



Pharmacology in Endodontics-Revisited

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Abstract

Antibiotics are very useful to treat microbial infections. But sound knowledge is important as to which antibiotic should be prescribed for a particular situation. Also, whether it is prudent to prescribe antibiotic also should be gauged before advising them. With the emergence of resistance strains to number of antimicrobials indiscriminate use of them must be avoided. The drugs are not without their side effects. Hence a collective approach is must before using them.

Keywords: Antibiotics; Antimicrobials; Prophylaxis; Special conditions

Introduction

The dental infections may be either primary due to odontogenic or secondary to systemic diseases. The clinician should diagnose the case thoroughly and appropriate antibiotics should be recommended to treat them. But the dentist should also be careful not to indiscriminately use the antibiotics which can lead to resistance development in the patient. The antibiotics should be used at times prophylactically to control the infection during the treatment procedures. The doctor should be well versed with drug interactions and the side effects. There is no hard and fast rule that antibiotics should be prescribed for all the patients. Proper clinical and radiographic diagnosis is must before prescribing drugs [1,2].

In daily practice we come across various patients like pregnant patients, patients who are already taking drugs for other systemic reasons, pediatric patients, prophylaxis, etc.

Many factors should be considered before prescribing antibiotics. These include the following [3]:

Microbiology of odontogenic infections: Often the causative is indigenous bacteria and mixed infection. Both aerobic (e.g., streptococci) and anaerobic bacteria are present. The most commonly found gram positive cocci are streptococci and peptostreptococci

and gram negative rods like bacteroides and fusobacterium.

- Systemic condition: People who are immunocompromised need antibiotics.
- Severity of the condition: Swelling, cellulitis, or fever that escalates with time may indicate that an infection is spreading.
- Benefits versus risks: The side effects and drug interactions must be addressed before prescribing antimicrobials. The side effects can vary from minor rash to life threatening anaphylactic reaction. Drugs prescription must be the last resort. In case of endodontic treatment, the cleaning and shaping procedure is more important than antibiotics.

Other factors like vital or non-vital teeth, sinus and past history of drugs taken is also important.

Bacteria commonly detected in odontogenic infections [4]

Based on Harbison H, Rose HS, Coen DM, Golan DE. Principles of antibacterial and antineoplastic pharmacology. In Golan DE, Tashji-an, Jr. AH, Armstrong EJ, Armstrong AW. Ed. Principles of pharmacology. The pathophysiologic basis of drug therapy. 2nd ed. 2008. Wolters Kluwer/Lippincott Williams & Wilkins. Baltimore, MD

- a. Inhibitors of Bacterial Cell Wall Synthesis: Penicillin
- b. Inhibitors of DNA Synthesis or Integrity: Metronidazole
- c. Inhibitors of Transcription or Translation: Tetracyclines

Gram staining and morphological characteristics	Facultative anaerobes	Obligate anaerobes
Gram positive cocci	Streptococcus enterococcus	Streptococcus Peptostreptococcus
Gram positive bacilli	Actinomyces lactobacillus	Actinomyces Lactobacillus Propriobacterium Bifidobacterium Eubacterium
Gram negative cocci	Neisseria	Viellonella
Gram negative bacilli	Capnocytophaga Eiknella	Porphyromonas Prevotella Fusobacterium Campylobacter Bacteroides
spirochetes		Treponema
Crescent shaped		Selenomonas

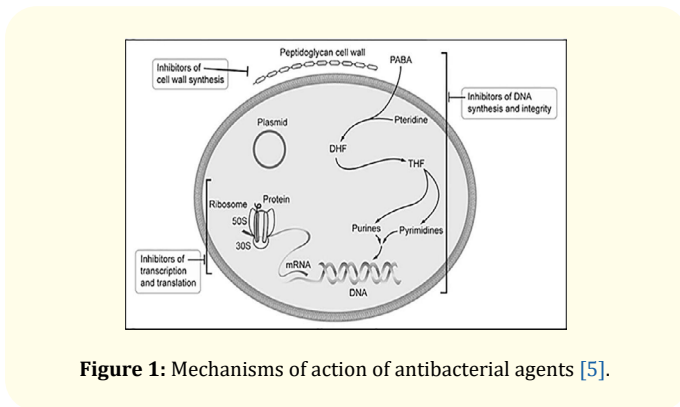


Figure 1: Mechanisms of action of antibacterial agents [5].

Antibiotic Strategies

- a. Use the most suitable drug.
- b. Prescribe the appropriate dose.
- c. Recommend the correct dosing schedule and duration.
- d. prescribe a loading dose to quickly achieve therapeutic levels in the blood.
- e. Avoid combinations of both bacteriostatic and bacteriocidal drugs.

