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Review Article

RECENT TRENDS IN ANTIBIOTIC THERAPY IN DENTISTRY – AN OVERVIEW

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ABSTRACT
The Golden era of antimicrobial chemotherapy began with clinical use of penicillin in 1941, which revolutionised health care over last seven decades. In spite of developing newer and broader spectrum of antibiotics, several of diseases are increasing in their incidence. The use of antibiotics as an adjunct in the management of orofacial infections is an important treatment option and when clinically indicated is of therapeutic benefit to the patient (Pogrel, 1994). However systemic antibiotics should be used with restraint because of the possibility of allergic reactions, toxicity, side effects and the development of resistant strains of microbes (Mata *et al.,* 1985). This article presents an overview of usefulness of older antibiotics compared with the newer one, with emphasis on spectrum of activity, side effects and cost. To provide a contemporary view of the drug-verses-microbe relationship, also covers principles of anti-microbial therapy; review of relevant articles and also about what is future in research of anti-microbial agents (AMA).

INTRODUCTION
The Golden era of antimicrobial chemotherapy began with clinical use of penicillin in 1941, which revolutionised health care over last seven decades. In spite of developing newer and broader spectrum of antibiotics, several of diseases are increasing in their incidence. The emergence of penicillin resistant anaerobes has become common in odontogenic infections. The bacteria are nearly infinitely adaptable and can become resistant if given sufficient sub lethal exposure to an antibiotic. When this resistance is achieved by even a few bacteria, it can easily be passed on to other bacterial cells. These genetically altered resistant organisms may continue to be well ahead of our efforts to control infectious diseases.
Considering above situation it is appropriate that we reassess antibiotics value and time has come to consider rational antibiotic therapy. The use of antibiotics as an adjunct in the management of orofacial infections is an important treatment option and when clinically indicated is of therapeutic benefit to the patient (Pogrel, 1994). However systemic antibiotics should be used with restraint because of the possibility of allergic reactions, toxicity, side effects and the development of resistant strains of microbes (Mata *et al.,* 1985). This article presents an overview of usefulness of older antibiotics compared with the newer one, with emphasis on spectrum of activity, side effects and cost. To provide a contemporary view of the drug-verses-microbe relationship, also covers principles of anti-microbial therapy; review of relevant articles and also about what is future in research of anti-microbial agents (AMA).

Rational Antibiotic Therapy
The medical literature abounds with studies illustrating the global increase in the burden of antimicrobial resistance among gram-negative pathogens. However, wide regional differences exist, accentuating the need to take into account the local epidemiology when making decisions about empirical therapy for serious infections (Arias and Murray, 2009; Pfeifer *et al.,* 2010). Successful use of antimicrobial agents must be rational, which is a process of providing essential drugs to those who need them at the right time, in right dose, at right cost and through the right route. The clinician should know enough about the AMA

to select the right one and to administer it by the right route, in the right amount, at the right interval, for the right length of time. Irrationalities in AMA's usage like over prescribing, under prescribing, use of ineffective/harmful drugs and combinations and improper diagnosis which forms the base of most of these irrationalities. The two most important considerations in rational antibiotic therapy are the type of the patient i.e. hosts factors like age, systemic conditions, immune status and the likely infecting organisms. The fight against microorganisms began with discovery of penicillin in 1928. Antibiotics cured or controlled tuberculosis, syphilis, pneumonia and other bacterial infections; however clinician must understand the impact of antibiotics on patients and on the quality of public health. As health care providers we all should understand above problem and write a safer and more effective prescription for the future.

