. History of Antibiotics

Hippocrates of Cos (460-377 B.C.) introduced the concept of disease as a natural phenomenon, rejecting the Greek healers' belief that prayer should be the primary way for making patients better. Hippocrates is best known for the Hippocratic Oath, a professional code of ethics. The term "antibiosis," from which the word antibiotic is derived, was coined by Louis Pasteur in 1889. In September 1928, Alexander Fleming discovered penicillin in London, and Norman Heatley, Howard Florey, Ernst Chain, and colleagues refined it at Oxford.[6] In 1945, Dorothy Hodgkin identified the β-lactam structure of penicillin, paving the way for semi-synthetic derivatives to overcome penicillin resistance. Selman Waksman was essential in finding soil-dwelling filamentous Actinomycetales ('Actinomycetes') as prolific

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makers of antimicrobial chemicals, defining an antibiotic as "a molecule created by a microbe to eliminate other microorganisms." From the 1940s to the 1960s, Waksman's work ushered in the Golden Age of antibiotic discovery.[7] Cephalosporin development began in 1945, when Professor Giuseppe Brotzu isolated a fungus, Cephalosporium acremonium, from seawater near a sewage outlet in Kaglara, Sardinia, and discovered that this organism inhibited the growth of a wide range of Gram-positive and Gram-negative bacteria after years of research.[8] In 1945, Lederle Laboratories, with the help of Septuagenarian Benjamin Minge Duggar, discovered chlortetracycline (Aureomycin), the first tetracycline antibiotic, and named it after its yellowish tint and the gold-colored Streptomyces strain from which it was isolated.[9] Tetracycline was patented by Lloyd Conover in 1955. The creation of an effective antitrichomonal medicine in the Rhonc-Poulenc laboratories in France resulted in Metronidazole, which was first used in a clinical trial on March 14, 1958.[10] Clavulanic acid was discovered in 1972 as a β-lactamase inhibitor with adequate potency and minimal antibacterial activity generated by Streptococcus clavuligerus. Amoxicillin was chosen as the antibiotic to be co-administered with clavulanic acid, and Augmentin was released in the UK in 1981 as a tablet formulation. Amoxicillin and potassium clavulanate tablets were patented by SmithKline Beecham.[11]

3. Types of Antibiotics Used in Children

3.1. Amoxicillin

It is a semi-synthetic acid stable antibiotic used to treat a variety of diseases caused by Gram positive and Gram negative bacteria. Its absorption is unaffected by food. There are just minor changes in the gut flora, thus there is no diarrhoea. It kills gram-positive bacteria such Non-Penicillin Resistant Streptococcal, Staphylococcal, and Enterococcal Species, as well as Helicobacter pylori. In people at risk of endocarditis, it can be administered for dental prophylaxis (single dose).[6]

3.1.1. Adverse effects

Skin reactions, gastrointestinal, hepatic, and haematological reactions.[12]

3.1.2. Contraindications

Penicillin allergy, Hypersensitivity reaction (anaphylaxis or Steven Johnson syndrome).[6]

3.1.3. Pediatric dosage:[6]

1. Children up to 10 years > 40 kgs - 125– 250 mg every 8 hours.
2. Children up to 10 years < 40 kgs - 20 – 40 mg/kg daily in divided doses every 8 hours or 25 - 45 mg/kg daily in divided doses every 12 hours.
3. Maximum dosage for Children: 2 g/day.
4. Infants < 3 months old - Maximum of 30 mg/kg daily in divided doses.

3.2. Amoxicillin and clavulanic acid

Clavulanic acid is a "suicide" inhibitor that forms a combination with beta-lactamase, rendering it inert. Its inclusion restores amoxicillin's natural spectrum and helps to prevent inactivation by beta-lactamases seen in Staphylococcus aureus, Haemophilus influenzae, Moraxella catarrhalis, E. coli, Proteus spp., and anaerobic bacteria like Bacteriodes fragilis. The new high dose preparation has a 14:1 ratio of amoxicillin to clavulanate, as opposed to the traditional 4:1 ratio (three-times-daily formulation). Amoxicillin-clavulanate has been recognised a safe medicine that is well tolerated in both adults and children.[13]

3.2.1. Adverse effects

Diarrhea, nausea, vomiting, loose stools, and abdominal discomfort.

