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Use of antibiotics in endodontics: A critical review

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Abstract

The main etiological factor in the pathogenesis and progression of pulpal and periradicular diseases is microorganisms especially bacteria. The main objective of root canal treatment is to create an environment in which remaining microorganisms cannot survive. This goal can be fulfilled by use of supplemental antibiotic therapy in conjunction with regular non-surgical root canal treatment. In endodontics both systemic and local antibiotics are broadly used. In endodontic infections the local administration of antibiotics are more efficient when compared to systemic administration. In a nutshell this article elaborates the use of antibiotics in endodontics.

Keywords: Antibiotics; Endodontic infections; Intracanal medicaments; Antibiotic prophylaxis

1. Introduction

Since the discovery of penicillin by Fleming in 1928, antibiotics have revolutionized the entire health-care system [1]. Endodontic infection is the infection of root canal system in which microorganisms play a prominent role in both pulpal and periapical disease. The primary endodontic infection is mixed, in which gram negative anaerobic rods are predominant, whereas in secondary infection comprise only one or few bacterial species –in which the most predominant is *Enterococcus faecalis* [2].

The ultimate aim of endodontic treatment is to eradicate as many micro-organisms and their by-products from the root canal space by using various antimicrobial agents to provide a micro-organism free environment [3]. In course of endodontic treatment antibiotics can be given either systemically or locally.

Only on the basis of defined indications systemic Antibiotics should be prescribed or used for dental infections [4]. Systemic antibiotics fail to reach the necrotic pulpless teeth, being lack of blood supply accordingly the local application of antibiotics is an effective mode of disinfection in endodontics [5].

2. History of antibiotics

In 1928 Antibiotics were first discovered, but clinically they were not routinely used until the early 1940s [6]. The foundation idea for antibiotics was laid down by Paul Ehrlich by introducing the term “magic bullets” for a chemical that would attach itself to the germ and kill it [7]. The term “antibiosis” that means “against life” for early antibacterial drugs was given by Jean Paul Vuillemin [8]. Louis Pasteur and Robert Koch first described the term antibiotics in 1877 [9].

3. Local applications in Endodontics

In endodontics Antibiotics can be used in various modes. Grossman - Father of Endodontics was the first person who used the applications of local Antibiotics in endodontics. He proposed poly antibiotic paste combination (PBSC) of

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penicillin, bacitracin, streptomycin and caprylate sodium suspended in silicon vehicle in 1951 [10]. Later Food and Drug Administration banned PBSC for endodontic use in 1975, due to the risk of sensitization and allergic reactions [11].

4. Rationale of systemic antibiotics

Endodontic infections are mostly polymicrobial infections categorized by anaerobic bacteria and to a large extent facultative anaerobes. The harmful effects of these bacteria leads to pulpal inflammation which ultimately leads to necrosis of pulp, which become reservoir of infection, characterized dead microbes and their noxious products enters the periapex leads to irritation of periapical region, that result in periradicular inflammation, leading to abscess and cellulitis. In such situations the rationale of locally used antibiotics in conjunction with systemic antibiotics plays a vital role [12]. In endodontics, use of antibiotics is a must to aid in the host defense in the elimination of the bacteria narrow spectrum of antibiotics should be the choice initially due to adverse, use of broad spectrum antibiotics result in antibiotic sensitive. Systemic application of antibiotics is indicated when there is a system involvement of infection such as fever, cellulitis, lymphadenopathy and swelling. Other indications for the use of antibiotics include antibiotic prophylaxis to prevent infective endocarditis, prosthetic joint infection and prophylactic coverage after sodium hypochlorite accident [13].

5. Indications for the use of systemic antibiotics

Systemic antibiotics are generally used in the indications like (i) acute periapical abscesses with signs of systemic involvement; (ii) acute periapical abscesses in immuno-suppressed patients; (iii) prophylaxis of infection associated with tooth avulsion; (iv) treatment of persistent symptomatology and/or exudation after the performance of all available options to control inter-radicular infection; (v) prophylaxis against bacteremia caused by endodontic treatment in immunosuppressed patients or patients susceptible to bacterial endocarditis; (vi) abscess dissemination; and (vii) endodontic flare ups etc.

