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Review Article

Dental Infections and Antimicrobials

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Abstract

The present study was intended to review antibiotic use in dental infections or diseases and its implications. This study was based on literature from Google Scholar, Google, Scihub, PubMed, and a link provided by AIMST and MAHSA Universities, Malaysia. Antimicrobials are extensively applied as therapeutic and prophylactic agents in dental infections. Inappropriate antibiotics use leads to anti-microbial resistance. The current study suggests periodontal disease and dental caries are the two leading causes for tooth loss that are considered as a maximum burden over oral health which affects 1/5 to 1/2 of the global population. This study suggests that irrational and overprescribing of antimicrobials in dental disease leads to anti-microbial resistance. Inclusion of the primary oral health care in national primary health care programs will promote dental health care.

Keywords: dental infection, antibiotics, microbes, resistance

Introduction

The first time treatment of patient with penicillin as the first antimicrobial agent was done in 1942 [1]. The World War II resulted in extreme production of penicillin in 1943 [2]. Although, antimicrobial discovery turned as milestone for health science and quality of life for humans, however high antimicrobials use resulted in antimicrobial resistance by microbial strains [3]. "An immense genetic plasticity of bacterial pathogens that trigger specific responses that result in mutational adaptations, acquisition of genetic material or alteration of gene expression producing resistance to virtually all antibiotics currently available in clinical practice" is known as the natural law [4]. For instance, due to antimicrobial resistance offered by Shigella strains, in the mid of 20th century Japan suffered with Shigellosis epidemic. Later, scientists explained that such resistance to multiple antibiotics developed very fast, instantaneously, and appeared to be transferred from resistant into sensitive strains [5]. Before commercialization of penicillin, the bacterial penicillinase enzyme called β lactamase was identified [6]. Based on the analysis of available bacterial genome sequencing, the fresh database accounts nearly 20,000 resistant genes or rgenes of 400 different types of bacteria [7]. Facts suggest microbial resistance to extend to all types of natural or synthetic antimicrobials. Therefore, antimicrobial resistance altogether affects the treatment against infectious diseases, healthcare policies and planning as well. Massive reports suggest that dental surgeons often imprudently and irrationally prescribe huge quantum of antimicrobials that leads to microbial resistance. Current study focuses on the facts related to dental infections (DI), antimicrobial use, microbial resistance, and their effects over global health [8].

Present review was based on literature from Google Scholar, Google, Scihub, PubMed, and scientific links provided by AIMST and MAHSA Universities, Malaysia. Some unpaid full paper manuscripts were procured from other libraries under cooperation with AIMST and MAHSA uni-

versities.

Di Epidemiology

The periodontal disease (PD) and dental caries (DC) are two leading causes for teeth loss that are considered as maximum burden over oral health which affects 1/2 to 1/5 of global population [9]. Studies report that in India for almost 80% of patients (above 30 years age) teeth loss is attributed to PD [10]. Supporting to this, fact suggest widespread of PD in West Bengal state of India [11]. In Asian, African and Middle East countries the DC is the major threat for oral health [12]. Some research claims that DC is reduced in modern countries population, whereas recent studies reports substantial increase in DC rates. Study over 1225 subjects from Libyan population aged between 18 to 34 years, disclosed that just 5% of population got healthy periodontium [13]. Numerous reports state that PD severity and occurrence increase with patient age and PD is common in males and persons with poor oral hygiene. In rural and urban population, the existence of dental and other oral infections is more prevalent in paediatric and adult males as compare to females [14].

Last 4 decades witnessed the significant reduction of DC in various countries. For example, a Duch study revealed the DC incidence significantly decreased during the year 1990 to 2009 among 8 to 21 year old population in lower and higher socioeconomic groups. One of the British reports claimed that during 1973 to 2013 there was high reduction (51%) in DC of 15 years age cluster of 69,318 children that were aged between 5 to 15 years. Apart from it, the study also revealed that despite of significant improvement, the DC remained an important liability for national health care system. A 15 years Norway study showed 81 to 52.2% decreases in DC in 12 years age group children during 1985 to 2000. But after 4 years during 2001 to 2004 the DC prevalence raised to 59.8% with annual growth rate of 3.3%. However, from 1997 to 2004 decayed, missing, and filled teeth (DMFT) index was steady that is 1.6. Quite same DMFT was noticed in other Scandinavian countries. For almost 80 years in epidemiological studies, DMFT index is considered as most reliable tool for assessment of DC [15,16].

