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Research Article

Antibiotics in Dentistry- A Boon or Bane?

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Abstract

The mortality rate due to infectious diseases was high ages ago. Millions and millions of lives were saved owing to the discovery of antibiotics. Antibiotics can be called as "life-saving drugs". However, inappropriate prescribing and excessive use of antibiotics are major factors in the emergence of antibiotic resistance. WHO recognized this growing global problem, announced theme for the year 2011 as "Antibiotic resistance: No action today, No cure tomorrow." Dental practitioners regularly prescribe antibiotics for therapeutic or prophylactic purposes to manage oral and dental infections. Antibiotics are not an alternative to dental intervention; they are adjunct and never the first line of treatment modality. Antibiotic overuse and misuse among dentists is substantial. Antibiotics are indicated when clinical signs of involvement are evident. Clinical situations that require antibiotic therapy on empirical basis are limited. Patient's expectation of an antibiotic prescription, convenience and demand necessitated by the social background of patients are considered unscientific reasons for prescription. There is an urgent need to raise public and professional awareness regarding the risks of antibiotic use not only in dentistry but all aspects of medical care. Overcoming barriers to more judicious prescribing will require development of materials to support change, implementation of effective strategies to catalyse such changes and development of supportive structures in healthcare organizations.

Keywords: Antibiotics; Prescribing; Antibiotic resistance; Misuse

Abbreviations

MRSA: Methicillin Resistant Staphylococcus Aureus; AHA: American Heart Association; AAOS: American Academy of Orthopaedic Surgeons; IE: Infective Endocarditis

Introduction

Since the discovery of penicillin, the first antibiotic, by Alexander Fleming in 1928 and its subsequent introduction to clinical practice by Florey in 1940, antibiotics have been used extensively in dentistry [1]. Dental practitioners regularly prescribe antibiotics for therapeutic or prophylactic purposes to manage oral and dental infections [2]. Antibiotic prescribing may be associated with unfavourable side effects ranging from gastrointestinal disturbances to fatal anaphylactic shock and development of resistance [3-5]. Additionally, inappropriate, indiscriminate and irrational use of antibiotics has led to the development of antibiotic resistance [6-8]. The increasing resistance problems are probably related to over or mis-use of broad spectrum agents such as cephalosporins and fluoro-quinolones [3]. Example of extensive resistance is methicillin-resistant staphylococcus aureus (MRSA), also known commonly as a 'superbug' [1]. The mortality rate due to infectious diseases was high ages ago. Millions and millions of lives were saved owing to the discovery of antibiotics. Antibiotics can be called as "life –saving drugs" [6].

Antibacterial resistance is a global clinical and public health problem that has emerged with alarming rapidity in recent years and undoubtedly will increase in near future. It is a problem in the community as well as in health care settings, where transmission of bacteria is greatly amplified, in both developed and developing countries [9]. Moreover, antibiotics are societal drugs that affect microbial resistance not only in the person taking drug but also everyone else, because resistance genes are easily passed via personal contacts, fomites, human and animal refuse. WHO has recognized this growing global problem, announced the theme for the year 2011 as "Antibiotic resistance: No action today, No cure tomorrow" [6].

With the emergence of bacterial species resistant to antibiotics there is a need to become vigilant about their prescription and with this, an urgent requirement for both professional and public understanding of the appropriate use of this life-saving component of treatment [7,8,10]. Consequently, surveillance of antibiotic resistance, monitoring of antibiotic usage and attempts to improve prescribing attitudes have become crucial [2,11].

Antibiotics are not an alternative to dental intervention; they are adjunct [11]. Therapeutic and prophylactic antibiotic prescribing practices are usually followed by dentists [2]. Antibiotics are indicated when clinical signs of involvement are evident. No benefit is seen from the use of antibiotic prophylaxis in low and moderate risk dental implant patients [12]. Antibiotics are indicated in dental practice for treating immune-compromised patients, evident signs of systemic infection and if the signs and symptoms of infection progress rapidly. Antibiotic treatment is an aspect of pharmacotherapy with the particularity of affording both etiological and curative action. Bacterial infections are common in dental and oral clinical practice; as a result, antibiotic use prescribed for their treatment is also frequent [13]. It is observed that countries with the highest per capita antibiotic consumption have the highest resistance rates. It is not only the amount of antibiotic used that select for resistance, but the number of individuals receiving the drug and the population density also

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matters. Thus, the astonishing effects of antibiotics, the occurrence of resistance and the considerable resources spent on antibiotics globally are convincing reasons for concern about ensuring adequate and proper use of these powerful agents [14].

