

## Antibiotic application in endodontics

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### Abstract

Endodontic therapy aims at infection control and management to provide a healthy environment to the tooth and the oral cavity. With the daily advances in endodontic procedures it is possible to control these infections clinically. But there are certain situations which require the need of a pharmacological intervention as an adjunct. In such cases antibiotics have proved to be a boon. Due to untoward use and mis guidance antibiotics are prescribed in an imprudent way. Therefore this paper throws a light on various conditions in endodontics that require antibiotic application and commonly used antibiotics that are prescribed to treat these conditions.

**Keywords:** Antibiotics, Antibiotic prophylaxis, Endodontic infections, Resistance.

### Introduction

Success of endodontic treatment not only depends on three dimensional obturation of root canal but also to a greater extent depends on infection control and pain management. Ideally root canal disinfection is achieved with antimicrobial irrigants and intracanal medicaments but due to the rapid growth of the resistant organisms found in the oral cavity pain and infection control has to be minimized by supplementing it with drugs such as analgesics, anti inflammatory and antibiotics.

Most common cause of pain and infection of pulpal and periapical origin is dental caries. The microorganisms associated with endodontic infections are polymicrobial in nature and the by products of these microorganisms are referred to as endotoxins and exotoxins which are responsible for spreading the disease. Endodontic infections are dominated by anaerobic bacteria in primary infections such as *Prevotella* and *asaccharolytic* species *Porphyromonas*. Other microorganisms such as *Tannerella forsythia*, *Dialister*, *Fusobacterium*, *Spirochetes*, Gram positive rods, Gram positive cocci such as *Streptococcus mitisi*, *Enterococcus faecalis* are also found in intraradicular endodontic infections.<sup>1</sup>

Pharmacology plays an important role in managing these infections. The best way to prescribe an antibiotic regime is to identify the mirorganisms associated with a particular endodontic infection and treat them with an adjunctive pharmacological therapy if and when required.

### Antibiotics used in endodontics

Antibiotics are the greatest boon for therapeutics in the 20th century. In any endodontic infection local therapy applied to the tooth is of utmost importance following which in some cases systemic antibiotics are required as an auxillary to combat infection.

### Beta lactam antibiotics

Beta lactam antibiotics are the first and the most commonly used antibiotics. They include penicillin V, Amoxicillin and clavulanic acid. They act by interfering with the synthesis of bacterial cell wall by binding at the site of penicillin binding proteins (PBPs).<sup>2</sup>

### Penicillin V

Penicillin V or phenoxymethyl penicillin are acid resistant penicillins which have a narrow spectrum of activity.<sup>2</sup> Its peak blood level is reached in 1 hour and plasma  $t_{1/2}$  is 30-60 minutes. Route of excretion is mainly by the kidneys. There is no recommended maximum dose and no side effects from overdose in non allergic patients.<sup>3</sup> A loading dose of 1,000 mg is recommended followed by 500mg every 4-6 hours.<sup>4</sup>

### Amoxicillin

The need of development of amoxicillin was due to the limited spectrum of activity of penicillin G and penicillin V. They are needed to be taken four times daily and were associated with rashes and rarely anaphylaxis.<sup>5</sup> Amoxicillin is the most commonly used acid stable, semisynthetic aminopenicillin that have a broad spectrum of activity which increases its chances of resistance.<sup>6</sup> Oral absorption of amoxicillin is good and food does not interfere with absorption. A loading dose of 1,000 mg is recommended followed by 500mg every 8 hours.

### Amoxicillin and clavulanic acid

To overcome bacterial resistance  $\beta$  lactamase inhibitors like clavulanic acid was introduced and used with amoxicillin as they donot have antimicrobial activity of its own. The betalactam ring of clavulanic acid prevents the inactivation of the penicillin group by binding irreversibly to bacterial beta-lactamase.<sup>7</sup> It has good oral absorption, broad antimicrobial spectrum and

is excreted through the kidneys<sup>8</sup> Dosage of 625 mg (500mg of amoxicillin and 125mg of clavulanic acid) should be given every 8 hours.<sup>9</sup>

### Macrolides

Macrolides act by inhibiting bacterial protein synthesis by binding with 50S ribosome subunits. Erythromycin was the earliest macrolide discovered and now newer generation macrolides like Azithromycin and Clarithromycin have been introduced which have a wider spectrum of activity and have gained popularity in endodontics.

### Erythromycin

The killing of bacteria by erythromycin slows down the manufacture of bacterial protein without altering the rate of human protein synthesis. Erythromycin has a narrow spectrum of activity and kills about the same bacteria as penicillins. Therefore macrolides are a wonderful alternative to patients allergic to penicillin as they have a different mechanism of action. Erythromycin is acid labile and cannot be taken with food as food delays its absorption. It is excreted mainly by bile in the active form and some amount is excreted through the kidneys.<sup>2</sup> It's given at a dosage of 500mg every 6 hours.<sup>10</sup>

### Azithromycin and clarithromycin

In an attempt to overcome the limitations of erythromycin like narrow spectrum activity, gastric intolerance, gastric acid lability, low oral bioavailability and short half-life, a number of semisynthetic macrolides have been produced, of which clarithromycin and azithromycin are most commonly used in endodontics.

