

Review Article

Use of Antibiotics in Endodontics

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ABSTRACT

Bacteria have been the main causative factor in the pathogenesis and progression of pulp and periapical diseases in the root canal system. The primary aim of endodontic treatment is to remove as many microorganisms as possible from the root canal system and to establish an environment in which remaining organisms cannot live. In cases where this cannot be achieved by the treatment procedure alone, antibiotics are needed along with endodontic treatment as either prophylactically, systemically, or locally. Owing to the inadvertent and overuse of antibiotics the emergence of antibiotic-resistant bacterial strains is a global concern. This paper elaborates on antibiotic use in the field of Endodontics and the current literature on the indications, various antibiotic-containing dental agents used in endodontics, and recommendations for their prescription in endodontic patients.

Keywords: antibiotics, endodontic infections, local antibiotics, root canal treatment

Introduction

Antibiotics are prescribed in the field of Endodontics for many conditions that may be inflammatory or infectious and sometimes related to revascularization treatment and traumatic injuries. The infections may be localized to pulp and periapical tissues, spreading to lymph nodes, or may have systemic involvement. The goal of endodontic treatment is to remove as many micro-organisms and their byproducts from the root canal space as by using various antimicrobial agents to provide an environment free of micro-organisms. Broad-spectrum antibiotics are prescribed

for cases like symptomatic irreversible pulpitis, necrotic pulps, and localized acute apical abscess.¹ Antibiotic, when indicated, is beneficial in the resolution of infection, prevention of the spread of disease, and minimizing complications. The routes for prescribing antibiotics are oral, parenteral, or topical.² Poor prescription practices, self-medication, over the counter sales of drugs and lack of awareness have created significant threats such as antimicrobial resistance and certain side effects.³ The side effects include allergic reactions, nausea, vomiting, diarrhoea, yeast infections in the mouth and vagina, and the development of *Clostridium difficile* infection. Odontogenic

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infections are polymicrobial rendering the prescription of an antibiotic empirical. This review article intends to give an overview of the antibiotics used in endodontics.⁴

Use of antibiotics in clinical situations:

Systemic use of antibiotics in endodontic infections

The effective management of the majority of infections of endodontic origin can be done without the use of antibiotics. Under certain conditions, an antibiotic is indicated as an adjunctive strategy in addition to debridement of the root canal harboring the infecting microbes and drainage of any accumulated purulence. An antibiotic regimen should be prescribed in conjunction with endodontic treatment when there are systemic signs and symptoms of infection or a progressive/persistent spread of infection like the presence of a fever (>100F), malaise, cellulitis, unexplained trismus, and progressive swelling. Once the source of the infection is removed patients with serious endodontic infections should be closely followed daily. Their conditions will usually improve rapidly. Antibiotics are not recommended for healthy patients with symptomatic pulpitis, symptomatic apical periodontitis, a draining sinus tract, localized swelling of endodontic origin, or following endodontic surgery.⁵

Where there is discrete and localized swelling, drainage by itself is considered sufficient without the need for additional medication. Lack of blood circulation in the root canal prevents antibiotics from reaching the area which makes them ineffective in eliminating the microorganisms.

The selection of antibiotics should be based on knowledge of bacteria associated with endodontic infections and their antibiotic susceptibility.⁶ The clinician must be knowledgeable about the benefits,

possible side effects, and possible sequelae of failing to take the recommended dosage of antibiotics. A loading dose is generally continued for 2 to 3 days following resolution of the major clinical signs and symptoms of the infection. Significant improvement in the patient's status should be seen in 24 to 48 hours following removal of the source of the infection and adjunctive antibiotic therapy. A prescription written for a 7-day regimen of antibiotic therapy is usually adequate. Seven day therapeutic prescription of antibiotics is usually adequate but culture and antibiotic susceptibility testing are advisable for medically compromised patients.⁷

The loading dose of 1,000 mg of penicillin VK administered orally followed by 500 mg every 4 to 6 hours is the antibiotic of choice in endodontics. It is effective against both facultative and anaerobic microorganisms commonly found in endodontic infections.⁸ Careful drug history is important as up to 10% of the population may be allergic to this medication,

The sustained serum level of amoxicillin with the oral loading dose of 1,000-mg followed by 500 mg every 8 hours or 875 mg every 12 hours as an expanded spectrum of activity that includes bacteria not routinely associated with infections of endodontic origin. It is ideal for use with medically compromised patients who require antibiotic prophylaxis. Clavulanate, a competitive inhibitor of beta-lactamase has shown excellent results against bacteria isolated from endodontic infections when clavulanate is used in combination with amoxicillin.⁹

Patients allergic to penicillin can be prescribed with erythromycin, but it is not effective against anaerobes associated with endodontic infections. Clarithromycin and azithromycin can have some advantages over erythromycin. They have activity against facultative bacteria and some anaerobic bacteria associated

with infections of endodontic origin with the advantage of a less gastrointestinal upset than erythromycin. The oral dosage for clarithromycin is 500-mg loading dose followed by 250 mg every 12 hours whereas for azithromycin it is 500-mg loading dose followed by 250 mg once a day.