History

The first antibiotic, Penicillin had unbelievable ability to treat the bacterial infections especially those caused by staphylococcus and streptococci without harming the host. Antibiotic resistance first became challenging shortly after penicillin gained extensive use in the 1940s. The period of late 1940s and early 1950s saw the discovery and introduction of broad spectrum antibiotics such as streptomycin, chloramphenicol and tetracycline and the age of antibiotic chemotherapy came into full being. These antibiotics were effective against the full array of bacterial pathogens including gram-positive and gram-negative bacteria, intracellular parasites and the tuberculosis bacillus. Development of antibiotic resistance was first reported in animal models in 1940s and subjectively reported among patients in the 1970s [14-16].

The oral microbiota

The oral cavity is colonized by a diverse range of micro-organisms. These comprise 300-500 species of bacteria, fungi and protozoa, of which only 10% are regularly, isolated using conventional culture techniques. Of the bacteria that are easily recovered upon routine culture, the alpha-hemolytic streptococci are among the most frequent isolates. Other bacteria found in oral commensal microbiota include coagulase-negative staphylococci, gram-negative cocci belonging to the families Neisseriaceae, Veillonellaceae, Lactobacilli, Spirochaetes, Corynebacteria and Mycoplasmas. Bacteria that are potentially pathogenic and that are sometimes found in the oral cavity include Staphylococcus aureus, Enterococcus faecalis, Streptococcus pneumoniae, Streptococcus pyogenes, Neisseria meningitides and members of the family Enterobacteriaceae, Haemophilus influenza and Actinomycetes. A complex ecosystem is formed in the oral cavity, and it changes constantly throughout life. Gram-positive aerobic cocci, alpha-hemolytic streptococci, peptostreptococci and gram-negative anaerobes are frequently isolated from oral infections. The antibiotics prescribed most commonly by dentists are penicillin, amoxicillin and metronidazole. These drugs have the potential to select for resistant bacteria within the commensal microbiota [17].

Therapeutic antibiotic prescribing by dentists

Most oral diseases presented to the dentist are primarily inflammatory conditions that are associated with pain. A considerable percentage of dental pain originates from acute and chronic infections of pulpal origin, which necessitates operative intervention, rather than antibiotics. Non-indicated clinical cases for antibiotic use include acute periapical infection, dry socket and pulpitis. Chronic inflammatory periodontal conditions are not indicated for antibiotics; systemic antimicrobials should only be used in acute periodontal conditions where drainage or debridement is impossible, where there is local spread of the infection or where systemic upset has occurred.

More common dental infections present in the form of pulpitis and periapical periodontitis, which require only operative measures like fillings, root canal therapy or extraction if the tooth is not restorable. Unfortunately, dentists still prescribe antibiotics for this condition [18,19]. A distressing finding was that a number of dentists prescribe antibiotics for viral infections like herpes simplex virus-1 infections [19].

Clinical situations that require antibiotic therapy on empirical basis are limited, and they include oral infection accompanied by elevated body temperature and evidence of systemic spread like lymphadenopathy and trismus. Facial cellulitis that may or may not be associated with dysphagia is a serious disease that should be treated by antibiotics promptly because of the possibility of infection spread via lymph and blood circulation, with development of septicemia. There are also a limited number of localized oral lesions that are indicated for antibiotic use and these include periodontal abscess, acute necrotizing ulcerative gingivitis and pericoronitis. Another aspect of antibiotic over-prescribing is prescribing based on non-clinical factors. Patient's expectation of an antibiotic prescription, convenience and demand necessitated by the social background of the patients are considered unscientific reasons for antibiotic prescription. The other side of the coin is that many doctors have been prescribing antibiotics in abundance for years and are following old habits.