Clarithromycin as compared to erythromycin is said to have increased activity against *Staphylococcus aureus* and streptococci.<sup>11</sup> It is more acid-stable and is rapidly absorbed than erythromycin. Presence of food delays absorption but does not decrease it. Recommended dose is a loading dose of 500mg followed by 250mg twice a day.<sup>12</sup>

Azithromycin, congener of erythromycin has an expanded spectrum of activity, it has increased activity against gram negative organisms when compared to

erythromycin<sup>17</sup> but has limited activity against gram positive cocci.<sup>2</sup> Azithromycin are acid stable, rapidly absorbed, has good tissue penetration, persistence and longer half lives due to which their dosage is limited to once or twice a day. Its recommended loading dose is 500mg followed by 250mg once a day.<sup>12</sup> Should not be taken for more than 5 days due to increased chances of arrhythmias.<sup>13</sup>

### Lincosamide antibiotic

#### Clindamycin

Next to penicillin, Clindamycin is considered as the second drug of choice in treating odontogenic infections. Clindamycin and erythromycin act by the same mechanism but act at different sites which are close to each other in the 50S ribosome. Its absorption is rapid and has a wide spectrum of activity. Excretion is through biliary tract and kidney. The oral adult dosage for serious endodontic infections is a 600 mg loading dose followed by 300 mg every six hours for five to seven days.<sup>14</sup>

### Nitroimidazoles

#### Metronidazole

In spite of its narrow spectrum of activity and ineffectiveness against aerobic and facultative organisms metronidazole is considered as the drug of choice in infections where anaerobic microorganisms predominate. If used alone it may lead to growth of aerobic and facultative organisms therefore they are used along with other antibiotics such as Penicillin V, amoxicillin and clindamycin as they show a synergistic action when used in combination.

A redox reaction takes place in the nitro group of metronidazole after it enters the anaerobic bacteria and gets converted to a free radical that exerts a cytotoxic effect on the organism. Its excreted through the kidneys and is contraindicated in the first trimester of pregnancy due to its mutagenic action and in chronic alcoholics as it causes disulfuram like reactions.<sup>2</sup> A loading dose of 1000mg followed by maintenance dose of 500 mg 6 hourly.<sup>15</sup>

A consolidated list of the drugs used and its dosage is given below. (Table 1)

**Table 1: Drugs used in endodontics and its recommended dosage**

Antibiotic	Loading dose (in mg)	Maintenance dose
Penicillin V	1000	500mg every 4-6 hourly
Amoxicillin	1000	500mg every 8 hourly
Amoxicillin with clavulanic acid	1000	625mg every 8 hourly
Erythromycin		500 mg every 6 hourly
Clarithromycin	500	250mg every 12 hourly
Azithromycin	500	250mg once a day
Clindamycin	600	300mg every 6 hourly
Metronidazole	1000	500mg 6 hourly

### Drug duration

The common dilemma associated with any antibiotic is that for how long it should be taken. Longer duration courses have greater tendency to destroy the normal oral and gut commensals, increases the growth of resistant bacteria while shorter duration of course may be just enough to combat the infection and decrease resistance, higher doses do not guarantee any absence of re-infection and no one can tell how long the infection will persist owing to the different bacterial behaviour and drug effect.<sup>16</sup> An antibiotic dose of 3-5 days will suffice including a loading dose if necessary. Re – evaluation of the patient should be done in 1-2 days as the decrease in patients symptoms is the only parameter that tells us about the condition of the patient and if the course needs to be continued.<sup>17</sup>

### Adverse effects of drugs used and antibiotic resistance

It is important that the advantages offered by any drug should outweigh its disadvantages and inadvertent use of any antibiotic can cause adverse effects and harm the patient. With the beta lactam group of antibiotics such as Penicillin V and amoxicillin there are chances of hypersensitivity, serum sickness, wheezing, angioneurotic oedema or exfoliative dermatitis. Doses of oral penicillins and macrolides taken in excess can cause gastrointestinal distress. The other important adverse effects associated with macrolides are ototoxicity when dosage of more than 4g/day is taken, acute pancreatitis, prolonged QT intervals leading to ventricular arrhythmias and rarely rashes and fever may occur.<sup>18</sup>

The minor side effects associated with clindamycin which is the preferred substitute for patients allergic to penicillin are nausea, vomiting, rashes, urticaria, abdominal pain, metallic taste, stomatitis but the major problem associated is diarrhoea and potentially fatal pseudomembranous enterocolitis due to *Clostridium difficile* superinfection. Frequently occurring side effects associated with metronidazole are anorexia, nausea, vomiting, abdominal cramps, rashes and metallic taste.