Conditions not requiring adjunctive antibiotics includes are (i) pain without signs and symptoms of infection; (ii) teeth with necrotic pulps and a radiolucency; (iii) teeth with a sinus tract (chronic periradicular abscess); and (iv) localized fluctuant swellings etc.

Penicillin, Erythromycin, Metronidazole, Clindamycin, Clarithromycin, Azithromycin, Tetra cycline, Doxycycline etc. are commonly used systemic antibiotics.

6. The rationale for local application of antibiotics

The systemic administration of antibiotics completely depends on patient consent with the dosing regimens the goal of the drug is to reach the infected site at a required concentration followed by absorption through the gastrointestinal tract and then distribution via the circulatory system. Hence, the infected area (i.e., the tooth root) needs a good and profound blood supply which is no longer available in case of teeth with a necrotic pulp, a pulp less and infected root canal system there by the need of local application of antibiotics within the root canal system came in to play. Since it may become a more effective mode for delivering these drugs to the site of infected area [15].

7. Locally used antibiotic agents in endodontics

In endodontics usually used antibiotics agent which are used locally includes (i) tetracyclines; (ii) MTAD; (iii) tetraclean; (iv) Ledermix paste; (v) combination of Ledermix paste and calcium hydroxide; and (vi) Triple antibiotic paste.

7.1. Tetracyclines

Tetracyclines are broad-spectrum antibiotics that are effective against a wide range of microorganisms. They are mainly bacteriostatic in nature [16, 17]. Since these drugs have four ("tetra-") hydrocarbon rings ("-cycl-") derivation ("-ine") they are called as tetracyclines. They are collectively known as derivatives of polycyclic naphthacene carboxamide [18]. Tetracyclines. In endodontics to remove the smear layer from instrumented root canal wall, tetracyclines have been used as part of an irrigant [19, 20]. For irrigation during periapical surgical procedures in retrograde preparations [21], and as an intracanal medicament. Pinheiro et al. [22] evaluated the antibiotic susceptibility of *Enterococcus faecalis* isolates from canals of root-filled teeth with periapical radiolucencies.

Tetracyclines readily attach to dentin and are subsequently released without losing their antibacterial activity. This property creates a reservoir of active antibacterial agent, which is then released from the dentin surface in a slow and sustained manner.

7.2. MTAD

Torabinejad et al has introduced MTAD to dentistry. It is composed of 3 % doxycycline, 4.25 % citric acid, and a detergent (0.5% polysorbate 80). MTAD is able to remove the smear layer without affecting the structure of a dentinal tubules [23, 24]. Newberry and coworkers demonstrated the antimicrobial efficacy of MTAD against 8 strains of *E. faecalis*. After irrigating the canals initially with 1.3% NaOCl, MTAD was for 5 mins used as a final rinse. It causes complete elimination of 7 out of 8 strains of bacteria [25].

7.3. Tetraclean

Tetraclean is a mixture of an antibiotic, an acid, and a detergent. However, it differ from those of MTAD in terms of concentration of the antibiotic, doxycycline (50 mg/ml), and the type of detergent (polypropylene Glycol) [26]. Studies on antibacterial activity of tetraclean were done by few people. Giardino and co-workers [27] compared the antimicrobial efficacy of 5.25% NaOCl, MTAD, and tetraclean against an *E. faecalis* biofilm generated on cellulose nitrate membrane filters.

7.4. Ledermix paste

Ledermix paste is a glucocorticosteroid- antibiotic compound the main reason for adding the antibiotic component to ledermix paste was to reimburse for what was perceived to be a possible corticoid-induced reduction in the host immune response [28].

Study by Bryson et al. showed that in treatment of traumatically injured teeth ledermix paste plays a vital role. In this study canals of replanted dog teeth were placed with ledermix medicament after a drying period of 60 minutes. Favorable healing and less root resorption were seen in teeth treated with ledermix paste when compared to the teeth treated with intra canal medicament like calcium hydroxide [29].

7.5. Combination of ledermix paste and calcium hydroxide

In cases of pulp necrosis, infected root canals and infection with incomplete root formation (as an initial dressing prior to using calcium hydroxide alone for apexification), perforations, inflammatory root resorption, and inflammatory periapical bone resorption and for treatment of large periapical radiolucent lesions a 50:50 mixture of ledermix paste and calcium hydroxide has been advocated as an intracanal dressing [30] without affecting the function of each component of both medicaments. It helps to maintain the sterility of the canal for longer duration and also maintains of all components within the canal at higher concentration.