Penicillin is the gold standard in treating dental infections. The most commonly used antibiotic in dental practice, penicillins in general, were found to be the most commonly prescribed antibiotics by dentists [20], the most popular one being amoxicillin [18,21], followed by penicillin V [19,22], metronidazole [18] and amoxicillin and clavulanate. The rationale for the choice could have been its wide spectrum, low incidence of resistance, pharmacokinetic profile, tolerance and dosage; combination with metronidazole enhances the anaerobic activity.

Short courses are preferred to long courses particularly when treating children, since children's compliance with conventional courses is poor. Short course antibiotic therapy requires that antibiotics have certain characteristics, such as: rapid onset of action, bactericidal activity, lack of propensity to induce resistant mutants, easy penetrability into tissues activity against non-dividing bacteria, not being affected by adverse infection conditions (low pH, anaerobiasis, presence of pus, etc.), administration at an optimal dose and optimal dosing regimen. Prolonged courses of antibiotics destroy the commensal microbiota. In addition, longer durations of upto 21 days may result in the selection of resistant strains and a reduction in the ability of the oral microbiota to resist the colonization by harmful micro-organisms that are not normal residents, leading to superimposed infections by multi-resistant bacteria and yeasts [3].

Adverse consequences of prescribing antibiotics include:

- Financial loss
- Emergence of resistant bacteria that can be more difficult to treat
- Increases patient expectations and their demand for antibiotics even when they are not indicated
- Potential of serious side-effects and drug interactions

Thus, antibiotics should be prescribed at the correct frequency, dose and duration so that the minimal inhibitory concentration is

Table 1: Antibiotic prophylaxis recommendations.

Situation	Agent	Regimen*
Standard general prophylaxis	Amoxicillin, Cephalexin**, or Cephradine	2.0g orally 30-60 minutes before procedure
Unable to take oral medications	Ampicillin Cefazolin	2.0g IM or IV 30-60 minutes before procedure 1.0g IM or IV 30-60 minutes before procedure
Penicillin-allergic	Clindamycin	600 mg orally 30-60 minutes before procedure
Penicillin-allergic and unable to take oral medications	Clindamycin	600 mg orally 30-60 minutes before procedure

*No follow-up dose recommended

** Cephalosporins should not be used in individuals with immediate type hypersensitivity reaction (urticaria, angioedema or anaphylaxis) to penicillins

For children, consult physician

IM- Intramuscular, IV- Intravenous

exceeded, and so that side effects and the selection of resistant bacteria are prevented [14,23,24,25].

Prophylactic antibiotic prescribing

Recommended Antibiotic Prophylaxis: Antibiotic Prophylaxis is recommended in various bacteremic dental procedures. Recommendations are based on the guidelines of American Heart Association (AHA) and the American Academy of Orthopaedic Surgeons (AAOS) [3]. (Table 1)

1) Dental procedures that involve manipulation of gingival tissue or the periapical region of the teeth or perforation of the oral mucosa

2) Scaling and root planning of teeth

3) Periodontal procedures

a) Curetting tissue

b) Periodontal probing

c) Periodontal surgery

d) Sub gingival placement of antibiotic fibers and strips

4) Tooth extraction

5) Suture removal

6) Biopsies

7) Prophylactic cleaning of teeth or implants where bleeding is anticipated

8) Dental implant placement [26] and replantation of avulsed teeth

9) Endodontic instrumentation or surgery only beyond the apex

a) Placement of orthodontic bands

b) Intra-ligamentary and intra-osseous local anaesthetic injections [22].

10) Prophylactic antibiotics, taken prior to a number of dental procedures, have been advocated to reduce the likelihood of postoperative local complications, like infection, dry socket or serious systemic complications like infective endocarditis (IE). In the case of bacterial endocarditis (IE), the absolute risk rate after dental treatment, even in at-risk patients, is considered very low [3]. This is consistent with recent guidelines from the British Society for Antimicrobial Chemotherapy, and the American Heart Association [27].

