

Antibiotic prescriptions in pediatric dentistry: A review

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ABSTRACT

Most commonly prescribed drugs in pediatric dentistry are “Antibiotics.” Among Dentists, there is a trend toward overuse of antibiotics for nonindicated clinical conditions. This insufficient knowledge of the appropriate clinical indications for antibiotic prescriptions promotes the overuse of antibiotics and contributes to the emergence of antibiotic resistance among children. According to the various surveys done on the dental students, dentists and pediatric dentists on the antibiotic prescribing practices, overall, adherence to the professional clinical guidelines was low. There was a wide variation in dosages for all the antibiotics prescribed and for prolonged periods which were inconsistent with the recommendations. This paper reviews the current literature from the year 2000 to 2019. An electronic literature search was conducted in MEDLINE/PubMed, EBSCO host, and Google Scholar databases. The data was also collected manually from comprehensive textbooks. Some recommendations were also based on the opinion of experienced researchers and clinicians. Thus, this review aims at highlighting clinical indications, dosages, and duration of therapeutic antibiotic prescriptions for orofacial infections in the pediatric outpatients and at the same time creating an awareness, regarding the necessity of strictly adhering to the clinical guidelines for antibiotic prescriptions.

Keywords: Antibacterial agents, antibacterial and pediatric dentistry, antibiotics, antibiotic prescriptions

Background

Dentists prescribe several categories of medications to manage a variety of oral diseases and conditions. Among these conditions are bacterial, fungal, and viral infections and pain. Antibiotics continue to be the most commonly prescribed drugs in children and adults.^[1] In England, for instance, it is estimated that 66.4% of dental prescriptions are antibacterial drugs.^[2]

Among Dentists, there is a trend toward overuse of antibiotics for nonindicated clinical conditions, like pain relief, irreversible pulpitis, and localized dentoalveolar abscess.^[3-5] This insufficient knowledge of the appropriate clinical indications for antibiotic prescriptions promotes the overuse of antibiotics^[4,6,7] and contributes to the emergence of antibiotic resistance among

children.^[8] Children as young as 4 years were found to harbor multidrug-resistant bacteria in their oral cavities.^[9,10]

The prescription of antibiotics has now become more complicated than in the past with clinicians dealing with an increasing number of issues such as microbial resistance to prescribed antimicrobials^[11,12] and drug interactions with an increase in the number of medications used by both adult and pediatric patients.^[13] The administration of drugs to pediatric patients is further complicated by the necessity to adjust the dosages of medications to accommodate their lower weight and body size.^[14]

Thus, this review aims at:

Highlighting clinical indications of therapeutic antibiotic prescriptions for orofacial infections in the pediatric outpatients and at the same time creating an awareness, regarding the necessity of strictly adhering to the clinical guidelines for antibiotic prescriptions.

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Search strategy

This paper reviews the current literature from the year 2000 to 2019. An electronic literature search was conducted in MEDLINE/PubMed, EBSCO host, and Google Scholar databases. MeSH terms used were: Antibacterial agents, Antibacterial agents AND Pediatric Dentistry. The data was also collected manually from comprehensive textbooks. Some recommendations were also based on the opinion of experienced researchers and clinicians.

Discussion

Klein *et al.* in 2018, analyzed the trends and drivers of antibiotic consumption from 2000 to 2015 in 76 countries and projected total global antibiotic consumption through 2030. They concluded that between 2000 and 2015, antibiotic consumption, expressed in defined daily doses (DDD), increased 65% (21.1–34.8 billion DDDs), and the antibiotic consumption rate increased 39% (11.3–15.7 DDDs per 1,000 inhabitants per day).^[15]