Clindamycin, effective against both facultative and strictly anaerobic bacteria is well distributed throughout the body. Clindamycin is rapidly absorbed even in the presence of food in the stomach. The oral adult dosage for serious endodontic infections is a 600-mg loading dose followed by 300 mg every 6 hours.¹⁰

Metronidazole is a valuable antimicrobial agent in combination with penicillin when penicillin alone has been ineffective. The usual oral dosage for metronidazole is a 1,000-mg loading dose followed by 500 mg every 6 hours.

Cephalosporins and Ciprofloxacin are usually not indicated for the treatment of endodontic infections instead doxycycline may be indicated in conditions where the above antibiotics are contraindicated. However, many strains of bacteria have become resistant to tetracyclines.

“Topical antibiotic use in endodontics.”¹¹

The use of topical antibiotics has been proposed for several endodontic treatments.

The first reported locally used antibiotic product was Grossman antibiotic paste, a polyantibiotic paste containing penicillin, bacitracin, streptomycin, and caprylate sodium (1951).

Broad-spectrum antibiotics effective against a wide range of microorganisms have been proposed as intracanal topical antibiotics. Taking into account that endodontic infections are polymicrobial,

BioPure MTAD (Manufacturer: Dentsply Sirona Endodontics; 5100 E Skelly Dr #300, Tulsa, 74135, United States) a mixture of doxycycline, citric acid, and a detergent (Tween 80). Tween 80 is polysorbate 80 (P80), polyoxyethylene sorbitan monooleate which is a non ionic detergent for solubilising proteins. The product has been proposed as a final irrigant because of its properties like antimicrobial activity, smear layer- and pulp-dissolving capability, the effect on dentine and adhesion, and biocompatibility. Microorganisms isolated from root canals have resistance against this group of antibiotics and the side effect of intra canal use of tetracyclines is that it may promote fungal growth and can cause discoloration of teeth.¹²

Septomixine forte and Ledermix paste are other commercial products for intracanal use. It contains antibiotics like doxycycline, neomycin, and polymyxin B sulfate, but the effect against endodontic flora is not better than with calcium hydroxide.

However, the use of topical antibiotics in root canal treatment has been proposed to prevent or reduce postoperative symptoms and they do not reduce the pain or swelling arising from teeth with symptomatic apical pathoses. Hence the evidence does not support the use of topical antibiotics during root canal treatment.

Traumatic injuries.¹³

In cases of traumatic dental injuries prevention of bacterial contamination is important as the prognosis may be dramatically affected when bacteria can access the site of injury and can lead to complications like inflammatory root resorption. Thus to obtain the best outcome, limiting the bacterial load during the healing phase is a logical approach in the management of traumatic injuries.

Tooth avulsion

The use of topical antibiotics on a tooth to be replanted after avulsion has been advocated to be beneficial to enhance healing in avulsion cases.

As inflammatory root resorption is one of the major challenges faced by clinicians during the management of a replanted tooth, topical antibiotic administration might serve as a helpful means to control infection eliminate this undesirable complication like inflammatory resorption. According to International Association for Dental Traumatology (IADT) guidelines, topical application of tetracyclines (minocycline or doxycycline, 1 mg per 20 ml of saline for 5 min) on the root surface before reimplantation has shown a beneficial effect in pulpal space revascularization and periodontal healing in case of avulsed immature teeth with open apices.”

Luxation injuries of the permanent dentition

Antibiotic administration might be indicated at the discretion of the clinician when the injury is accompanied by soft tissue trauma or in certain medical conditions of the patient requiring intervention. IADT guidelines do not recommend the use of systemic antibiotics in the management of luxation injuries or teeth with root fractures.

Hence, systemic antibiotic administration may be a useful adjunct for avulsed permanent teeth according to the age and weight of the patient. In traumatic injuries such as fracture or luxation injuries, antibiotic administration does not appear to offer any additional advantage unless the patient's medical status or the degree of soft tissue injury necessitates its application.