Antibiotics for odontogenic infections

Bascones et al. [28] suggested that treatment should be provided in some acute situations of odontogenic infection pulp origin as a complement to root canal treatment, in ulcerative necrotizing gingivitis, in periapical abscesses, in aggressive periodontitis and in severe infections of the fascial layers and deep tissues of the head and neck. They do not recommend antibiotic treatment in chronic gingivitis or periodontal abscesses (except in the presence of dissemination) [13].

Antibiotics for non-odontogenic infections

The non-odontogenic infections require a prolonged treatment. They include infections such as tuberculosis, syphilis, leprosy and non-specific infections of bone [2].

Non-odontogenic infections include specific infections of the oral cavity (tuberculosis, syphilis, leprosy), and nonspecific infections of the mucosal membranes, muscles and fascias, salivary glands and bone. Bone infections are included on the basis that many of them may be of dental origin. These processes require prolonged treatments, and drug associations are used that usually include clindamycin, due to its capacity to reach high concentrations in bone and fluoroquinolones (ciprofloxacin, norfloxacin and moxifloxacin) to extend the bacterial spectrum to include gramnegative bacilli, grampositive aerobic cocci and, in the case of third generation fluoroquinolones (moxifloxacin), anaerobes [13].

Antibiotic resistance

Causes: Patient related factors are major drivers of inappropriate use of antibiotics. Many patients believe that new and expensive medications are more efficacious than older agents. This perception increases the unnecessary health care expenditure and encourages the selection of resistance to these newer agents as well as to older agents in their class. Patient's misperception about the utility of antibiotics in self resolving viral infections, poor compliance where patient forgets to take medication or interruption of treatment when they begin to feel better or may be unable to afford the treatment, self medication which may be unnecessary or often inadequately closed, are major factors contributing to resistance [2]. Insufficient training in infectious diseases and antibiotic treatment, difficulty of selecting the appropriate anti-infective drugs empirically and need for self reassurance are promoting the use of drugs [29].

Two of the main factors associated with development of resistance are duration of therapy and dose of drug. Individuals within the community can harbor resistant bacterial strains for upto three months following antibiotic usage and as such, represent a high level of resistance within the general population [30-32]. Epidemic and endemic infections caused by multiple resistant strains followed intense antibiotic use in many hospitals particularly in intensive care unit which is the major breeding ground for antibiotic resistance [2,33,34].

There are various factors that contribute to the occurrence of resistance such as; incorrect use of antibiotics, patient related factors, prescriber's prescriptions, use of monotherapy, hospitals, veterinary prescriptions, commercial promotion, over the counter sale of antibiotics, under use of microbiological testing and globalization [2] which stimulates the international circulation of goods and people and plays an important role in dissemination of pathogens including resistant strains [14].

Microbes are living organisms that evolve over time. Their primary function is to reproduce, thrive, and spread quickly and efficiently. Therefore, microbes adapt to their environments and change in ways that ensure their survival. If something stops their ability to grow, such as an antimicrobial, genetic changes can occur that enable the microbe to survive. Several ways through which this happens include:

Selective Pressure: In the presence of a drug, microbes are either killed or, if they carry resistance genes, survive. These survivors will replicate, and their progeny will quickly become the dominant type throughout the microbial population.

Mutation: Most microbes reproduce by dividing every few hours, allowing them to evolve rapidly and adapt quickly to new environmental conditions. During replication, mutations arise and some of these mutations may help an individual microbe survive exposure to an antibiotic.

Gene Transfer: Microbes also may get genes from each other, including genes that make the microbe drug resistant.

Inappropriate Use: Selection of resistant microorganisms is exacerbated by inappropriate use of antibiotic. Alongwith patient related factors, sometimes healthcare providers will prescribe antimicrobials inappropriately, wishing to placate an insistent patient who has a viral infection or an as-yet undiagnosed condition.

Inadequate Diagnostics: More often, healthcare providers use incomplete or imperfect information to diagnose an infection and thus prescribe an antimicrobial just-in-case or prescribe a broad-spectrum antimicrobial when a specific antibiotic might be better. These situations contribute to selective pressure and accelerate drug resistance.