3.2.2. Contraindications

Prior history of amoxicillin or clavulanic acid-induced hepatic dysfunction, previous hypersensitivity reactions to amoxicillin, clavulanic acid, or other beta-lactam antimicrobials.[14]

3.2.3. Pediatric dosage:[6]

1. For Severe infections 45mg/kg/day every 12 hours or 40 mg/kg/day every 8 hours.
2. For less severe infections 25 mg/kg/day every 12 hours or 20 mg/kg/day every 8 hours.
3. Maximum dosage: For children < 40 kg, 1000 - 2800 mg Amoxicillin/ 143 - 400 mg Clavulanic acid.

3.3. Metronidazole

Metronidazole was developed as an anti-trichomonal agent (antiprotozoal drug that kills trichomonas parasites) with a broad spectrum of activity. It eliminates pathogenic anaerobes and is effectively absorbed after oral treatment without disrupting the beneficial aerobic flora. At relatively low doses, metronidazole destroys organisms. Microorganisms that are vulnerable to metronidazole use a nitro-reductase to convert the nitro group of the drug to a cytotoxic derivative that binds to DNA and inhibits protein synthesis. Because aerobic bacteria lack this nitroreductase, they are resistant to metronidazole.[15] Metronidazole is susceptible to anaerobic bacteria such as Bacillus fragilis, Bacillus melaninogenicus, Fusobacterium, Clostridium perfringens, Clostridium difficile, Peptococcus, Peptostreptococcus, Prevotella, Veillonella, Campylobacter,

Helicobacter pylori, and Spirochetes.[16] People with a history of central nervous system problems (e.g., seizures) should be cautious since the medicine is neurotoxic and can aggravate the current sickness, as well as patients with a history of blood dyscrasias because they may cause leukopenia.

3.3.1. Adverse effects

Stomach pain, nausea, sometimes vomiting, anorexia, furred tongue, drowsiness, dizziness, pruitis, rashes, headache, and unpleasant taste sensations.

3.3.2. Contraindications

Consumption of alcohol or hypersensitivity to metronidazole.

3.3.3. Pediatric dosage:[6]

1. Mg/kg/day in 3 divided doses.
2. Age 7 - 10 years: 300 mg in three divided doses.
3. Age 3 – 7 years: 200 mg in three divided doses.
4. Age 1 – 3 years: 150 mg in three divided doses.
5. Maximum dosage for Children: 2 g/day.

3.3.4. For anaerobic skin and bone infection

Children: 30/mg/kg/day in divided doses every 6 hours (maximum 4 g/24 hours)

Adolescents and adults: 7.5 mg/kg every 6 hours (maximum 4 g/24 hours)

3.3.5. For periodontal disease, including necrotizing ulcerative gingivitis

Adolescents and adults: 250 mg every 6-8 hours for 10 days in combination with amoxicillin

3.3.6. For aggressive oral infections, may be used in combination with amoxicillin

250 mg 3 times/day with amoxicillin (250-375 mg 3 times/day) for 7-10 days.[17]

3.4. Azithromycin

As azithromycin is concentrated in neutrophils, macrophages, and especially fibroblasts, it can play a triple role in the treatment and resolution of periodontal diseases, suppressing periodontopathogens, anti-inflammatory activity, and healing by persisting at low levels in macrophages and fibroblasts in periodontal tissues even after a single course of three tablets.[16,18] It is extremely effective against H. influenza, as well as a few anaerobes as Peptostreptococcus and Clostridia. This medication is a penicillin or cephalosporin replacement for people who have a Type I penicillin or cephalosporin allergy.

3.4.1. Adverse effects

Mild gastric upset, abdominal pain (less than erythromycin, headache, and dizziness

3.4.2. Contraindications

Cardiac arrhythmias in patients with pre-existing cardiac conditions, macrolide hypersensitivity.[17]

3.4.3. Pediatric dosage

1. Children >6 months up to 16 years: 5-12 mg/kg on day 1, single dose, (maximum 500 mg/day), followed by 5-6 mg/kg once daily for remainder of treatment (2-5 days).
2. Endocarditis prophylaxis: 15 mg/kg (maximum 500 mg) 30-60 minutes before procedure.[17]
3. Recommended antibiotic regimen for penicillin-allergic patient with periodontal diseases (3 days): 10 mg/kg daily.[19]

3.5. Doxycycline

Doxycycline is a semi-synthetic tetracycline of the second generation. Doxycycline binds to the 30s subunit at the A site in a reversible manner. When aminoacyl t-RNA binds to m-RNA, the addition of new amino acids to the developing peptide chain is inhibited, and the translation process is stopped.[15,20] Antibacterial spectrum is broad including gram-positive and gram-negative organisms like Streptococci, Staphylococci, Gonococci, Meningococci, H. influenza, Brucella, V. cholerae, Campylobacter, Y. pestis and many anaerobes. They also inhibit Rickettsiae, Chlamydiae, Mycoplasma, Actinomyces, E. histolytica and Plasmodia.[20]