7.6. Triple antibiotic paste

Due to the complexity of the root canal infection, it is fortunate that any single antibiotic could result in sound disinfection of the canal. Triple antibiotic paste would also decrease the likelihood of the development of resistant bacterial strains could be decreased by a combination of antibiotics. The combination that consists of metronidazole, ciprofloxacin, and minocycline appears to be most promising [31]. Hoshino et al. [32] investigated the antibacterial effect of a mixture of ciprofloxacin, metronidazole, and minocycline on bacteria taken from infected dentin of root canal walls and found that it was able to consistently sterilize all samples. Hoshino *et al.* recommended metronidazole (500 mg) minocycline (100 mg) and ciprofloxacin (200 mg) at 1:1:1 ratio for triple mix formulation. The carrier is propylene glycol and macrogol ointment at 1:1 ratio [15]. Even though TAP is effective medicament, it has its own drawback. TAP paste is shown to be most cytotoxic to human periodontal ligament fibroblasts.

8. Antibiotic prophylaxis

Antibiotics must be administered one hour (oral route) or 30 minutes (intravenous route) before the procedure according to the protocol proposed by the American Heart Association (Table - 1). Below table 1 shows regimens of antibiotics used for dental procedures.

Table 1 Regimens of antibiotics for dental procedures [33]

Situation	Agent	Regimen-Single dose (30-60 minutes before procedure)	
		Adults	Children
Oral	amoxicillin	2 gm	50 mg/kg
Unable to take oral medication	Ampicillin or	2 g IM or IV	50 mg/kg IM or IV
	cefazolin or ceftriaxone	1 g IM or IV	50 mg/kg IM or IV
Allergic to penicillins or ampicillin (oral)	Cephalexin * # or	2 g	50 mg/kg
	clindamycin or	600 mg	20 mg/kg
	azithromycin or clarithromycin	500 mg	15 mg/kg
Allergic to penicillins or ampicillin (unable to take oral medications)	cefazolin or ceftriaxone or	1 g IM or IV	50 mg/kg IM or IV
	clindamycin	600 mg IM or IV	20 mg/kg IM or IV

* Other first or second generation oral cephalosporin in equivalent adult or pediatric dosage; # cephalosporins should not be used in an individual with a history of anaphylaxis, angioedema, or urticarial with penicillins or ampicillin.; IM- intramuscular; IV- intravenous

Conditions requiring antibiotics prophylaxis includes (i) previous history of endocarditis; (ii) total joint replacement; (iii) complex and cyanotic congenital heart diseases; (iv) surgically constructed pulmonary shunts; (v) rheumatic heart diseases; (vi) mitral valve prolapse; (vii) valvular regurgitation; (viii) prosthetic valve replacement; and (ix) uncontrolled diabetes mellitus etc. [34].

Dental procedures at high risk of bacteremia includes (i) dental extractions; (ii) periodontal procedures – surgeries, SRP; (iii) dental implants placement, re-implantation of avulsed tooth; (iv) endodontic instrumentation beyond apex; (v) endodontic surgery, placement of retraction cord; (vi) placement of orthodontic bands; and (vii) intraligamentary and intraosseous injections etc.

Dental procedures at low risk of bacteremia includes (i) restorative procedures; (ii) intracanal endodontic treatment and post placement and core; (iii) placement of rubber dam, removable partial dentures; (iv) orthodontic appliance adjustments; AND (v) Taking oral impressions, oral radiographs, and fluoride gels application etc. [35].

9. Conclusion

In order to avoid the over using of antibiotics in endodontics the use of systemic antibiotics should be restricted to specific cases. They should be used as a supplemental in the treatment of acute apical abscesses with systemic involvement, and in progressive and persistent infections in order to limit the spread of the infection. Complication arising from endodontic infections are more susceptible in medically compromised patients. Hence systemic antibiotics should not be prescribed until and unless there is a systemic involvement or immune compromised conditions. Within the root canal system local application of antibiotics may be a more effective mode than systemic routes of administration for delivering the drugs to infected areas.

Compliance with ethical standards

Disclosure of conflict of interest

The authors have stated explicitly that there are no conflict of interests in connection with this article.

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