



Antibiotic resistance and antibiotics in endodontics

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Antibiotic resistance has been called one of the world's most pressing public health problems (1). Antibiotic resistance is not a new problem. Resistant disease strains began emerging not long after the discovery of antibiotics more than 50 years ago. Penicillin and other antibiotics, which were initially viewed as miracle drugs for their ability to cure such serious and often life-threatening diseases as bacterial meningitis, typhoid fever, and rheumatic fever, soon were challenged by some defiant strains (2). Antibiotic resistance is a major contributor to the disease, death, and costs resulting from hospital-acquired infections. One report placed the annual cost of antimicrobial resistance among a single pathogen (*Staphylococcus aureus*) at \$122 million (3). Antibiotic resistance has made potential killers out of bacteria that previously posed little threat to mankind. The indiscriminate and reckless use of antibiotics has led to a fast-approaching crisis in which human dominance of the planet is threatened by single, elementary cells of the microbial world (4). Reasons for the development of antimicrobial resistance fall into two broad categories: over-prescription by health-care providers and improper use by patients. Although physician over-prescription for upper respiratory infections is the single largest reason for the development of resistant microbial strains (5), over-prescription for dental problems and/or dental pain is emerging as a growing threat. The purpose of this clinical update is to review the Centers for Disease Control and Prevention (CDC) recommendations regarding antibiotic use and to review the literature regarding antibiotic use in endodontics.

How resistance occurs

The ability of antibiotics to stop an infection depends on killing or halting the growth of harmful bacteria. Some bacteria have developed a natural resistance to antibiotics, long before the development of commercial antibiotics. If they are not naturally resistant, bacteria can become resistant to drugs in a number of ways. They may develop resistance to certain drugs spontaneously through mutation. Mutations are changes that occur in the genetic material, or DNA, of the bacteria. These changes allow the bacteria to fight or inactivate the antibiotic (6).

Bacteria also can acquire resistant genes through exchanging genes with other already resistant bacteria. The bacteria reproduce rapidly, allowing resistant traits to quickly spread to future generations of bacteria. This means that resistance can spread from one species of bacteria to other species, enabling them to develop resistance to multiple classes of antibiotics (6).

The emergence of a resistant population of bacteria in a patient as a result of antibiotic use generally occurs through a process termed "selective pressure." Studies using special culture techniques show that healthy persons normally harbor small numbers of bacteria that are intrinsically resistant to antibiotics. The larger numbers of antibiotic-susceptible organisms usually keep resistant bacteria in check. The use of any antibiotics eliminates organisms susceptible to that drug at the site of infection and at all sites in the body into which the drug penetrates in adequate concentrations. Selective

pressure occurs when the administration of an antibiotic decreases the numbers of normal flora, allowing resistant bacteria to proliferate (5).

Recommendations for the prudent use of antibiotics

Misuse of antibiotics increases the chances of superinfections, mutations, genetic transfer, and the development of multi-drug resistant strains of bacteria (7). The CDC estimates that about 100 million courses of antibiotics are prescribed by office-based physicians each year, and that approximately one half of those prescriptions are unnecessary (5). To curb the widespread overuse of antibiotics, the CDC has published broad guidelines regarding the prescription of antimicrobials.

CDC's recommendations for appropriate antibiotic use for health care providers (1):

- Only prescribe antibiotic therapy when likely to be beneficial to the patient
- Use an agent targeting the likely pathogens
- Use the antibiotic for the appropriate dose and duration

It is up to health-care providers to educate patients on the risks and benefits of proper antibiotic use. Clinicians should explain to patients that antibiotics are potentially harmful in the following ways:

- Increased colonization and infection with resistant pathogens in patients with prior antibiotic therapy
- Increased antimicrobial resistance in the community
- Unwanted allergic reactions and adverse effects of antibiotics
- Cost of unnecessary therapy

Empathize with patients about the effect of symptoms on their daily activities, provide them with educational materials and prescribe therapies to alleviate their symptoms.