If all the countries continue to increase their antibiotic consumption rates at their compounded annual growth rates, the estimated total consumption would increase 202% to 128 billion DDDs, while the antibiotic consumption rate would increase 161% to 41.1 DDDs per 1,000 inhabitants per day. The increase comes mainly from low- and middle-income countries (LMICs). The leading LMIC consumers were: India, China, and Pakistan. The highest-consuming LMICs saw large increases. Between 2000 and 2015, antibiotic consumption increased from 3.2 to 6.5 billion DDDs (103%) in India, from 2.3 to 4.2 billion DDDs (79%) in China, and from 0.8 to 1.3 billion DDDs (65%) in Pakistan. 7%–11% Of all antibiotics are prescribed by dentists.^[7,15]

It has been found out that approximately one-third of all outpatient antibiotic prescriptions are unnecessary leading to the overuse of antibiotics.^[16] According to the various surveys done on the dental students, dentists and pediatric dentists on the antibiotic prescribing practices, overall, adherence to the professional clinical guidelines was low.^[3,17-20] There was a wide variation in dosages for all the antibiotics prescribed and for prolonged periods which were inconsistent with the recommendations.^[12,17]

As per the WHO, the ideal dentist-population ratio is 1: 7500. But, in rural India, this ratio of the dentist-population is about 1:1,50,000. According to WHO, minor facilities are available for oral health care of the rural population and the tooth-related problems of the patients are taken care of by the primary health care providers rather than the dentists due to their scarcity. For the acute dental problems, general medical practitioners and nurses are more likely to prescribe antibiotics for which they are not even required. They should understand that most of the dental problems require local interventions for the treatment of the cause of the infection.^[20-25]

Because of the overuse of the antibiotics, the extent of the antibiotic resistance is so much that some bacterial species are resistant to the full range of antibiotics presently available, with the methicillin-resistant *Staphylococcus aureus* being the most widely known example of extensive resistance.^[26]

Other complications associated with inappropriate antibiotic prescriptions in pediatric population are: the risk of developing diabetes in children due to sugar-containing medications, risk of development of allergy and asthma in children treated with antibiotics.^[27,28] Early-life exposure to antibiotics is also thought to change intestinal microbiota, with subsequent adverse long-term effects like obesity,^[28] superinfections with *Candida* species^[29] and photosensitivity.^[30,31] Children are also at risk of gastrointestinal disturbances, like diarrhea, which is generally more frequent with three-times-daily than twice-daily regimens.^[32] Exposure to amoxicillin during early infancy may be linked to developmental enamel defects on both permanent first molars and maxillary central incisors.^[33]

Joseph and Rodvold summarized the 4 D's of antimicrobial therapy they are: right Drug, right Dose, Deescalation to pathogen directed therapy, and right Duration of therapy.^[34] An important consideration in starting antimicrobial therapy is to assess if the infection is localized and if the patient has an adequate immune response to control the bacteria if supported surgically. These considerations are summarized in Table 1.

Following clinical situations have to be considered while prescribing the antibiotics:

Oral wound

Facial lacerations and puncture wounds may require topical antibiotic agents.

Intraoral puncture wounds and lacerations that appear to have been contaminated by extrinsic bacteria, debris (e.g. dirt, soil, gravel), foreign body, open fractures, and joint injury have an increased risk of infection and should be managed by systemic antibiotics.

Tetanus immunization status should be determined. If it is decided that antibiotics would be beneficial to the healing process, the timing of the administration of antibiotics is critical to supplement the natural host resistance in bacterial killing. The drug should be administered as soon as possible for the best result.

If the infection is not responsive to the initial drug selection, a culture and sensitivity testing of a swab from the infective site or, in some cases, blood microbiology, culture, and sensitivity may be indicated.^[36,37]

Irreversible pulpitis, necrotic pulps, and localized acute apical abscesses

Antibiotics are unnecessary in irreversible pulpitis, necrotic pulps, and localized acute apical abscesses with no systemic signs and