Antibiotic treatment is a double edged sword that alters the natural balance of organisms. Each time antibiotic is used to eliminate bacteria other pathogens gain strength with resistance increasing proportional to amount of time drug is used. Antibiotic are one of the few kinds of drugs that affect not only a single patient but entire populations of individuals through their collective effects on microbial ecology. By stimulating the development of resistant strains of bacteria, these medications permanently alter the microbial environment. Dentist, physicians and patients have a serious responsibility to understand why antibiotics must be administered with caution and adhere to principles that govern their appropriate use. In a study which investigated the prescribing of antibiotics to emergency dental patients by primary healthcare workers concluded that both general medical and general dental practitioners had prescribed antibiotics inappropriately to patients with dental emergencies (Thomas *et al.,* 1996). Evidence from further studies further suggests that antibiotics are being prescribed inappropriately within general dental practice (Palmer *et al.,* 2000; Palmer *et al.,* 2000; Palmer *et al.,* 1998; Baker and Qualtrough, 1987; Abbot, 2000).

Pulpitis, Apical periodontitis, draining sinus tract or localized swelling can usually be treated endodontically without antibiotics. The circulation within the pulp is compromised in the presence of inflammation/infection. Because an antibiotic is carried by vascular system, its ability to reach bacteria in a therapeutic concentration will be limited. This environment diminishes the efficiency of the antibiotic. Endodontic treatment/access opening of tooth and removing the bacteria and their by products thoroughly debriding the root canal system-effectively eliminates the infection, curtails the inflammation and promotes healing. Swelling can be drained through the tooth/through soft tissue incision.

Pain alone/localized swellings do not require antibiotic treatment. Patient in poor health/who are immune compromised are more likely to need antibiotics. Swelling/fever that escalates within 24 to 72 hours period may indicate that an infection is spreading. A useful indicator for the use of antibiotics is elevation of temperature by 1.5° C. A large, diffuse swelling may require antibiotics as well as surgical drainages. Patients who have cellulites/extra oral swelling, lymphadenopathy, elevated body temperature, malaise/unexplained fever usually require antibiotic therapy and surgical drainage. Antibiotics can safely be discontinued after 2 to 3 days provided that satisfactory drainage has been achieved, the temperature returned to normal and the swelling is resolving. For periodontal surgery antibiotics are indicated for most patients with compromised immune system. When the defence are down antibiotics are sound. Antibiotics are an adjunct to treatment. The patient's own immune system provides cure. The use of antibiotic prophylaxis during placement of implant is controversial. But antibiotic prophylaxis in 3rd molar removal has no value unless the immune system compromised.

Penicillin is effective against most aerobic and anaerobic bacteria that are commonly present in the oral environment. Amoxicillin, a derivative, has a broader spectrum of activity and is a good choice for immune compromised patient. However, treatment with amoxicillin increases likelihood of inducing antibiotic resistance.

ß-Lactam / ß-Lactamase Inhibitor Combinations

Classic ß-lactam inhibitors, such as sulbactam and clavulanate, have variable inhibitory activity. In a study the cure rate of patients with cystitis treated with amoxicillin-clavulanate was 93% suggesting that

amoxicillin clavulanate may be successful in the treatment of simple infections (Rodriguez-Bano *et al.,* 2008). Studies suggest that the use of cephalosporins, including cephamycins and cefepime, is associated with a worse outcome compared with the use of carbapenems, despite apparent in vitro susceptibility (Zanetti *et al.,* 2003). Cephalosporins are therefore not recommended in patients with suspected or confirmed infections with Extended-Spectrum ß-Lactamase (ESBL) Producing Enterobacteriaceae. Carbapenems are considered first-line agents in treating infections caused by ESBL-producing organisms (Zanetti *et al.,* 2003). Some studies have observed a suboptimal response to quinolones vs carbapenems in ESBL-producing isolates with retained susceptibility to quinolones (Endimiani *et al.,* 2004). Aminoglycosides, fluoroquinolones, and trimethoprim-sulfamethoxazole should be used with caution. Clindamycin is an appropriate substitue if the patient is allergic to penicillin. It is a B-lactamase inhibitor highly effective against orofacial infections. Erythromycin, which is commonly prescribed for penicillin allergic patients, has been shown to be ineffective against most of the anaerobes associated with orofacial infections. Other antibiotics are now preferred. Clarithromycin is another acceptable penicillin substitute. It has some advantage over erythromycin. It is effective against facultative anaerobes and some of the obligate anaerobes. Metronidazole is a synthetic antibiotic that is highly effective against obligate anaerobes but is not effective against facultative anaerobic bacteria. Also active in vitro against ESBL-producing organisms are the ß-lactams temocillin (Glupczynski *et al.,* 2007) and pivmecillinam (Nicolle and Mulvey, 2007) the carbapenems biapenem (Jia *et al.,* 2010), faropenem (Mushtaq *et al.,* 2007), and tomopenem (Koga *et al.,* 2005). More data are needed to support their use in the clinical setting.

