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Review Article

Application of omics in personalized oral health care: A paradigm shift

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ABSTRACT

Periodontal disease and Dental caries are the most common oral diseases in adult populations worldwide and is a major public health concern due to its substantial cost to the oral health care system. During recent years a significant amount of evidence has been produced on the pathogenesis and risk factors of oral disease and its association with systemic diseases and general health. Personalized medicine is an emerging field within health care that uses an individual's genomic information and its resulting products RNA, proteins and metabolites to customize care that is specific to that individual. Customized oral health care is cost effective individualized strategies for oral diseases. The goals of Customized oral health care are to determine a person's susceptibility or risk of developing disease, establishing a diagnosis, determining disease patterns and prognosis, determining appropriate interventions, predicting and monitoring therapeutic response, and predicting an individual's response to environmental and microbial challenges. This review highlights the holistic approach to improve oral health care.

Keywords: Customized, Genetics, Microbiomics, Personalized medicine

INTRODUCTION:

Periodontal disease and Dental caries are the most common oral diseases in adult populations worldwide and is a major public health concern due to its substantial cost to the oral health care system.[1] Dental caries is slowly progressing and prevalent in all age groups. It is a chronic disease with localized destruction of susceptible dental hard tissues by acidic by-products from the bacterial fermentation of dietary carbohydrates.[2]

Periodontitis is a complex disease with multi factorial etiology which includes modifiable and non modifiable factors. It is characterized by inflammation and destruction of tooth supporting structures, in severe cases leading to tooth loss. It is also highly associated with systemic inflammation resulting in an increased risk for chronic diseases such as cardiovascular diseases, diabetes, metabolic syndrome, pneumonia and rheumatoid arthritis.[3]

Although definitive mechanisms still remain unclear the inflammation and infection via outgrowth of multiple opportunistic microbes in the oral environment including Porphyromonas gingivalis, Tannerella forsythus, Aggregetebacter actinomycetemcomitans are the contributing factor.[4] While the presence of microbial pathogens is a factor leading to this condition, it is not solely sufficient to cause periodontitis. It was recently proposed that dysbiosis of the oral microbiota leads to periodontitis via interference of the host-microbial homeostasis, rather than simple outgrowths of a few pathogens.

Lifestyle related factors such as smoking and dietary patterns as well as oral hygiene have also been correlated with the prevalence of periodontitis. Response of inflammatory reaction in periodontal diseases depends on its intensity and duration, also depends on the nature of the existing oral microbiome and the impact of environmental and genetic factors characteristic to every host. Inter individual variability as a consequence of host environment microbial interactions give rise to a specific clinical phenotype represents biologic reactions unique to each individual.[5]

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Current oral care practices rely on the emergence of signs and symptoms prior to the initiation of treatment procedures. Despite of high costs associated, long term morbidity and prognosis may often be poor. This is due to inadequate control of the disease manifestations treatment failure, disease recurrence and the reappearance of severe secondary complications contributing to relatively low quality of life for the treated persons and resulting in tooth loss. [6,7]

Change of concept:

Traditional treatment methods have enabled to better manage disease, but for the most part it has been ineffective in dealing with the complex chronic diseases which lacks personalized plan for disease prevention and oral health promotion.

From Reactive To Preventive:

Reactive methods of Treatment:

This method of treatment is cause related therapy. In this method the cause of the disease is identified and treated.(Figure 1) There will be some amount of uncertainty in treatment out come and stability. This method has got its own limitations like the identification of multiple factors and prediction of occurrence of disease.

Figure 1: Traditional methods of treatment

Table 1: Traditional methods of dental evaluation
Chief complaint
History of present illness
Medical and Dental history
Examination
Diagnosis and treatment

Figure 2: Customized methods of treatment

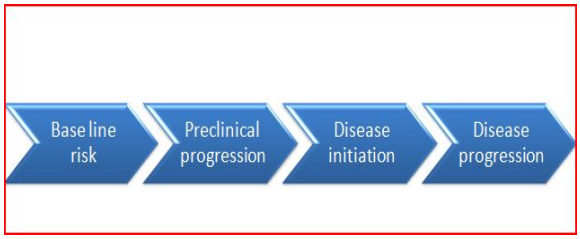

Table 2: Customized methods of evaluation
Oral health profile
Present oral health status
Oral health risk analysis
Disease susceptibility
Treatment plan

Traditional methods of oral evaluation (Table 1) depend on the chief complaint of the patient and the elaboration of history of present illness. After recording the medical and dental history depending on the clinical features the case will be diagnosed and treated. Whereas prospective method of evaluation is based on the oral health profile. The present oral health status is recognized and the risk will be analyzed.(Figure 2) Depending on the likely hood of developing disease strategic health plan will facilitate new form of health care.