Antibiotics used in regenerative endodontic procedures.¹⁴

Ciprofloxacin, amoxicillin, and metronidazole are antibiotics used in

regenerative endodontic therapy (RET). Apart from the disinfection of the root canal system, the combination of ciprofloxacin and metronidazole also exerts an immunomodulatory effect, which may aid in periapical healing. Lipopolysaccharide causes the production of pro inflammatory cytokines interleukin 1 beta and tumour necrosis factor-alpha by macrophages which gets suppressed by both ciprofloxacin and metronidazole.¹⁵

Triple antibiotic paste (TAP) or ‘3 mix’ consisting of ciprofloxacin, metronidazole, and minocycline (100 µg ml of each antibiotic, 300 µg ml of the mixture) has been the most widely used intracanal medicament in regenerative endodontic procedures.

The use of antibiotics as intracanal dressings in regenerative endodontic procedures may have several side effects such as dentine discoloration in case of the intraoral use of triple antibiotic paste containing minocycline. The incorporation of cefaclor or calcium hydroxide into a triple antibiotic paste, instead of minocycline can avoid discoloration.

Available guidelines and regulations regarding the use of antibiotics in endodontics.

American Association of Endodontics (AAE) guidelines.^{16,17}

1. Penicillin VK and amoxicillin, both beta-lactam antibiotics, are the first line of antibiotics chosen as adjunct therapeutic agents in endodontics in the United States of America and Europe. These drugs are highly effective against isolates from infected root canal systems that are composed primarily of facultative and obligate anaerobes.
2. The dose regimen for amoxicillin is 500 mg three times a day (with or without

a loading dose of 1,000 mg) for adults. Most practitioners usually prescribe antibiotics in courses of 3 to 7 days.

3. Clindamycin is the first drug of choice for patients with a history of hypersensitivity to penicillin drugs. The recommended dosage of clindamycin for infections of endodontic origin is 600 mg as a loading dose followed by 300 mg every 6 hours, whereas in children, this dose must be adjusted to four equal doses of 10-30mg/Kg (dose/body weight).
4. Patients with a history of penicillin allergy and severe gastrointestinal reactions to clindamycin require alternative antibiotics such as macrolides, quinolones, or tetracyclines. Endodontic pathogens have lesser susceptibility to these alternative antibiotics with an increased prevalence of resistant strains.
5. Studies have demonstrated more resistance to clindamycin, which has typically been the drug of choice for penicillin-allergic patients. In patients reporting with or known allergy to penicillin, drugs like moxifloxacin or azithromycin are considered.

Italian Guidelines.¹⁸

Clinical Guidelines in Dentistry, published by the Ministry of Health in 2017, Italy, has suggested that antibiotics use may be considered for the following situations –

1. Systemic side effects after paediatric oral surgery;
2. Orthograde endodontic therapy, to control pain;
3. Tooth replantation;
4. Side effects of acute apical abscess;
5. Antimicrobial therapy for severe periodontitis.

European Guidelines¹⁸

According to the European Society of Endodontology, antibiotics can be administered in the following situations:

1. Acute apical abscess in medically compromised patients.
2. Acute apical abscess with systemic involvement.
3. Progressive infections.
4. Replantation of avulsed permanent teeth.
5. Soft tissue trauma requiring treatment.

Administration of antibiotics should be avoided in the following situation:

1. Symptomatic irreversible pulpitis.
2. Pulp necrosis.
3. Symptomatic apical periodontitis.
4. Chronic apical abscess.
5. Acute apical abscess without systemic involvement.

Prophylactic antibiotics recommendations¹⁹

- Compared with previous recommendations, there are currently relatively few patient subpopulations for which antibiotic prophylaxis may be indicated before certain dental procedures.
- For infective endocarditis prophylaxis, current guidelines support premedication for a relatively small subset of patients. This is based on a review of scientific evidence, which showed that the risk of adverse reactions to antibiotics generally outweighs the benefits of prophylaxis for many patients who would have been considered eligible for prophylaxis in previous versions of the guidelines.

Concern about the development of drug-resistant bacteria also was a factor.