Di and Common Microbes

The PD and DC are most common chronic infectious dental diseases that are caused by microbes of oral cavity. Human oral microbiota is known to compose of more than 700 microbes, of which around 50% are non-cultivable. Various anatomical region, their bathing liquid, and saliva encompasses oral microbiota that comprises normal flora, for example: bacteria, fungi, archaea, viruses, and protozoa. Oral microbes freely float in saliva and constitute a complex ecological biofilm (BF) that attaches with various surfaces of oral cavity. This BF often accounts for numerous systemic and local diseases. A study claimed varied infection of anaerobes with facultative anaerobes. Study identified viridans streptococci (streptococcus gram positive bacteria) as principle microbe that causes PD, dento-alveolar (DA) infection, and pericoronitis (PC). Studies identified Peptostreptococcus micros, Fusobacterium, Prevotella and Porphyromonas species as principle microbes to cause DA infection; Peptostreptococcus micros to cause PD; Prevotella species (around 34%) to generate beta lactamase; anaerobic microbes to cause 90% of root canal (RC) infections; and polymicrobial flora to frequently involve with Gram negative anaerobic bacteria [17].

Di and Nutritional Causes

Diet performs an active role in DC and erosion of enamel. A study explained DC as a state that involves demineralization of inorganic portion of tooth with dissolution of organic matter attributed to multi factor etiology. Another study explained DC as multi factor state attributed to interaction of host, DC associated bacteria, and cariogenic diet. Demineralization of dentine and dental enamel is related to organic acids that are generated in dental plaque (DP), which is attributed to anaerobic microbes that metabolizes sugar diet. Dietary acids assist in development of enamel defects, for example: enamel hypoplasia, and fluorosis. As soft drink comprises acids and sugars, so possess acidogenic and cariogenic property that leads to enamel erosion (EE) and DC. Many studies suggested positive correlation of consuming soft drinks with DC and EE. Report suggest 2 to 10 years children consuming high amount of soft drink possess high rate of DC compare to children that consumes high juice, milk, and water in diet [18].

A study reported that 14 to 15 years boys consumed high sugar drinks compare to female counterpart. The two or more glass of sugar drinks exhibits significant relation with dental caries. Moreover, high sugar drink consumption was correlated with gender, family income, and mother education. Another study suggested that high intake of fizzy or soda pop drink by children is major reason for higher DC rates. Studies reveals that poor intake of micronutrients like copper and vitamin B2, B12 and D are associated with high rate of DC and PD. Less consumption of milk and dairy products are linked to DC in children. The high consumption of non-alcoholic carbonated drink and less consumption of milk and dairy products during children and adolescence stage increase the risk for systemic diseases and DC [19].

Numerous studies claimed that milk consumption assures intake of several macro and micronutrients that further promote and protect the health from several diseases. Facts suggest that when sugar consumption was less among inuit population of Ethiopia, Alaska, Nigeria, Sudan, and Ghana (who often lead traditional life) have negligible rate of DC; but as economic condition of these geographical population improved the amount of sugar and carbohydrate increased in their diet which parallelly increased the DC rate. Many studies revealed that frequent consumption of fermented sugars assists in DC formation, like sucrose on fermentation produces lactic acid that lowers pH, which disturbs the oral environment and affects the normal demineralizing and remineralizing processes that finally leads to dental EE [20].