3.5.1. Adverse effects

Hepatotoxicity, hypersensitivity reactions, phototoxicity, gastrointestinal irritation, nausea, vomiting and diarrhoea, renal toxicity, metabolites of outdated tetracyclines and are teratogenic.[21]

3.5.2. Contraindications

This drug can cause enamel hypoplasia in developing teeth, and hyperpigmentation of the soft tissues.[17]

3.5.3. Pediatric dosage:[17]

Children >8 years who weigh <45 kg: 2.2 mg/kg every 12 hours on day 1, then 2.2 mg/kg once/day; for severe infections, 2.2 mg/kg every 12 hours until infection resolves

Children >8 years who weigh >45 kg and adults: 100 mg every 12 hours on day 1, then 100 mg once/day; for severe infections, 100 mg every 12 hours until infection resolves.

4. Choice of Antibiotics i n Pediatric Population

The majority of orofacial infections are odontogenic in nature, and treatment usually entails removing the underlying cause. It can spread to the extra oral parts of the face if left untreated. Children have more water in their tissues, as well as more sponginess in their bones, which creates favourable conditions for infection to spread more quickly. Food for children has a higher sugar content, which encourages the growth of bacteria in the mouth.[22] Several studies have looked at the occurrence and degree of bacteraemia in children after various dental treatments.[23] In this regard, teeth brushing have been linked to bacteraemia in more than one-third of children, and the fitting and removal of wedges / splints, braces, and bands has been linked to bacteraemia in a large number of paediatric instances. Antibiotic prescriptions are based on the pathogens against which the drug is effective, the mechanism of action, and the positive and negative effects of the drugs in question. Medical conditions, age, mode of administration, weight, taste, odour, and colour of the medicine, as well as body surface area, must all be taken into account when prescription drugs for children.

5. Management of Diseases Based on the Use of Antibiotics

Antibiotics should be administered in paediatric dentistry with the following considerations in mind:

1. When the dentist sees the kid, the severity of the infection.
2. The condition of the patient's immune system. Immune compromised children may not be able to withstand a transient bacteremia following invasive dental procedures.[24]
3. If the inflammation is moderate and the process is proceeding quickly, with moderate to severe pain, or if the child has a fever, the existing data advises prescribing antibiotics in addition to treating the afflicted tooth.
4. Infection in a child with a medical problem
5. An infection that has spread to the face's extra-oral areas. The infection is sufficiently aggressive in these cases to have gone beyond the lips, indicating that the host's defensive mechanism has failed to control it. In severe cases, hospitalisation may be required.[22]

5.1. Irreversible pulpitis

Generally penetration of the bacteria takes place through the dentinal tubules, dentinal cracks, or defective dental restorations present in a tooth [24]. Antibiotics are useless in eliminating bacteria because they cannot reach the area due to a lack of blood circulation in the root canal. Drainage alone is regarded to suffice in the case of discrete and restricted oedema. When signs and symptoms are present, amoxicillin or amoxicillin and clavulanic acid combinations may be prescribed.

5.2. Apical abscess / Odontogenic abscess

If an acute odontogenic abscess is associated with generalised swelling and pyrexia over the last 24 hours, it indicates a systemic response to the infection, antibiotics should be administered depending on the severity and breadth of the illness. Antibiotic treatment may not be necessary for healthy children who require the extraction of a single deciduous tooth with an abscess or endodontic treatment of a permanent tooth. Immune-compromised children or those with a heart disease, on the other hand, may need antibiotic treatment even if infection is a remote possibility.

5.3. Oro-facial swelling of dental origin/facial cellulitis

The doctor must be aware of the development of cellulitis in situations of acute apical abscess, where the transudate and exudates disseminate via interstitial and tissue gaps. As an adjuvant to evidence of systemic involvement and septicemia, emergency treatment and antibacterial medicine should be given (e.g. fever, malaise, asymmetry, facial oedema, lymphadenopathy, trismus, tachycardia, dysphagia, respiratory distress). The drainage incision is the best option in this situation because it allows the antibiotic to permeate deeper into the affected area.[19] As a result, drainage has two advantages: it relaxes the patient by removing hazardous materials, and it makes it easier for the antibiotic to enter the affected area. The antibiotics of choice include amoxicillin, metronidazole, or azithromycin.