Hospital Use: Critically ill patients are more susceptible to infections and, thus, often require the aid of antibiotics. However, the heavier use of antibiotics in these patients can worsen the problem by selecting for resistant microorganisms. The extensive use of and close contact among sick patients creates a fertile environment for the spread of resistant germs.

Consequences of antibiotic resistance

Infections caused by resistant microbes fail to respond to treatment resulting in prolonged illness and greater risk of death, longer periods of hospitalization and infections which increases the number of infected people moving in the community. When an infection becomes resistant to first line antibiotic, treatment has to be switched to second or third line drugs, which are always much more expensive and sometime more toxic as well [14].

Impact of resistance on public health and economy

Due to the selection pressure caused by antibiotic use, a large pool of resistant genes has been created and this antibiotic resistance places an increased burden on society in terms of high morbidity, mortality and cost [2]. The cost of patient care also increases due to the need for costlier second line drugs, longer duration of hospital stay, increased need for intensive care and diagnostic testing, higher incidences of complications and expenses incurred by use of isolation precaution. Antibiotic resistance is driving up health care cost, increasing the severity of disease and death rates of some infections. The economic and health costs of resistance, serious enough in the industrialized world, are often more severe in developing countries [14].

Control and Prevention

The key elements should include a public relations campaign, clinic based education and community outreach activities. A successful public relations effort will require expertise in marketing and communication skills. Educational information can be disseminated through community organizations, schools, childcare centers and pharmacies. National goals should be developed to reduce unnecessary use and progress towards goals should be monitored. Economic factors must be considered. Appropriate diagnostic testing should be encouraged [14].

Strategies to reduce inappropriate use of antibiotics

Overcoming barriers to more judicious prescribing will require development of materials to support change, implementation of effective strategies to catalyse such changes and development of supportive structures in healthcare organizations [15].

Use of diagnostic microbiology laboratories by general dental practitioners

Diagnostic microbiology laboratories can provide information to assist in therapeutic decisions, resistance surveillance and the development of local policies and guidelines [35]. In a study [36], a number of respondents felt that when short of time, it was acceptable to prescribe antibiotics without further investigation. The immediate relief of the patient seems to be an important factor when considering treatment. This may also be fuelled by patient expectation. From the laboratory perspective, there are also logistical difficulties when processing dental specimens, owing to the lack of standard methodologies and he need to preserve the integrity of small specimens containing diverse populations of anaerobic bacteria during transport to the laboratory. Overall, reveals a lack of communication between general dental practitioners and diagnostic microbiology laboratories [35-37].

Intervention strategies and approaches [38]

- Clinical practice guideline for appropriate use of antibiotics must be developed in each community and must be supported by other educational activities [39].

- Peer education: To recruit trained and educated personnel who could deliver and cater to the territorial and local needs

- E-mailing lectures: Helps in flow of information and various opinions

- A multifaceted approach is needed to increase the public understanding of antibiotic resistance and to change expectations about the use of antibiotics.

- Multidisciplinary coordination and cooperation between hospital administrator, clinician, infection control team, microbiologist and hospital pharmacist

- Updating education on antibiotic use for clinicians, nurses and pharmacists regularly [14,40] and Detection of patients colonized with communicable resistant bacteria

Summary and Conclusion

Antibiotic overuse and misuse among dentists is substantial [6]. It is of global concern because of the spreading and developing resistance of most common bacteria to most inexpensive generic antibiotics. Antibiotic resistance now has been universally identified as public health priority and necessary plan of action to combat resistance should be developed. Improving the quality, not just the quantity of medication will require public and professional education towards rational use of antibiotics. Better diagnostic tests, promotion and evaluation of medical and veterinary practice guidelines, restriction of antibiotic use as growth promoters in food and animals, development of novel antibiotics are required.

There is an urgent need to raise public and professional awarenesss regarding the risks of antibiotic use not only in dentistry but all aspects of medical care. Ignoring these problems will undoubtedly result in an increase in incidence of untreatable dental infections and most importantly, death of patients from dental disease in the future [1]. Patient providers and health care leaders must make a serious commitment to change the dynamics of outpatient prescribing.

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