Di and Biofilm

Investigators identified huge consortium of microbes in the oral BF that comprises about 1000 distinct microbial species of bacteria, fungi, and virus. The BF is functionally and structurally organized microbial community in 3D configuration, surrounded by extracellular material matrix. In oral BF many microbes are natural inhabitants, and some of them have quality to damage mineralized and soft tissues of gums and teeth [21].

The 17th century witnessed the first report over DP and oral BF. The DP is responsible for DC, and PD. Facts suggest each mg of dental plaque to contain 1011 microbes. Growth of several microbes and BF formation is promoted by three major factors, namely mouth cavity (rich with nutrition), temperature 35/36°C, and pH 6.75-7.25. After brushing and rinsing of teeth, the oral cavity saliva proteins forms thin film over teeth surface. Microbes using microfilaments attach to such thin film of proteins. Any alteration in oral environment that is favorable for microbes increases the microbial population and communication through secretion of signal molecules thereby creates a community. Microbial secretory proteins, nucleic acids, polysaccharides, and other substances of extracellular matrix comprising proteins and nutrients from saliva forms BF matrix. The key microbial species contained in DP of unhealthy region are different in comparison to those of healthy region. However, in healthy region of mouth cavity, the disease causing microbes are still found but in low quantum. Formerly two hypothesis were proposed, firstly DC is caused by high quantum of microbes in DP called as Non-specific Plaque Hypothesis; secondly DP comprises specific type of cariogenic bacteria (like: Streptococcus mutans and Streptococcus sobrinus) in DP called as Specific Plaque Hypothesis. Two hypotheses were reunified called as Ecological Plaque Hypothesis. Present hypothesis of DC formation explains the stressing of normal oral microbes environment to alter certain disease related microorganisms [22,23].

Di and Antimicrobial Associated Resistance

The DI is commonly treated with antimicrobial agents. The antimicrobials are widely abused in the dental and medical treatment. Unsuitable use of antimicrobial drugs leads to serious adverse events and antimicrobial resistance. Antimicrobial agents play an important role in the treatment of DI against microbes particularly bacteria. The increased antimicrobial burden is attributed to their cost and detrimental effects. For progressive DI, the antimicrobials are considered as the first choice, but they offer the increased incidence of antimicrobial resistance. As per WHO report, the pandemic countries with high use of antibiotics may lead to community issues. Previous study also shows a drastic increase in DI associated resistance cases on high use of antimicrobials. In supercomplex oral cavity, there exists large number of microbes in a form of biofilm. The composite of ecosystem causes progression of disease conditions involving different microbial species. All the microorganisms do not cause the odontogenic infections as some of the microbial species are non-pathogenic. Antibiotic treatment should be more rational for dental care at the individual and community level. An antimicrobial treatment must consider safety, efficacy, affordable cost, selection method, formulation, and duration of drug response to avoid toxicity and resistance. The ideal antimicrobial treatment mainly focuses on administration of right drug, at right time, in right dose and for right duration of treatment.

While prescribing antibiotics the dentists must consider the pharmacokinetics and pharmacodynamics parameters. Recently many newer antimicrobial drugs are established in the market, of which only few drugs are suitable for dental infections. Among antimicrobials, the penicillin class is considered as the most suitable for the treatment of various dental infections. However, the inappropriate use of antimicrobials leads to antibiotic resistance. Previous study reveals that combination of amino penicillin and metronidazole exerts synergistic effect against the anaerobic infections. Preferably, there is a need to go for microbial cultures and sensitivity test before initiating the antibiotic therapy. After laboratory analysis, the antibiotic treatment should be started empirically. The selection of antibiotic treatment is generally based on severity of infections. For example, in case of severe odontogenic infections one may choose combination of penicillin and metronidazole [24,25].

Dosage/Frequency and Duration of Antimicrobials

To achieve a therapeutic effect, it is important to consider the dosage and duration of antibiotic treatment. The antibiotic treatment approaches such as TDK (time dependent killing) and CDK (concentration dependent killing) plays an important role in the lysis of bacteria. As TDK achieves drug effect at particular time period, so maintenance of therapeutic levels for a longer period of time would exert the greatest effect. Moreover, as TDK do not involve concentration dependent effect, thus it is mainly recommended to increase the frequency of drug administration rather than dose adjustment, for example penicillin class of antibiotics. The CDK is associated with bacterial cell death and concentration of drug. An increase in dose would enhance the killing effect for example metronidazole. Recent literature advocates the use of antimicrobials in high dose for a shorter period [26].