- Infective endocarditis prophylaxis for dental procedures should be recommended only for patients with underlying cardiac conditions associated with the highest risk of adverse outcome from infective endocarditis. Antibiotic prophylaxis is recommended for dental procedures involving gingival tissue or the periapical region or breach of oral mucosa.²⁰

Prophylaxis is reasonable before dental procedures that involve manipulation of gingival tissue, manipulation of the periapical region of teeth, or perforation of the oral mucosa. Antibiotics prophylaxis regimen for various conditions are shown in table 1 and table 2.

According to the American Dental Association guidelines, there is no association between dental procedures and the occurrence of periprosthetic joint infections.

Prophylactic antibiotics for adult patients should be given in those with health conditions that may predispose them to infective endocarditis or patients who have prosthetic joint with risk of developing haematogenous infections at the site of the prosthesis.

Limiting the use of antibiotics^{21,22}

Antibiotics use in dentistry can be limited by the following measures:

The conservative shorter courses of use of antibiotics are administered or prescribed only when indicated to lower the risk of

Table 1: Antibiotics prophylaxis for medically compromised patients.

Condition	Clinical data	Antibiotics as adjunct
Patients with immunodeficiency ²³	Leukemia, HIV/AIDS	Yes
Chronic disease ²⁴	End stage renal disease Dialysis Uncontrolled diabetes	Yes
Medications ²⁴	Chemotherapy, Radiation, Steroids	Yes
Immunosuppressive medications ²³	Post transplant	Yes
Neutropenia ²³	Counts fall to < 500 IL	Yes
Infective endocarditis ²⁵	Routine dental procedures	Yes
Infective endocarditis ²⁵	Gingival or periapical region of the teeth or perforation of the oral mucosa, including scaling and root canal procedures	Yes
Patients with complex congenital heart defects, prosthetic cardiac valve ²⁶	Previous recent infection of the joint and cases with massive oral infections.	Yes
Jawbones exposed to high dose of radiation for cancer treatment ²⁷	Dental treatment with a risk to translocation of infection to the bone in high-dose exposed areas.	Yes

Table2 Recommended antibiotic prophylaxis regimens in Endodontics
(American Heart Association guidelines)²⁴

Situation	Agent	Adults	Children
Able to take oral medication	Amoxicillin	2g	50 mg/kg
Unable to take oral medication	Ampicillin or Cefazolin or Ceftriaxone	2g IM or IV 1g IM or IV	50 mg/kg IM or IV 50 mg/kg IM or IV
Allergic to penicillins or ampicillin- Oral	Cephalexin or Clindamycin or Azithromycin or Clarithromycin	2g 600 mg 500 mg	50 mg/kg 20 mg/kg 15mg/kg
Allergic to penicillin/ amoxicillin/ampicillin and unable to take medication.	Cefazolin or Ceftriaxone or Clindamycin	600mg IM or IV 1g IM or IV	20mg/kg IM or IV 5mg/kg IM or IV

developing resistance to current antibiotic regimens.

1. Dentists should avoid prescribing antibiotics to delay the appointment, or to retain the patient.
2. A precautionary discussion with the patient and educating them to consume antibiotics exactly as prescribed and briefing patients about managing anticipated post endodontic pain using analgesics can change the attitude toward placebo role antibiotic plays in managing dental pain.
3. The government can support in reduced use of broad-spectrum antibiotics, improved appropriate antibiotic selection and dosing, minimal prescribing errors, antibiotic cost, and reduced antibiotics resistance by adopting computerized decision making. Systems like "MIND ME" which is an initiative by Government of South Australia is a guiding system for advising clinicians regarding prescribing antibiotics.

4. Antimicrobial stewardship program has been well improved in the medical field, but not in the field of dentistry are conducted to improve the appropriate use of antimicrobials. These programs should be promoted and dentists should be trained about appropriate usage of antibiotic drugs, their dose, dosing interval, and duration of intake to make them more confident in antibiotic use and prescribing them.
5. In most of the developing countries like India, antibiotics are often easily available without a physician's prescription and this has elevated the condition of antibiotic resistance among people. The rule of "prescription only medicines" should be in practice and should be strictly reinforced.

Conclusion

Over-prescription of antibiotics should be avoided. They should be limited to be used when indicated such as adjunct in the treatment of apical periodontitis to prevent

the spread of the infection only in acute apical abscesses with systemic involvement, in progressive persistent infections, and medically compromised patients. Penicillin VK, possibly combined with metronidazole to cover anaerobic strains, is still effective in most cases, amoxicillin (alone or together with clavulanic acid) is recommended because of better absorption and lower risk of side effects. Lincosamides, such as clindamycin, are the drug of choice in case of confirmed penicillin allergy.

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