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ANTIBIOTIC RESISTANCE IN ORAL AND MAXILLOFACIAL SURGERY: A REVIEW

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INTRODUCTION

Orofacial infections have plagued humankind for as long as our species has existed. Most of these infections are odontogenic in origin and one of the most frequently occurring infectious processes known both to the antiquity and present day health practice.[1] Antibiotics can destroy bacteria (bacteriocidal) or sometimes just nullify growth (bacteriostatic). Most antibiotics in human use as antibacterials are natural products, elaborated by one species of microbe (bacteria or fungi) as chemical weapons, often in times of crowding, to destroy other microbes in the neighbouring microenvironment. Over the past 60–70 years most antibiotics have been discovered by screening of soil samples for such natural products that destroy bacteria, including known pathogens, first on culture plates and then in animal infections. These include penicillins and cephalosporins from fungi and a host of antibiotics from different strains of the filamentous bacterium Streptomyces, such as streptomycin, erythromycin, tetracycline and vancomycin. Semisynthetic modifications have produced second- and third generation b-lactams of both the penicillin and cephalosporin classes whereas total synthesis has created the second-generation erythromycins — clarithromycin and azithromycin. As of the end of 1999, only the fluoroquinolones (for example, ciprofloxacin) represent a totally synthetic, significant class of antibiotic.[2]

Antibiotics are usually prescribed when symptoms first appeared without first determining either the cause of the disease or the chemotherapeutic susceptibility of the microbe. Consequently, there has been a significant rise in the antibiotic resistance of important pathogenic genera and today, infectious diseases are the leading cause of death worldwide.[3] In t day's scenario more than 95% of Staphylococcus aureus isolates globally are resistant to penicillins. An initial response to penicillin resistance was the development of methicillin, a semisynthetic penicillin. By the late 1980s even methicillin resistant Staphylococcus aureus had become prevalent in many hospitals and difficult to treat.[4]

Resistance is defined as bacteria that are not inhibited by usually achievable systemic concentration of an agent with normal dosage schedule and/ or fall in the minimum inhibitory concentration ranges. Likewise the multiple drug resistance is defined as the resistance to two or more drugs or drug classes. Acquisition of resistance to one antibiotic conferring resistance to another antibiotic, to which the organism has not been exposed, is called cross resistance.

There are four specific mechanisms by which bacteria acquire resistance genes:

1. Spontaneous mutation

This is the original source for all antibiotic resistance, because bacteria have maintained genes that encode for resistance of naturally occurring antibiotics of other species.[5]

2. Gene transfer

Bacteria can undergo conjugation with a transfer of genes as plasmids, which are a composition of cytoplasmic loops of DNA that encode for antibiotic resistance, and transposons, which are able to insert themselves into the genome of the recipient cell.

3. Bacteriophage

Viruses infect bacteria and can insert genetic material and take control of the host's genetic and metabolic machinery, which may encode for antibiotic resistance mechanisms.

4. Mosaic genes

Bacteria can absorb directly the fragments of the virally altered genome of dead members of related species to form a "mosaic genome" of genetic material from varying

sources. This type of gene derivation is responsible for the non–β-lactamase penicillin resistance in Streptococcus pneumonia and meningococci and ampicillin resistance in Haemophilus influenzae and gonococci.[5]

Antibiotic resistance mechanisms

Once the genetic machinery is in place, bacteria exert antibiotic resistance by various pathways that are broadly classified in four ways.

1. Drug inactivation or modification

The destruction or inactivation of the antimicrobial agent is accomplished by the induction of specific drug-inactivating enzymes, such as those that inhibit b-lactams or aminoglycosides. Numerous gram-positive and gram-negative bacteria, such as Staphylococcus aureus, Enterococcus faecium, Escherichia coli, Pseudomonas aeruginosa, H. influenzae, Bacteroides, and many strains of Prevotella have this capability. Another method used by bacteria to withstand antimicrobial attack is the ability to synthesize neutralizing enzymes.

2. Alteration of microbial membrane permeability

Alterations in membrane permeability can cause decreased uptake or increased efflux of the antibiotic. The types of antibiotics most often affected by this mechanism are the b-lactams, quinolones, tetracyclines, erythromycin, and the aminoglycosides. The gram-negative rods E. coli, P. aeruginosa, and Salmonella typhimurium also have this capability. Porins within the transmembrane protein matrix are specific for various antibiotics, and the loss of a specific porin confers resistance. E. coli and Staphylococcus epidermidis also can resist tetracyclines, macrolides and quinolones by this mechanism.[6]

3. Alteration of target site

Enzymes responsible for cell wall synthesis, the transpeptidases, can be altered slightly to produce less affinity for penicillins. These altered penicillin-binding proteins are most often seen in S. aureus and S. pneumoniae.[7]

4. Alteration in the concentration of drug target receptors

Many of the gram-negative rods have the ability to alter the number of drug receptors that bind antibiotics. The sulfonamide family is affected by such a mechanism.[6]

Newer antibiotics of interest

1. **New fluoroquinolones:** Moxifloxacin and gemifloxacin are two new fluoroquinolones whose spectrum includes the Viridans streptococci, oral anaerobes, and actinomyces. They are also effective against sinus pathogens, Staphylococci, Enterobacteriaceae, and B. fragilis. Their broad spectrum is a relative disadvantage when the target is a fairly small range of bacteria.

2. **Oxazolidinones:** Linezolid is the prototype of this new class of antibiotics. Its effectiveness against methicillin and vancomycin-resistant staphylococci and enterococci indicates that it should be reserved for these highly resistant organisms.[8]

3. **Ketolides:** Telithromycin is the first representative of this new class, which is related to the macrolides. Its spectrum includes the pathogens against which the macrolides have been historically effective, including S. pneumoniae, Mycoplasma, H. influenzae, Chlamydia pneumoniae, and Legionella pneumophila.

4. **Pristinamycins:** Quinupristin/dalfopristin, a combination of two pristinamycin antibiotics, is especially effective against vancomycin resistant Staphylococci. Its use generally has been reserved for infections caused by these organisms.[6]

Reversing resistance

Consumers also should refrain from demanding antibiotics for colds and other viral infections and might consider seeking nonantibiotic therapies for minor conditions, such as certain cases of acne. Physicians, for their part, can take place immediate steps to minimize any resistance ensuing from required uses of antibiotics. When possible, they should try to identify the causative pathogen before beginning therapy, so they can prescribe an antibiotic targeted specifically to that microbe instead of having to choose a broad-spectrum product. Washing hands after seeing each patient is a major and obvious, but too often overlooked, precaution. To avoid spreading multidrug-resistant infections between hospitalized patients, hospitals place the affected patients in separate rooms, where they are seen by gloved and gowned health workers and visitors. Reversal of resistance requires a new awareness of the broad consequences of antibiotic use, a perspective that concerns itself not only with curing bacterial disease at the moment but also with preserving microbial communities in the long run, so that bacteria susceptible to antibiotics will always be there to outcompete resistant strains.

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