Approaches of Antibiotic Treatment and Management in Di

The conditions of uncomplicated endodontic lesion suggest the use of antibiotics in dental practice (Table 1) [27-34].

During treatment of infectious diseases when dentist prescribes the antimicrobial drugs to inhibit or eradicate the bacteria, it often leads to simultaneous increase in antimicrobial resistance. This is commonly attributed to inappropriate prescriptions of dental surgeons, wherein they massively prescribe the antimicrobial drugs for the treatment and prevention of DI. This consistent increase in antimicrobial drugs develops the high antimicrobials resistance and further worsens the patient quality of life. Antibiotic

use of immunocompromised patients has a high risk of unwanted effects, which necessitates the need to monitor the blood components especially neutrophils count. In case of any deviation from the normal values, one must restrict the specific antimicrobial drug. Generally, the treatment strategies and therapeutic response differs from case to case. Oral infections are generally caused by the complex form of microbes (bacteria and fungi) associated with the biofilms, and these microbes enhances the synthesis of cytokine thereby promotes the inflammation. Oral infections are mainly caused by poor oral health and involve different age groups. Due to poor dental health, the progression of dental disease is associated with several other diseases such as head and neck cancers, endocarditis, eating disorder and Sjogren's syndrome. With the advent of emerging antimicrobial resistance, the dental surgeons must improve their practice of antimicrobial prescription and must strictly follow the guidelines and need for public awareness before prescription of antimicrobials [35].

Table 1: Antimicrobial drugs useful in dental practice

Condition	Treatment approach
Acute Necrotizing Ulcerative Gingivitis	The primary choice is metronidazole in addition to penicillin group [27]
Odontogenic infection	Preferred fluoroquinolones particularly moxifloxacin [28]
Gram negative odontogenic infections	Aminoglycosides [29]
Bone and gingival tissues infections	Tetracyclines [30]
Anaerobic bacteria infections	Clindamycin [31]
Obligate anaerobes infections	Metronidazole [32]
Oral infection, but not type I hypersensitivity to penicillin group of drugs.	Cephalosporins [33]
Odontogenic infections	Amoxicillin+clavulanate [34]

Primary Health Care (Phc) and Primary Oral Health Care (Pohc)

Health is considered as human right (HR). The HR is conserved and warranted by all countries for individuals and cluster against activities that are restricted with self-determinations and HR. The HR is universal. The PHC assures both health care and HR in developed and developing countries. At present necessary oral health services, oral health education program and continuous dental care program, with intervention were lacking across globe in LMIC. POHC is integral part of PHC and countries require development of POHC program to address the global issue of dental care [36].

Conclusion

The oral cavity is a native terrain for different microorganisms, that often act as a resource pool for pathogenic microorganisms causing oral, dental, systemic, and local infections. Unnecessary, excessive, and overprescription of antimicrobials contributes to the development of resistant microorganisms. Numerous studies claim that a minimum of 30-50% of antimicrobials is prescribed with no scientific grounds. Multiple studies supported that dentists must prescribe antimicrobials to control the well-documented local/ systemic infections, but not for inflammation. In dental diseases, the antimicrobials use as prophylactic were suggested only in case of suspected systemic infections. The resistance offered by antimicrobials is a natural phenomenon that occurs with microbial evolution. Humans' actions enhanced the pace of microorganism development and resistance dissemination. The inappropriate antimicrobials use contributes to developing microbial resistance. Therefore, while prescribing antimicrobials, healthcare professionals must acknowledge that antimicrobials may lead to resistance emergence and dissemination. The present study recommends that POHC inclusion in national PHC will promote the rationality of dental care.

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