Other educational points to convey to patients include:

- Don't demand an antibiotic when the health-care provider determines one isn't appropriate.
- Finish each prescription. Even when the symptoms of an illness have disappeared, some bacteria may still survive and reproduce if the patient doesn't complete the course of treatment.
- Don't take leftover antibiotics or antibiotics prescribed for someone else. These antibiotics may be inappropriate for the current infection, and taking the wrong medicine could delay getting appropriate treatment and allow bacteria to multiply.

Indications for antibiotic therapy in endodontics

The first point to consider is that antibiotics should only be used as an adjunct to definitive non-surgical or surgical endodontic therapy. Removal of the etiology is ultimately the goal of treatment. Pulpal debridement and/or surgical access are the primary treatment for all endodontic infections. Even then, the rationale for antibiotic therapy is a severe infection in which the organism is not known and

major consequences would ensue if therapy is not initiated before culture and sensitivity tests are available.

Accordingly, the primary indications for antibiotic use are:

- Compromised host resistance
- Systemic involvement
- Fascial space involvement
- Inadequate surgical drainage

Other indications for the use of antibiotics include the prophylactic treatment for preventing endocarditis and prosthetic joint infection, as well as prophylactic coverage following a sodium hypochlorite accident (8). If multiple appointments are planned for patients requiring antibiotic prophylaxis, scheduling should allow for a minimum of 10 days between appointments in order to minimize the odds that bacterial strains will develop resistance (9). When multiple appointments in succession are needed, changing the class of antibiotic (i.e. from amoxicillin to clindamycin) will help curb the risk of bacterial resistance (10).

Proper antibiotic selection is critical. An antibiotic with a broad enough spectrum to cover the bacterial etiology is essential, but not too broad in which to kill beneficial normal flora. Hence, penicillin is still the drug of choice in endodontic infections. A recently published study reported that penicillin V was effective in 81% of acute endodontic infections. The same study found that metronidazole was effective in 88%, and clindamycin in 89% of infections. When penicillin V and metronidazole were combined the effectiveness increased to 93.2% (11).

After drug selection, the next important step is selection of the appropriate dose and duration. Studies within the past few years have shown that up to 40% of providers are using inappropriate adult doses (12,13). The proper adult dosages for commonly prescribed antibiotics are as follows (without renal impairment):

- Penicillin V 500mg
Sig: 2 p.o. STAT; then 1 p.o. every 6 hours for 7 days
- Metronidazole 500mg
Sig: 1 p.o. every 6 – 8 hours for 7 days
- Clindamycin 150-300mg
Sig: 1 p.o. every 6 hours for 7 days

In a year 2000 survey of members of the American Association of Endodontists (AAE), a loading dose of penicillin was reported by 85% of providers; hence, its inclusion in the above recommendations (14).

When not to prescribe antibiotics

Endodontic diagnoses in which the prescription of antibiotics are not warranted include irreversible pulpitis with or without acute periradicular periodontitis, necrotic pulp with or without acute periradicular periodontitis, necrotic pulp with a draining sinus tract, and a necrotic pulp with chronic periradicular periodontitis without swelling. Research has shown that penicillin does not reduce pain, percussion sensitivity, or the amount of analgesics required in untreated teeth diagnosed with irreversible pulpitis; and therefore, should not be prescribed in cases of irreversible pulpitis (15). The reason is that irreversible pulpitis is an immune system mediated event, which is most often not due to a bacterial infection, but rather is a result of inflammatory mediators overcoming the host defenses (16). The prophylactic use of antibiotics to prevent potential flare-ups has also been shown to have no effect on their occurrence, and

cannot be recommended as routine protocol in the treatment of asymptomatic necrotic teeth (17).