Antibiotic Choice

Narrow Spectrum Antibiotics	Broad Spectrum Antibiotics
<ul style="list-style-type: none"> a. Specific for the particular strain of microbe. b. Less harmful to other microbes. c. Minimal side effects. d. Quick effect seen in case of sensitive strains. e. E.g.: Pen VK, Pen G, Erythromycin 	<ul style="list-style-type: none"> a. Both Gram positive and Gram negative bacteria are sensitive, appropriate for mixed infections. b. Sometimes effectiveness for Gram positive is lost to gain effectiveness for Gram negative. c. E.g.: Amoxicillin, Ampicillin

Principles of Antibiotic Therapy

- 1. Therapeutic effectiveness Clinical indications Pharmacodynamics, pharmacokinetics Age and extent of infection

Patient factors

- 1. Age, allergies, compliance, pregnancy risk
- 2. Patient function Renal, hepatic, immunosuppression, route applicability
- 3. Cost Brand name, length of course, alternatives?

Management of odontogenic infections

Uncomplicated odontogenic infections which primarily manifest as dental caries, reversible pulpitis or periapical periodontitis. Symptoms of such conditions include pain, erythema, edema, and difficulty chewing.

Complicated odontogenic infections: when an uncomplicated condition not properly intervened at right time the symptoms aggravate with the disease extending to surrounding tissues resulting in cellulitis, osteomyelitis, and space infections. There may also be trismus, lymphadenitis, and difficulty in breathing and swallowing [6,7].

Reversible pulpitis: NSAIDs’

Irreversible pulpitis: In case of vital teeth NSAIDs’ are sufficient.

Acute Apical Periodontitis [1]

Apical periodontitis lesions originating from pulp are precipitated by the immune system and are consequent to intraradicular

infections. In most cases, this inflammatory process successfully removes the microbes enter in the periapical region through the canal and stops them from spreading in the periapical region. This process is initially mediated by the polymorphonuclear leukocytes which kill bacteria by phagocytosis. Asymptomatic apical periodontitis originating from pulp do not routinely require systemic antibiotic therapy for complete resolution and healing. Proper cleaning and shaping with thorough irrigation using copious amount of irrigant is enough from healing. Once the source of infection is removed prescribing antibiotics no longer have any benefit. NSAIDs' must be prescribed to reduce the recovery time.

Acute Apical Abscess: NSAIDs'

Draining Sinus Tract: Thorough cleaning and shaping eliminates most of the infection. NSAIDs' are recommended to shorten the recovery time.

Gingival Abscess: It is most commonly due to secondary to food lodgment. Removal of the etiology is first line of treatment. Followed by topical anesthetic application and periodic warm water gargling. Routine antibiotic therapy is of no use.

Necrotizing Ulcerative Gingivitis: First, gentle irrigation with warm saline is recommended. Followed by meticulous curetting of necrotizing ulcerative lesion and root surfaces is done. Patients should be advised to rinse their mouth with warm saline and repeat curetting of lesion if needed during the next visit. Antibiotics are of no use. For severe lesions, gingivoplasty is recommended [8].

Concomitant antibacterial Chemotherapy: Timely intervention and proper first line of treatment including removal of etiology and cleaning and shaping where necessary reduces most of the infection. When these interventions are not done at right time, antibiotics may be needed. Also in case of immunocompromised patients it is recommended.

Penicillin VK or ampicillin, single or along with metronidazole and clindamycin are acceptable empirical choice to consider for treating complicated odontogenic infections. Azithromycin is also an empirical option in some cases. Lastly, the empirical drug of choice must be an effective formula with the most narrow spectrum and the least side effects due to drug intake.

First Line of Antibacterial Chemotherapy [9,10]

The empirical drug of initial choice for treating dental infections is narrow spectrum penicillin V K. Majority infections need atleast

5 days course of antibiotics. the starting loading dose is followed by maintenance doses for the remaining period. It is wise to review the patient after 2 to 3 days. This will enable the clinician to assess patient's response to treatment. Hypersensitivity reactions are potentially the most serious adverse drug effects.

Indications for Adjunctive Antibiotics

- a. Fever > 100°F
- b. Malaise
- c. Lymphadenopathy
- d. Trismus
- e. Increased Swelling
- f. Cellulitis
- g. Osteomyelitis
- h. Persistent Infection

Conditions where Adjunctive Antibiotics are not recommended

1. Pain without signs and symptoms of infection
 - a. Symptomatic irreversible pulpitis
 - b. Acute periradicular periodontitis
2. Teeth with necrotic pulps and radiolucency
3. Teeth with a sinus tract (chronic periradicular abscess)
4. Localized fluctuant swellings

A small localized swelling with no systemic signs and symptoms of infection or spread of infection regimen of antibiotics is not indicated in an otherwise healthy patient.