Table 1: Considerations for antimicrobial therapy³⁶

Indicated clinical conditions for antibiotic therapy	Nonindicated clinical conditions for antibiotic therapy
1. Pyrexia within last 24 h-indicates a systemic response to the infection	1. Pain-(analgesics/antiinflammatory drugs are indicated)
2. Systemic symptoms like malaise, fatigue, weakness, dizziness, rapid respiration and local tender lymphadenopathy-indicate an impending sepsis	2. Edema-(antiinflammatory drugs indicated)
3. Trismus-indicates spread to peri mandibular spaces and can extend to secondary spaces that can be potentially dangerous. Also, trismus makes intraoral procedures difficult, which must wait until the trismus is relieved.	3. Redness/heat-(antiinflammatory drugs indicated)
4. As a prophylaxis in patients with systemic conditions like rheumatic heart disease, endocarditis, heart/orthopaedic prosthesis	4. Purulence-(resolved by drainage of pus/debridement)
5. In patients with any kind of immunocompromise-AIDS, cancer, autoimmune diseases, corticosteroid therapy, patients with immune-compromised diseases like cyclic neutropenia, pancytopenia, uncontrolled diabetes to name a few common ones.	5. Abscess-localized (e.g, alveolar abscesses, periodontal abscesses)-(Resolves by incision and drainage)
6. After solid Organ transplant/grafts (cardiac/renal/bone marrow/liver/osseous	6. Draining sinus tract. (Removal of foci of infection resolves drainage and sinus tract may heal on its own or may have to be surgically excised.)

symptoms.^[5,38,39] Lack of blood circulation in the root canal in these scenarios prevents antibiotics reaching the area, that is, they are ineffective in eliminating the microorganisms.^[38] Where there is discrete and localized swelling, drainage by itself is considered sufficient without the need for additional medication.

Evidence has shown that antibiotics have no effect on the pain associated with dentoalveolar infection.^[39,40-42] For the pain relief, analgesics/antiinflammatory drugs are indicated^[43] and not the antibiotics. For edema, antiinflammatory drugs are prescribed. For redness/heat, antiinflammatory drugs are indicated and purulence should be resolved by drainage of pus/debridement.^[44]

Soft tissue swelling of endodontic origin (apical abscess/alveolar abscess)

If acute odontogenic abscess with diffuse swelling is associated with pyrexia within the last 24 h, it indicates a systemic response to the infection; antibiotics should be prescribed in such cases.^[1,40,41,44]

Acute facial swelling of dental origin/facial cellulitis

The clinician must be cautious about the development of cellulitis in cases of acute apical abscess in which the transudate and exudate spread via interstitial and tissue spaces. Signs of systemic involvement and septicemia (e.g. fever, malaise, asymmetry, facial swelling, lymphadenopathy, trismus, tachycardia, dysphagia, respiratory distress) warrant emergency treatment and antibiotic therapy should be prescribed as an adjunct.^[4,36,37,40] In such cases, the incision for drainage is of utmost importance, as it will enhance the diffusion of the antibiotic into the affected area. Thus, the advantages of drainage are twofold: both for the relief of the patient by the removal of toxic products and for the antibiotic to penetrate into the infected space more readily. The antibiotic of choice is amoxicillin (2–3 days, max 5 days): Children >3 months and < 40 kg: 20–40 mg/kg/day in divided doses 8 hourly and children > 40 kg: 250–500 mg 8 hourly or phenoxymethyl penicillin (2–3 days, max 5 days): children <12 years: 25–50 mg/kg/day in divided doses 6 hourly and children ≥12 years: 250–500 mg 6 hourly. Recommended antibiotic regimen for penicillin-allergic patient

metronidazole (3 days): children 30/mg/kg/day in divided doses 6 hourly, or azithromycin: children >6 months up to 16 years: 5–12 mg/kg daily for 3 days, or clarithromycin (7 days): 7.5 mg/kg 12 hourly. In case of successful drainage, antibiotics offer little help, and their use should be reserved for patients with acute apical periodontitis and systemic symptoms or to medically challenged or immunocompromised patients.