Another major issue associated with careless and unnecessary use of antibiotics is its resistance. Unnecessary antibiotic prescription such as in cases of

no infection, inappropriate dosage or duration and excessive use in prophylaxis leads to genetic alterations like changes in gene expression, Horizontal gene transfer and mutagenesis.<sup>19</sup> Emergence of superbugs i.e bacterial resistance to the class of antibiotics used for their treatment due to multiple mutations and multi drug resistance have further worsened the condition.<sup>20</sup> Therefore keeping in mind the seriousness of the situation check on the antibiotic usage is utmost important.

### Endodontic implication of antibiotics

Majority of endodontic infections can be managed efficiently without the use of systemic antibiotics. It should be clear that antibiotics are an adjunct in these infections and not all the conditions require a course of antibiotics. Healthy patients with irreversible pulpitis, necrotic pulps, symptomatic apical periodontitis, draining sinus tract or localized swelling of endodontic origin do not require an additional use of antibiotic.<sup>12</sup> In these cases conventional root canal therapy will suffice and there is no use of systemic antibiotics. In cases of abscess formation the main aim should be drainage of the pus by incision and drainage or drainage through the tooth following which there is no need to prescribe antibiotics. Antibiotics in such cases should only be prescribed if the patient shows sign of local spread or systemic involvement.

Antibiotic regimen is indicated in patients with irreversible pulpitis, necrotic pulps, apical periodontitis, sinus formation only if there is systemic involvement which includes signs such as fever greater than 100°F, malaise, lymphadenopathy and trismus or in cases of immunocompromised patients. They are also an useful adjunct in cases of persistent and progressive infections such as increasing swelling, cellulitis and Osteomyelitis.<sup>3</sup>

According to the guidelines given by International academy of dental traumatology systemic antibiotics are contraindicated in luxation injuries and root fractures whereas they can be prescribed in cases of avulsed tooth after they have been replanted since experimentally they have shown to be useful in pulpal and periodontal healing. A summary of the indications and contraindications of antibiotics is given below (Table 2)

**Table 2: Indications and contraindications of antibiotics in endodontics**

Antibiotics Contraindicated	Antibiotics Indicated	
Symptomatic irreversible pulpitis	Systemic involvement (Fever, malaise, lymphadenopathy, trismus) /immunocompromised patients associated with irreversible pulpitis pulpal necrosis Acute apical periodontitis Acute and chronic periapical	Amoxicillin is the first choice of drug. ALLERGIC TO PENICILLIN Clindamycin or Azithromycin or Clarithromycin may be used If amoxicillin is not effective after 2–3 days of use metronidazole to be recommended as

	abscess	a supplemental medication
pulpal necrosis	Progressive infections like cellulitis, lymphadenopathy	Amoxicillin with clavulanic acid and metronidazole
Acute apical periodontitis	Persistent infection that does not subside by conventional endodontic procedures	
Acute periapical abscess and Chronic periapical abscess with no systemic involvement	Avulsion	Doxycycline or Amoxicillin
Luxation injuries and root fracture		

### Antibiotic prophylaxis

Antibiotic prophylaxis (Table 3) is given to individuals with risk of systemic spread of infection or in order to prevent local spread of infection. Recommended Preventive antibiotics prior to a dental

procedure are advised for patients with Artificial heart valves, Infective endocarditis, Congenital heart conditions, immunocompromised patients, patients with joint surgery, haemophilia, prior to endodontic surgery, Following the avulsion and replantation of teeth.<sup>21</sup>

**Table 3: Prophylactic regimen for dental practice<sup>22</sup>**

Situation	Agent	Regimen: Single Dose 30 to 60 min Before Procedure	
		Adults	Children
Oral	Amoxicillin	2 g	50 mg/kg
Unable to take oral medication	Ampicillin OR Cefazolin or ceftriaxone	2 g IM* or IV+ 1 g IM or IV	50 mg/kg IM or IV 50 mg/kg IM or IV
Allergic to penicillins or ampicillin—oral	Cephalexin φδ OR Clindamycin OR Azithromycin or clarithromycin	2 g 600 mg 500 mg	50 mg/kg 20 mg/kg 15 mg/kg
Allergic to penicillins or ampicillin and unable to take oral medication	Cefazolin or ceftriaxoneδ OR Clindamycin	1 g IM or IV 600 mg IM or IV	50 mg/kg IM or IV 20 mg/kg IM or IV
* IM: Intramuscular + IV: Intravenous φ Or other first- or second-generation oral cephalosporin in equivalent adult or pediatric dosage. δ Cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticaria with penicillins or ampicillin.			

### Conclusion

The use of antibiotics in endodontics is not mandatory and most of the cases can be managed by conventional root canal therapy. It is utmost important to make use of these antibiotics judiciously and only in selective cases where there is systemic involvement or as a prophylactic measure. This would not only protect the patient from hypersensitivity and potential toxicity

but may also contribute in prevention of antibiotic resistance.

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