Combating antibiotic resistance

ADA COUNCIL ON SCIENTIFIC AFFAIRS

ABSTRACT

Background. The ADA Council on Scientific Affairs developed this report to provide dental professionals with current information on antibiotic resistance and related considerations about the clinical use of antibiotics that are unique to the practice of dentistry.

Overview. This report addresses the association between the overuse of antibiotics and the development of resistant bacteria. The Council also presents a set of clinical guidelines that urges dentists to consider using narrow-spectrum antibacterial drugs in simple infections to minimize disturbance of the normal microflora, and to preserve the use of broad-spectrum drugs for more complex infections.

Conclusions and Practice Implications. The Council recommends the prudent and appropriate use of antibacterial drugs to prolong their efficacy and promotes reserving their use for the management of active infectious disease and the prevention of hematogenously spread infection, such as infective endocarditis or total joint infection, in high-risk patients.

For the past 70 years, antibiotic therapy has been a mainstay in the treatment of bacterial infectious diseases. However, widespread use of these drugs by the health professions and the livestock industry has resulted in an alarming increase in the prevalence of drug-resistant bacterial infections.

Worldwide, many strains of *Staphylococcus aureus* exhibit resistance to all medically important antibacterial drugs, including vancomycin,[1,2] and methicillin-resistant *S. aureus* is one of the most frequent nosocomial pathogens.[3] In the United States, the proportion of *Streptococcus pneumoniae* isolates with clinically significant reductions in susceptibility to β lactam antimicrobial agents has increased more than threefold.[4,5] Even more alarming is the rate at which bacteria develop resistance; microorganisms exhibiting resistance to new drugs often are isolated soon after the drugs have been introduced.[6] This growing problem has contributed significantly to the morbidity and mortality of infectious diseases, with death rates for communicable diseases such as tuberculosis rising again.[7,8]

Any perceived potential benefit of antibiotic prophylaxis must be weighed against the known risks of antibiotic toxicity, allergy and the development, selection and transmission of microbial resistance.

Disease etiologies also are changing. In recent studies, staphylococci, particularly *S. aureus,* have surpassed viridans streptococci as the most common cause of infective endocarditis.[9] Resistance among bacteria of the oral microflora is increasing as well. During the past decade, retrospective analyses of clinical isolates have clearly documented an increase in resistance in the viridans streptococci.[10] Further, strains of virtually every oral microorganism tested exhibit varying degrees of resistance to various antibacterial agents.[11]

This increase in antibacterial resistance has been attributed primarily to two different processes. First, reduced susceptibility may develop via genetic mutations that spontaneously confer a newly resistant phenotype.[12] Alternatively, the exchange of resistant determinants between sensitive and resistant microorganisms (of the same or different species) may occur.[13] Regardless of the genetic basis of resistance, the selective pressure exerted by widespread use of antibacterial drugs is the driving force behind this public health problem. It is only through the prudent and appropriate use of antibacterial drugs that their efficacy may be prolonged.

Antibacterial drugs should be

TABLE 1

NARROW-SPECTRUM* ANTIMICROBIAL AGENTS ENCOUNTERED IN DENTISTRY.†

GENERIC NAME	CHARACTERISTICS‡	COMMON INDICATIONS FOR USE
Clindamycin	Bacteriostatic (bactericidal at higher doses); active against some aerobic gram-positive cocci (including *Staphylococcus aureus*, *S. epidermidis*, streptococci and pneumococci), some anaerobic gram-negative bacilli, many anaerobic gram-positive non–spore-forming bacilli, many anaerobic gram-positive cocci and clostridia	Indicated for the treatment of infections caused by susceptible microorganisms; used as a prophylactic antibiotic in high-risk patients allergic to penicillin for the prevention of both bacterial endocarditis and infections of total joint replacements
Metronidazole	Bactericidal; active against most anaerobic cocci and both gram-negative bacilli and gram-positive spore-forming bacilli	Has been used as adjunct in treatment of periodontitis and acute necrotizing ulcerative gingivitis; commonly coprescribed with amoxicillin (Note: its combined use with amoxicillin or amoxicillin/clavulanic acid has not been approved by the U.S. Food and Drug Administration)
Penicillin V Potassium	Bactericidal; cell-wall synthesis inhibitor that is active primarily against gram-positive cocci (including *S. aureus*), gram-positive and gram-negative bacilli, and spirochetes	Use is limited to treatment of minor infections such as ulcerative gingivostomatitis, and to the prophylaxis and continued treatment of streptococcal infections