Dental trauma

Systemic antibiotics have been recommended as adjunctive therapy for avulsed permanent incisors with an open or closed apex.^[45-48]

Tetracycline (doxycycline twice daily for 7 days) is the drug of choice, but consideration of the child's age must be exercised in the systemic use of tetracycline due 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.^[36,37]

For luxation injuries in the primary dentition, antibiotics are not indicated.^[36,37]

Pediatric periodontal diseases

Dental plaque-induced gingivitis, eruption gingivitis, pubertal gingivitis, gingivitis related to mouth breathing, and primary herpetic gingivostomatitis are managed by appropriate local therapeutic interventions including professional oral hygiene and reinforcement of brushing twice daily for at least 2 min and no antibiotics should be prescribed.^[36,37,49]

Patients diagnosed with aggressive periodontal disease (now periodontitis) may require adjunctive antimicrobial therapy in conjunction with localized treatment.^[4,36,37,49,50] The antibiotic of choice for aggressive periodontitis are amoxicillin (50 mg/kg/day) and metronidazole 30 mg/kg/day 8 hourly for 7 days. Recommended antibiotic regimen for penicillin-allergic patient is azithromycin (3 days): 10 mg/kg daily or metronidazole.

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, in some cases, treatment may involve antibiotic therapy. In severe and refractory cases, extraction is indicated. Culture and susceptibility testing of isolates from the involved sites are helpful in guiding the drug selection.^[36,37]

Viral diseases

Conditions of viral origin such as acute primary herpetic gingivostomatitis should not be treated with antibiotic therapy unless there is strong evidence to suggest that a secondary infection exists.^[36,37]

Salivary gland infections

For acute salivary gland swellings of bacterial nature, antibiotic therapy is indicated. If the patient does not improve in 24–48 h on antibiotics alone, incision and drainage may be warranted.

Amoxicillin/clavulanate is used as empirical therapy to cover both staphylococcal and streptococcal species as most bacterial infections of the salivary glands originate from oral flora. Clindamycin is appropriate for penicillin-allergic patients.^[36,37]

Clinical conditions in which antibiotics are used or not used as an adjunct are summarized in Table 2.

Choice of the antibiotics may be challenging to the dentist. Tables 3 and 4 show the recommendations of the various researchers, experts, and professional guidelines for the types of antibiotics prescribed in pediatric dental practice.

Certain antibiotics should be avoided in children, like fluoroquinolones, which can lead to chondrotoxicity in growing cartilage, and tetracycline, which can cause discoloration of permanent teeth. Further, choosing amoxicillin-clavulanic acid should cover a broader spectrum than amoxicillin. However, the use of clavulanic acid in the pediatric population has been associated with gastrointestinal disturbances (diarrhea), but these can be reduced by using the two-daily rather than the three-daily regimen.^[51]

Prescribing medications that can be given once or twice daily will improve patient's compliance to the treatment,^[52] that is, antibiotics with a long half-life like azithromycin become useful, as they only need to be taken once daily for 3 days and are well tolerated in children. On the other hand, azithromycin is more expensive than amoxicillin and clindamycin.^[53] Furthermore, care should be taken when prescribing azithromycin, as it may lead to the growth of azithromycin-resistant bacteria, and it may be associated with proarrhythmic effects. Amoxicillin, on the other hand, is considered safer, especially when less frequent doses are used. A recent study found that using once or twice daily doses of amoxicillin, with or without clavulanate, were comparable with three doses for the treatment of acute otitis media in children. The applicability of this finding in the treatment of dental infections needs to be further explored.