Nearly all groups of practitioners are guilty of over-prescribing. In the AAE survey mentioned above, for cases of irreversible pulpitis, 16.76% of responders prescribed antibiotics. In cases of a necrotic pulp, acute apical periodontitis, and no swelling, 53.93% prescribed antibiotics. Nearly 12% prescribed antibiotics for necrotic pulps with chronic apical periodontitis and a sinus tract (14).

Conclusions

Antimicrobial therapy is an invaluable and sometimes life-saving adjunctive therapy. Inappropriate and indiscriminate use, has led to wide-spread antibiotic resistance, which if not curbed, will lead to bacteria that are resistant to all present antibiotics (18). Prudent usage of antibiotics rests upon providers. Meeting this responsibility will ultimately help to determine whether we have effective antimicrobials in the future.

References:

1. <http://www.cdc.gov/drugresistance/community/> CDC Background on Antibiotic Resistance. 2003.
2. Nordenberg T. Miracle Drugs vs. Superbugs. FDA Consumer Magazine, 1998 Nov-Dec 32(6):22-5.
3. www.cdc.gov/ncidod/HIP/aresist/am_res.htm, Antimicrobial resistance: A growing threat to public health. 1999.
4. Harrison JW, Svec TA. The beginning of the end of the antibiotic era? Part II. Proposed solutions to antibiotic abuse. Quintessence Int. 1998 Apr;29(4):223-9.
5. Colgan R, Powers JH. Appropriate antimicrobial prescribing: Approaches that limit antibiotic resistance Am Fam Physician. 2001 Sep 15;64(6):999-1004.
6. Bren L. Battle of the bugs: fighting antibiotic resistance. FDA Consum. 2002 Jul-Aug;36(4):28-34.
7. Harrison JW, Baumgartner JC, Svec TA. Incidence of pain associated with clinical factors during and after root canal therapy. Part 1. Interappointment pain. J Endod. 1983 Sep;9(9):384-7.
8. Hales JJ, Jackson CR, Everett AP, Moore SH. Treatment protocol for the management of a sodium hypochlorite accident during endodontic therapy. Gen Dent. 2001 May-Jun;49(3):278-81.
9. Leviner E, Tzukert AA, Benoliel R, Baram O, Sela MV. Development of resistant oral viridans streptococci after administration of prophylactic antibiotics: time management in the dental treatment of patients susceptible to infective endocarditis. Oral Surg Oral Med Oral Pathol. 1987 Oct;64(4):417-20.
10. Dajani AS, Taubert KA, Wilson W, Bolger AF, Bayer A, Ferrieri P, et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. Clin Infect Dis. 1997 Dec;25(6):1448-58.
11. Khemaleelakul S, Baumgartner JC, Pruksakorn S. Identification of bacteria in acute endodontic infections and their antimicrobial susceptibility. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2002 Dec;94(6):746-55.
12. Epstein JB, Chong S, Le ND. A survey of antibiotic use in dentistry. J Am Dent Assoc. 2000 Nov;131(11):1600-9.
13. Roy K, Bagg J. Antibiotic prescribing by general dental practitioners in the greater Glasgow Health Board Scotland. Br Dent J. 2000 Jun 24;188(12):674-6.
14. Yingling NM, Byrne BE, Hartwell GR. Antibiotic use by members of the American Association of Endodontists in the year 2000: report of a national survey. J Endod. 2002 May;28(5):396-404.
15. Nagle D, Reader A, Beck M, Weaver J. Effect of systemic penicillin on pain in untreated irreversible pulpitis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2000 Nov;90(5):636-40.
16. Bergenholtz G. Pathogenic mechanisms in pulpal disease. J Endod. 1990 Feb;16(2):98-101.
17. Pickenpaugh L, Reader A, Beck M, Meyers WJ, Peterson LJ. Effect of prophylactic amoxicillin on endodontic flare-up in asymptomatic necrotic teeth. J Endod. 2001 Jan;27(1):53-6.

18. Slavkin HC. Benefit-to-risk ratio: the challenge of antibiotic drug resistance. J Am Dent Assoc. 1997 Oct;128(10):1447-51.

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