Antibiotics are not a substitute for surgical procedures like endodontic treatment, extraction, incision and drainage and scaling and curettage. Only when the infection is diffuse, the source can't be identified and a situation where immediate treatment is not possible to control the spread of infection antibiotic is administered [11].

There is no hard and fast rule that bactericidal drugs are always better than bacteriostatic drugs. Bactericidal drugs are useful in case of immunocompromised patients. Post antibiotic effects (PAEs-persistent inhibition of bacterial growth after previous exposure to antibiotics) are more predictable and reliable with bacteriostatic agents (erythromycin, clindamycin) than with

bactericidal agents (betalactamase) because the clinical effects of bacteriostatic agents are less dose-dependent.

Proper Use of Antibacterial Drugs clinically [12]

1. The drug dosage should be optimum. The patient should be administered the required drugs only for the required number of days.
2. The minimal inhibitory concentration of drug for a particular causative organism should be attained at the site of infection.
3. Antibiotic therapy should be started with a loading dose that is more than needed for maintaining the drug later.
4. Oral antibiotic should ideally be administered at dosing intervals of three to four times its serum half-life, particularly if
5. When steady-state blood levels are desired, the antibiotic should be administered orally for at least 3 to 4 times in periodic intervals corresponding to its serum half life.

Endodontic conditions where antibiotics are not recommended [13,6]

- a. Vital pulp
- b. Pulp necrosis with acute apical periodontitis
- c. Pulp necrosis with acute periradicular abscess (localized, antibiotic recommended in medically compromised patients)

Endodontic conditions where antibiotics are recommended

Pulp necrosis with acute periradicular abscess (spreading): Amoxicillin 500 mg every 8 hours or Clindamycin 300 mg every 8 hours for 5-7 days is recommended for adults. If condition doesn't subside, change antibiotic to macrolide or include Metronidazole 500 mg every 12 hours for 5 days.

Drugs for pregnant patients [4]

- a. Antibiotics must be the last resort. As the side effects are more than the desired effects especially during pregnancy.
- b. Drugs must not be prescribed during first trimester
- c. Only time tested drugs must be prescribed
- d. Only the minimum required dose must be prescribed
- e. Above all, thorough endodontic treatment is primary and pivotal. If cleaning and shaping is done well using copious amount of irrigants and calcium hydroxide intracanal dressing is placed antibiotics are not needed.

Indications	Adult dosages
First line of treatment	Penicillin V potassium 500
No history of allergy to beta lactum antibiotics	Initial loading dose of 1000 mg followed by three times a day for 5 days
Patient did not respond favorably to Penicillin VK in 2-3 days	Metronidazole 500 mg tablets Four times a day
2 nd line of treatment	Azithromycin 250 mg tablets
Patient allergic to beta lactum antibiotics	Initial loading does of 500 mg followed by one tablet 250 mg for five days
3 rd line of treatment	Clindamycin 300 mg capsules
Patient allergic to beta lactum antibiotics	Initial loading dose of 600 mg followed by 300mg
Infection not resolved after taking beta lactum antibiotics	daily for five days.
Empirical drug initially for treating serious infections	
Pediatric dosage Penicillin V Potassium 25-50 mg/kg day divided quarterly 6-8h, metronidazole 30 mg/kg/day divided quarterly 6h, Azithromycin 5-10 mg once daily, Clindamycin 10 mg/kg, quarterly 8h, pediatric dosage must not be more than adult dosage. Metronidazole is added in addition to Penicillin V regimen.	

Table 1: Empirical antibacterial drugs for the treatment of complicated odontogenic infections [14].

Drugs for pediatric patients

Calculation of pediatric dosage:

Child's weight lb (or kg) × adult dose = child's dose 150 lb (or 70 kg)

Infection type	Preferred antibiotic
Early (first 3 days of infection)	Penicillin VK Amoxicillin Cephalexin (or other first generation cephalosporins) 1
No improvement in 24-36 hours	Beta lactamase stable antibiotic Clindamycin or amoxicillin/ clavulanic acid combination
Penicillin allergy	Clindamycin Cephalexin (if penicillin allergy is not anaphylactoid type) Clarithromycin ²
Late (> 3 days)	Clindamycin Penicillin VK-Metronidazole, Amoxicillin- Metronidazole
Penicillin allergy	Clindamycin

Table 2: Empiric Antibiotics of Choice for Odontogenic Infections [6].

For better patient compliance, 2nd generation cephalosporin (cefactor, cefuroxime), at twice daily dose has been recommended. A macrolide is useful for patients who are sensitive to penicillin, recommended two times a day for better patient compliance [8].