Table 2: Clinical conditions in which antibiotics are used or not used as an adjunct^{40,50}

Pulpal/periapical/periodontal/conditions	Clinical signs and symptoms	Antibiotics as an adjunct
Irreversible pulpitis	Pain No other signs and symptoms of infection.	NO
Pulpal necrosis	Nonvital teeth	NO
Acute Apical periodontitis	Pain Pain to percussion and biting. Widening of periodontal space	NO
Chronic apical abscess	Teeth with sinus tract Periapical radiolucency	NO
Acute apical abscess with no systemic involvement	Localized fluctuant swellings	NO
Acute apical abscess with systemic involvement	Localized fluctuant swellings Elevated body temperature (>38°C) Malaise Lymphadenopathy Trismus	YES
Cellulitis	Rapid onset of severe infection (less than 24 h)	YES
Osteomyelitis	Cellulitis or a spreading infection Osteomyelitis	
Eruption gingivitis	Gingival inflammation	NO
Pubertal gingivitis	Swelling of interdental papilla with spontaneous gingival hemorrhage	NO
Gingivitis related to mouth breathing	Gingival inflammation and halitosis	NO
Acute necrotizing ulcerative gingivitis	Strong continuous pain and fetid odor. Generalized systemic manifestation including low grade fever, lymph adenopathy and malaise.	YES
Primary herpetic gingivostomatitis	Painful gingival inflammation and vesicles that are formed mainly on dorsum of the tongue, hard palate, and gingiva.	NO
Aggressive periodontitis	Rapid loss of connective tissue attachment and alveolar bone.	YES

Table 3: Recommendations of the various researchers, experts, and professional guidelines for the antibiotics prescribed in pediatric dental practice

Author/Year	Type of Infection	Antibiotic of Choice
Palmer ^[3] (2006)	Acute odontogenic abscess associated with raised axillary temperature and diffuse swelling	Amoxicillin (2-3 days, max 5 days) Phenoxymethyl penicillin (2-3 days, max 5 days) Penicillin-Allergic Patients: Metronidazole (3 days) Erythromycin (2-3 days) Azithromycin (2-3 days)
Steven Schwartz ^[1] (2017)	Odontogenic infections	Early (or first 3 days of infection) PenicillinVK, Amoxicillin Clindamycin Cephalexin (Or other first generation cephalosporin) No improvement in 24-36 h Clindamycin Amoxicillin/clavulanic acid (Augmentin) Penicillin allergy: Clindamycin Cephalexin Clarithromycin Late (>3 days) Clindamycin PenicillinVK- Metronidazole/ Amoxicillin-Metronidazole Penicillin allergy: Clindamycin
AAPD Guidelines ^[35,36]	Acute facial swelling of dental origin	Penicillin derivatives remain the empirical choice for odontogenic infections; however, consideration of additional adjunctive antimicrobial therapy (metronidazole) can be given where there is anaerobic bacterial involvement. Cephalosporins could be considered as an alternative choice for odontogenic infections.
Dar Odeh <i>et al.</i> ^[4] (2018)	Cellulitis	Amoxicillin (2-3 days, max 5 days) OR Phenoxymethyl penicillin (2-3 days, max 5 days) Recommended Antibiotic Regimen for Penicillin-Allergic Patient: Metronidazole (3 days) OR Azithromycin OR Clarithromycin (7 days)

Table 4: Recommendations of the various researchers, experts, and professional guidelines for the antibiotics prescribed in pediatric dental practice

Author/Year	Periodontal Disease	Antibiotic Of Choice
Al-Ghutaimel <i>et al.</i> ^[49] (2014) 50	Acute Necrotizing Ulcerative Gingivitis Aggressive periodontitis	Penicillin or erythromycin (for 5 days) Flagyl (Metronidazole)- eliminates acute symptoms rapidly Tetracycline alone or with metronidazole followed by metronidazole in combination with amoxicillin in the presence of tetracycline resistance.
Dar-Odeh <i>et al.</i> ^[4] (2018)	Aggressive Periodontitis Necrotizing Ulcerative Gingivitis Pericoronitis	Amoxicillin AND Metronidazole Patients allergic to penicillin: Azithromycin (3 days) OR Metronidazole Amoxicillin (3 days) Penicillin allergic patients: Metronidazole (3 days) Amoxicillin (3 days) Penicillin allergic patients: Metronidazole (3 days)
AAPD Guidelines ^[35,36]	Localized Aggressive periodontitis and chronic periodontitis Necrotizing ulcerative gingivitis/ periodontitis	Tetracyclines or Combination of tetracycline and metronidazole. Metronidazole in combination with amoxicillin has also been utilized If the patient is febrile- Metronidazole and penicillin.