* Active against a small number of organisms.
† Adapted in part from Ciancio.[17]
‡ Bactericidal drugs directly kill an infecting organism; bacteriostatic drugs inhibit the proliferation of bacteria by interfering with an essential metabolic process.

reserved for the management of active infectious disease and considered for the prevention of hematogenously spread infection, such as infective endocarditis or total joint infection, in high-risk patients (as defined by the American Heart Association[14] and the American Dental Association and the American Academy of Orthopedic Surgeons[15]). One example of their use in managing infectious disease is in the treatment of aggressive periodontal disease, which use has become well-accepted for optimal control of the disease process.[16] The Council encourages further research on the appropriate use of antibacterial therapy in the management of oral diseases.

GUIDELINES FOR PRESCRIBING ANTIBIOTICS

The following guidelines should be observed when prescribing antibacterial drugs:

(1) make an accurate diagnosis;

(2) use appropriate antibiotics and dosing schedules;

(3) consider using narrow-spectrum antibacterial drugs (Table 1) in simple infections to minimize disturbance of the normal microflora, and preserve the use of broad-spectrum drugs (Table 2) for more complex infections[17];

(4) avoid unnecessary use of antibacterial drugs in treating viral infections;

(5) if treating empirically, revise treatment regimen based on patient progress or test results;

(6) obtain thorough knowledge of the side effects and drug interactions of an antibacterial drug before prescribing it;

(7) educate the patient regarding proper use of the drug and stress the importance of completing the full course of therapy (that is, taking all doses for the prescribed treatment time).

Furthermore, the diagnosis and antibiotic selection should be based on a thorough history (medical and dental) to reveal or avoid adverse reactions, such as allergies and drug interactions. Any perceived potential benefit of antibiotic prophylaxis must be weighed against the known risks of antibiotic toxicity, allergy and the development, selection and transmission of microbial resistance.[15]

It remains incumbent on dental practitioners, as health care providers, to use antibacterial drugs in a prudent and appropriate manner. Adherence to the principles outlined here will aid in extending the efficacy of the antibacterial drugs that form the treatment foundation for many infectious diseases. ■