If penicillin is ineffective after 48 to 72 hours, metronidazole is a valuable anti-microbial agent for combination antibiotic therapy. Proper dosage and selection of an antibiotic with the right spectrum of activity are equally important. Treatment regimens should be short and aggressive to minimise the development of resistant bacteria and to achieve a therapeutic concentrations. The patient must understand clearly that adherence to the dosing schedule is critical to eliminate the infection. A loading dose of 1000 mg of penicillin VK should be followed by 500 mg every 6 hours for five to seven days. Consider contacting the patient 24 hours after administration of antibiotics to assess the patient condition. If there is no improvement after 48 hours, penicillin can be supplemented with a dosage of metronidazole. The recommended oral dosage of metronidazole is 250 mg (500 mg loading dose every 6 hours). The usual adult dose of clindamycin begins with a loading dose of 300 mg followed by 150 mg every 6 hours. Clarithromycin may be given in a dose of 250 – 500 mg every 12 hours.

Principles of Antibiotic Dosing for Orofacial Infections

Use high dose for a short duration for dose dependent AMA's. Antibiotic success depends on monitoring the blood and tissue concentration above MIC for the target organism, are more critical with the dose dependent AMA's. It is more critical with the B-lactom prolonged dosing beyond, which is necessary only increases antibiotic toxicity, allergy, and antibiotic resistance. The bacteriostatic agents including macrolides, tetracycline and clindamycin act at any reasonable concentrations. Achieving blood levels of antibiotic 2 to 8 times of MIC is necessary to compensate for the tissue barriers that impede antibiotic penetration to the site of infection, as one has to consider variabilities in gender, age, sex etc. Using an oral antibiotic loading dose is desirable as without loading dose it takes 6 to 12 hour to achieve maximum thereapeative blood and tissue levels via oral route. The AMA's are terminated when the host defences have gained control of the infection.

Some explanations can be put forward as to why antibiotics are being prescribed irrationally first being, that the practitioners may have a poor understanding of the pathological processes involved in pulp and periapical diseases (Palmer *et al.,* 1998). Furthermore, there could be a lack of knowledge of the indications for effective antibiotic use.

It is possible that facilities were not available in the primary health care centres for the provision of surgical treatment. In a recent study (Thomas *et al.,* 1996) lack of time and uncertainties of diagnosis were cited as reasons for antibiotic prescribing. Qualitative research is required to find out why this

problem of inappropriate antibiotic prescribing is so intractable. Methods also need to be developed to enable practitioners to change their prescribing behaviour.

CONCLUSION

Future Direction

Researchers believe that studying of bacterial function at the molecular level holds the key to rapid new drug development. Future antibiotics may "customized" to disarm bacteria genetically and prevent development of resistant strains. Scientists are using high tech tools such as super computers x-ray crystallography to study enzymes that promote bacterial resistance. Over 100 naturally occurring antibacterial peptides have been identified. Eventually peptides may form new category of antibiotic that not only kills bacteria, but also neutralizes enzymes that make bacteria resistant. Genetic is another promising area of exploration. Scientists discovered how the genetic trigger works for diphtheria. Antibiotics preventing this trigger/virulence could be developed. Techniques to enhance host immune response are also the promising area.

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