Contd...

Table 4: Contd...

Author/Year	Periodontal Disease	Antibiotic Of Choice
Muppa <i>et al.</i> ^[50] (2016)	Localized Aggressive periodontitis	Amoxicillin along with metrogl for 15 days.
SDCEP	Necrotizing Ulcerative Gingivitis and	Metronidazole: (3-day regimen).
Clinical guidelines ^[40]	Pericoronitis	or Amoxicillin

Short courses are preferred to long courses particularly when treating children, since children's compliance with conventional courses is poor. One of the methods to halt the increase in resistance may be shorter courses of antibiotics.^[54] Higher dose of antibiotic given for a shorter duration is advocated in recent years.^[7]

Other forms of abuse in prescribing antibiotics include prescribing broad-spectrum antibiotics for infections that can be treated by narrow-spectrum antibiotics and adopting in appropriate dosing regimens.

Sugar-containing medications are expected to increase patients' adherence. However, sugar increases susceptibility to dental decay, tooth erosion, and associated complications, such as pulpitis and dentoalveolar abscess, emphasizing the importance of performing optimum oral hygiene activities during antibiotic therapy and beyond.

Other inappropriate clinical practices that must be avoided are antibiotic prescribing for viral infections.^[37,38] Although many childhood diseases, like primary herpetic gingivostomatitis and infectious mononucleosis, may present with oral and systemic manifestations, they are still viral infections that should be treated by palliative treatment, rather than antibiotics.

Because of the lack of patience and training of dentist in dealing with difficult children, children may also show the lack of cooperation when receiving dental treatment. Operative interventions should remain the first line of treatment for the management of dental/periodontal infections in children. However, these interventions are highly resisted by children, especially when treatment entails performing local anesthetic injections, extractions, and preparing cavities or root canals for fillings. The situation may get complicated when parents' faulty beliefs and perceptions encourage children's dental phobic attitudes. All the aforementioned factors may help initiate antibiotic prescriptions by dentists, particularly those who lack patience and training in dealing with difficult children.

Nonclinical factors also contribute to the overuse of antibiotics, such as unavailability of close appointments,^[5] for the sake of seeking parental satisfaction;^[5] worried parents may sometimes complicate the problem by expecting antibiotics and putting pressure on dentists to meet their expectations. In addition, parents' lack of understanding of the diagnosis might hinder children's intake of medications.^[54]

Conclusion

- Conservative use of antibiotics is indicated to minimize the risk of developing resistance to current antibiotic regimens.
- Consequently, an urgent need arises to create more concrete awareness of guidelines for dental antibiotic prescriptions in children.
- Indications for antibiotics in otherwise healthy children include: necrotizing ulcerative periodontal disease, aggressive periodontitis, periodontal abscess, pericoronitis, postoperative sialadenitis, neonatal sialadenitis, and facial cellulitis.
- Contraindications for antibiotics in otherwise healthy children include: dental caries, apical periodontitis, localized dentoalveolar abscess, and pulp polyp.
- Proper dosing regimens of antibiotics should be prescribed.
- One should not prescribe broad-spectrum antibiotics for infections that can be treated by narrow-spectrum antibiotics and short courses should be preferred over long courses.
- Prescribing medications that can be given once or twice daily rather than three times a day will improve patient's compliance to the treatment.
- It may seem more suitable to prescribe analgesics to supplement operative treatment for patients in pain rather than prescribing antibiotics.
- In case antibiotics were prescribed, children should be followed up for a few days to evaluate response to treatment, and the development of unwanted side effects.

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