TABLE 2

BROAD-SPECTRUM* ANTIMICROBIAL AGENTS ENCOUNTERED IN DENTISTRY.†

GENERIC NAME	CHARACTERISTICS‡	COMMON INDICATIONS FOR USE
Amoxicillin (Semisynthetic Penicillin)	Bactericidal; active against many gram-negative and gram-positive organisms; not effective against β-lactamase–producing bacteria	Commonly used as an empirical antibiotic for oral infections, sinusitis and skin infections; used as a prophylactic antibiotic in high-risk patients for the prevention of bacterial endocarditis and infections of total joint replacements
Amoxicillin With Clavulanic Acid	Bactericidal; active against a wide spectrum of gram-negative and gram-positive organisms, including β-lactamase–producing bacteria	Used for the treatment of sinus, oral and respiratory infections
Ampicillin (Semisynthetic Penicillin)	Bactericidal; active against many gram-negative and gram-positive organisms; not effective against β-lactamase–producing bacteria	Commonly used as an empirical antibiotic for oral infections, sinusitis and skin infections; used as a prophylactic antibiotic in high-risk patients unable to take oral medication for the prevention of both bacterial endocarditis and total joint infections
Cefadroxil (First-Generation Cephalosporin)	Bactericidal; active against β-hemolytic streptococci, staphylococci, *Streptococcus pneumoniae, Escherichia coli, Proteus mirabilis, Klebsiella* and *Moraxella*	Indicated for the treatment of infections caused by susceptible microorganisms; used as a prophylactic antibiotic in high-risk patients for the prevention of bacterial endocarditis and infections of total joint replacements; caution should be exercised when prescribing cephalosporins for patients sensitive to penicillin§
Cefazolin (First-Generation Cephalosporin)	Bactericidal; active against group A β-hemolytic streptococci, *Haemophilus influenzae, S. pneumoniae, E. coli, Enterobacter aerogenes, P. mirabilis* and *Klebsiella*	Used for the treatment of respiratory, urinary tract, skin and biliary infections and for the treatment of septicemia and endocarditis; used as a prophylactic antibiotic in high-risk patients who are unable to take oral medications for the prevention of both bacterial endocarditis and infections of total joint replacements; caution should be exercised when prescribing cephalosporins for patients sensitive to penicillin§
Cephalexin (First-Generation Cephalosporin)	Bactericidal; active against β-hemolytic streptococci, staphylococci, *S. pneumoniae, E. coli, P. mirabilis, Klebsiella* and *Moraxella*	Indicated for the treatment of infections caused by susceptible microorganisms; used as a prophylactic antibiotic in high-risk patients for the prevention of bacterial endocarditis and infections of total joint replacements; caution should be exercised when prescribing cephalosporins for patients sensitive to penicillin§
Cephradine (First-Generation Cephalosporin)	Bactericidal; active against group A β-hemolytic streptococci, *H. influenza, S. pneumoniae, E. coli, E. aerogenes, P. mirabilis* and *Klebsiella*	Used as a prophylactic antibiotic in high-risk patients for the prevention of bacterial endocarditis and infections of total joint replacements; caution should be exercised when prescribing cephalosporins for patients sensitive to penicillin§
Azithromycin (Macrolide)	Bactericidal; active against a wide range of aerobic gram-negative and gram-positive organisms	Indicated for the treatment of mild-to-moderate infections caused by susceptible microorganisms; used as a prophylactic antibiotic in high-risk patients allergic to penicillin for the prevention of bacterial endocarditis
Clarithromycin (Macrolide)	Bactericidal; active against a wide spectrum of aerobic and anaerobic gram-positive and gram-negative organisms	Indicated for the treatment of mild-to-moderate infections caused by susceptible microorganisms; used as a prophylactic antibiotic in high-risk patients allergic to penicillin for the prevention of bacterial endocarditis
Erythromycin (Macrolide)	Bacteriostatic; active against gram-positive bacteria, particularly gram-positive cocci; provides limited activity against gram-negative bacteria	Indicated for the treatment of infections of upper and lower respiratory tract, skin and soft-tissue infections of mild-to-moderate severity; alternative to penicillin G and other penicillins for treatment of gram-positive coccoid infections in patients with hypersensitivity to penicillins; used as a prophylactic antibiotic in high-risk patients allergic to penicillin for the prevention of bacterial endocarditis
Tetracycline (Doxycycline, Minocycline)	Bacteriostatic; active against gram-positive and gram-negative bacteria, mycoplasmas, rickettsial and chlamydial infections	Indicated for the treatment of periodontitis and acute necrotizing ulcerative gingivitis (Note: to avoid the gastrointestinal side effects of oral tetracyclines, localized delivery systems of doxycycline and minocycline are marketed for the treatment of periodontitis)

* Used as empirical antibiotics or when culture and sensitivity testing are not available.
† Adapted in part from Ciancio.[17]
‡ Bactericidal drugs directly kill an infecting organism; bacteriostatic drugs inhibit the proliferation of bacteria by interfering with an essential metabolic process.
§ Cross-hypersensitivity has been documented and will occur in up to 10 percent of patients who have a history of penicillin allergy.[18]

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