Antibiotic	Pediatric dosage < 12 years	Adult dosage >12 years
Penicillin V potassium	250 mg orally every 8-12hr for 10 days	250-500 mg orally every 6hr for 5-7 days
Amoxicillin	15 mg/kg every 8h for 5-7 days Maximum dose per day 2 grams	500 mg every 8h for 5-7 days Maximum dose per day 2 grams
Amoxicillin + clavulanic acid	45 mg/kg every 12h every 8h for 5-7 days Maximum dose per day 2 grams	875 mg every 12g every 8h for 5-7 days Maximum dose per day 2 grams
cephalexin	25 to 50 mg/kg in divided doses total daily dose may be divided and administered every 12 hours For 10 days maximum.	Dosage ranges from 1 to 4 g daily in divided doses. 250 mg every 6 hours.
clindamycin	10 mg/kg every 8h At least 10 days	150-300 mg every 8h for At least 10 days

Table 3: Antibiotics of Choice for Odontogenic Infections [10].

Antibiotic Prophylaxis Recommendations

prophylactic chemotherapy is recommended for cardiac diseases that may arise due to initial endocarditis who undergo dental treatment [5]

- Prosthetic cardiac valve or prosthetic material used for cardiac valve repair
- Previous infective endocarditis
- Congenital heart disease (CHD)
- Unrepaired cyanotic CHD, including palliative shunts and conduits
- Completely repaired heart defect that are congenital repaired with prosthetic material or device by surgery or by catheter

intervention, for the first 6 months after the treatment.

- Repaired congenital heart disease with defects not completely healed at the site or next to the surgical region where prosthetic part or prosthetic equipment (which retard endothelialization) is present.
- patients with cardiac transplantation who eventually grow cardiac valvulopathy.

Prophylaxis recommended	Prophylaxis not recommended
<ul style="list-style-type: none"> Procedures that include manipulation of gingival, periapical tissues of teeth or repair of perforation 	<ul style="list-style-type: none"> Routine anesthetic injection at the site where infection is absent Radiographic procedures Orthodontic appliance placement and removable prosthesis insertion Orthodontic bracket placement Orthodontic appliance adjustment Primary teeth shedding Lip and tongue trauma resulting in bleeding

Drugs that should be part of a medical emergency kit

- Albuterol (one metered dose inhaler and a spacer for children, if applicable)
- Aspirin (two packets of powdered aspirin {325 mg})
- Diphenhydramine (two 1 ml ampules or vials of 50 mg/ml)
- Epinephrine 1:1000 (two preloaded, self-injecting syringes for patients weighing more than 66 lbs, 0.3 mg, and two preloaded, self-injecting syringes for patients weighing between 33 lbs and 66 lbs, 0.15 mg, if applicable)
- Glucose (one tube of glucose gel)
- Nitroglycerine (one bottle of the metered dose spray or one bottle of sublingual tablets, 0.4 mg/spray or tablet)

Immunocompromised patients

Immunocompromised patients may not be able to resist transient bacteremia following invasive dental procedures. These non-cardiac causes can make patient vulnerable for distant-site

infection due to dental procedure. This category includes, but is not limited to, patients with the following medical conditions [8]:

- Immunosuppression secondary to:
 - Human immunodeficiency virus (HIV);
 - severe immunodeficiency that lead to multiple disorders related to immune system
 - neutropenia;
 - Cancer chemotherapy;
 - Hematopoietic stem cell or solid organ transplantation
- Head and neck radiotherapy
- Autoimmune disease (e.g., juvenile arthritis, systemic lupus erythematosus)
- Sickle cell anemia;
- Asplenism or status post splenectomy;
- Chronic steroid usage;
- Diabetes;
- Bisphosphonate therapy.

Resistance to antibiotics

Despite these drugs have very potent effect on bacteria; they do have effect on the human body if used irrationally. The inappropriate excessive use of antibiotics where it's not justified has lead to a critical situation due to strains resistant to treatment because of mutations in the bacterial gene. The most common example is staphylococcus aureus, which has developed resistance to majority of commonly used antibiotics which includes strains resistant to Daptomycin, and Methicillin-resistant S. aureus has become obvious as one of the most common pathogens in infections aquired in hospitals. The increasing number of resistant strains of bacteria has lead to morbidity and mortality of infectious diseases, mainly nosocomial infections [2].

Conclusion

Antibiotics are definitely changed the success of various surgical procedures but we should never misuse the strength of antibiotics. Accurate diagnosis is paramount to the treatment followed by timely intervention and good surgical procedure. Antibiotics are only an adjunct and not a substitute for routine surgical procedures. With the emergence of resistant strains the clinician should always use individual rather than combination of antibiotics and go for bacteriostatic drugs where appropriate.

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