5.4. Trauma of teeth

Systemic antibiotics have been recommended as an adjuvant therapy for avulsed permanent incisors with an open or closed apex. Tetracyclines are used sparingly in dentistry as it enhances the vascularisation of the pulp and reduces root resorption.[22] Since they can stain teeth, they should not be given to children under the age of eight.[17] Antibiotics are not advised for primary dentition luxation injuries. Antibiotic coverage is essential in children who have dental avulsions that can be re-implanted. Due to the treatment of systemic antibiotics, the incidence of external root resorptions has decreased in these instances. The anti-tetanus vaccination must be addressed when trauma occurs with oral wounds.[19]

5.5. Pediatric periodontal diseases

Dental plaque gingivitis, eruption gingivitis, pubertal gingivitis, mouth breathing gingivitis, and primary herpetic gingivostomatitis can all be treated with appropriate local

therapeutic interventions such as professional oral hygiene and reinforcement of brushing twice daily for at least 2 minutes.[19] Antibiotics should be avoided. Patients with severe periodontal disease may require further antibiotic medication in addition to targeted treatment. Antibiotics like as amoxicillin and metronidazole are used for aggressive periodontitis. For penicillin-allergic patients, azithromycin or metronidazole are the antibiotics of choice. In paediatric periodontal disorders associated to systemic disease, the immune system is unable to control the growth of periodontal bacteria, and antibiotic therapy may be required in some cases. In severe and refractory cases, extraction is advised.

5.6. Salivary gland infections

Acute bacterial salivary gland swellings should be treated with antibiotics. If the patient does not improve after 24–48 hours on antibiotics alone, incision and drainage may be required. Because oral flora causes the majority of bacterial infections of the salivary glands, amoxicillin and clavulanate are used as an empirical therapy to treat both staphylococcal and streptococcal species.

5.7. Triple antibiotic paste

As root canal infection contains both aerobic and anaerobic bacteria, any single antibiotic is unlikely to result in effective canal sterilisation. So far, the most promising combination has been Metronidazole, Ciprofloxacin, and Minocycline. Sato et al. evaluated this triple antibiotic regimen for the first time in 1996.[6] Triple antibiotic paste (TAP) is used as a dressing in the endodontic regenerative process (ERP), an alternative clinical approach to apexification. The purpose of inducing bleeding is to establish a matrix for new vital tissue to grow in the pulp canal space.[25] LSTR (lesion sterilization and tissue repair) is a way of treating oral infections such dentinal, pulpal, and periapical lesions with a mixture of antibiotics that disinfects the wounds and encourages tissue regeneration through the host's natural tissue recovery mechanism.

5.7.1. Use

Medicated sealer, pulp revascularization and regeneration, periapical lesions therapy, intracanal medicament, additive to gutta-percha sites in root canal obturation.

5.8. Contraindications

1. Sensitivity to ciprofloxacin, minocycline, or metronidazole, or allergic reactions to these antibiotics
2. Perforation of the pulpal floor
3. Excessive interior or exterior root resorption as determined by radiography
4. Excessive bone loss in the furcation area with underlying tooth germ involvement
5. Permanent tooth with a non-restorable crown that makes post-placement and core buildup impossible
6. Exfoliation of the primary tooth is nearing[26]

6. Pediatric Considerations in Use and Misuse of Antibiotics

Antibiotic use has increased dramatically among medical and dental workers since the discovery of penicillin. Bacterial strains are also thought to be experiencing mutation and genetic alterations as a result of increased antibiotic use. It's also been observed that antibiotics are sometimes prescribed to youngsters with orofacial infections when they don't need them. Resistance might develop as a result of drug overuse or ineffective use. One of the main explanations for observed prescribing behaviour in paediatric dentistry could be due to parental pressure and the desire to suit the needs of the parent rather than the patient. According to studies, practitioners believe that prescribing antibiotics is the quickest way to postpone treatment.[27] Antibiotics can be administered as supplements in some cases, according to the American Academy of Pediatric Dentistry, after a thorough review of the infection's spread and patient risk factors.

7. Conclusion

The need to enhance awareness of the guidelines for oral antibiotic prescriptions in children is critical. In otherwise healthy children, antibiotics are used to treat necrotizing ulcerative periodontitis, aggressive periodontitis, periodontal abscess, pericoronitis, postoperative sialadenitis, newborn sialadenitis, and face cellulitis. The American Association of Pediatric Dentistry's (AAPD) guidelines for administering antibiotics sparingly are based on scientific data and must be followed by all dental professionals.[28]

8. Conflict of Interest

None.

9. Source of Funding

None.

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