The emerging concept of customized oral health care (Table 2) focuses more on prevention, risk assessment, and preemptive intervention. It addresses the need to reduce costs, increase efficiencies, and improve patient care, especially for those patients presenting with chronic oral disease.

The recognition of the factors involved in various diseases helps explain why there are a high number of no responders to certain treatment. This in turn leads to an increase in the number of patients needed to treat, leading to dentists adopting trial-error paradigms when treating patients. Inter-individual variability in patient responses can also increase adverse events and

reduce effectiveness, or both, leading to sub-optimal care and adding to the costs of care.

Environmental, behavioral and genetic factors influence the progression of oral diseases. These diseases differ in the susceptibility and response in each individual.

Chronic pathology generally triggered at the molecular level with consequent symptomatic manifestation of disease. A laboratory based detection of pathology of specific molecular patterns would create a well founded basis for the desirable predictive care giving an opportunity for optimal dental care. This requires application of innovative biotechnologies to predict pathology, and devising of appropriate and timely preventive strategies and individual treatment planning. [8,9,10]

Personalized medicine:

A medical model that proposes the customization of heath care with all decisions and practices being tailored to the individual patient by use of genetic or other information.[11]

Personalized medicine can serve in [12]

1. Diagnose disease in an individual
2. Assess an individual's risk of disease
3. Identify whether an individual will benefit from particular interventions
4. Tailor dosing regimens to individual variations in metabolic response

Personalized medicine in oral health care refers to application of cost effective and individualized strategies for diagnosis, monitoring and treating disease. It is not the pledge of the future; it is becoming the current state in diagnostics and therapeutics, Innovations based on genetic and molecular designs offer patients better care at lower cost because conditions are predicted sooner, diagnosed more accurately and treated more effectively

Thus the current traditional concept 'ONE SIZE FIT TO ALL' might no longer be valid in a few years. There is much evidence in literature that a person's health and behavior will be modified by his or her unique genetic composition and the epigenetic factors. Furthermore, there is evidence that psychosocial factors that are unique to the individual play a role in the etiology of pathogenesis and disease progression.[13,14]

Individualized treatment approach can allow screening, early intervention and treatment to be concentrated on those who will benefit reducing expense and side effects for those who are not likely to benefit.[15,16]

Customized oral health care can facilitate disease prediction, prevention & treatment strategies by;

1. Determining if someone is at increased risk of developing a disease, followed by promotion of and support for compliance with available preventive strategies
2. Diagnosing disease earlier in development using optimal surveillance there by allowing more effective interventions and treatment options
3. Enhancing therapeutic efficacy by ensuring the most appropriate drug is used and that the dosing regimen takes into consideration any genetic variants which may influence metabolism of drug
4. Avoiding preventable drug related complications and side effects.

Omics and customized oral health care:

Omic technology offers very good potential to shift from the traditional methods to Individualized approaches.

Microbiomics[17]

The emerging field of research that targets the microbiome for therapeutic purposes.

Microbiomics aims to understand how microorganisms interplay with its host's physiology and health by analyzing their distinct functions and interrelationships.

Microbiome is the biomarker of disease activity. Genomes collected through metagenomic techniques helps in engineering of therapeutic agents needed to manipulate the microbiome according to personal needs. Understanding changes in the microbiome at the early stages of chronic oral diseases would allow clinicians to diagnose & treat an unhealthy oral cavity before the appearance of any periodontal pockets. Additionally, the use of probiotics or other biological antimicrobial agents at early stages of disease could naturally restore microbial equilibrium and thus minimize need for antibiotics. Pharmacogenomics: Describing how human genetic variants influence drug response phenotypes.

Genetic variations of drug metabolism related genes have a significant effect on drug clearance.

Some individuals are poor metabolizers where as others metabolize drugs rapidly. Therefore patient's genetic profiles are of great interest to predict the efficacy of drug therapy and minimize its side effects.[12]

Genetics: Focuses on the effects of single genes in isolation.
Genomics: Focuses interaction between all genes in the genome with environmental factors.

Currently two forms of Chronic periodontitis, Aggressive periodontitis are distinguishable only by physiological and histological observations and don't include genomic and proteomic differences. Microarray technologies may provide a more accurate and reliable method of identifying periodontal disease subtypes through characterization of differences in gene expression profiles.[14]

Genomic analysis currently enables the identification of microorganisms associated with periodontitis that were previously unable to culture in lab.[15]

Proteomic analysis allows identification of different levels of protein expression in response to bacteria induced periodontitis can be detected & used in early diagnosis and prevention of disease progression. The information provided through the genomic and protemic technologies has the potential to dramatically improve oral health.

Epigenetics: Molecular mechanisms that link the genetic code and environment.

Barriers in clinical integration of genomics
Skepticism by providers and payers of the added value of genomics to improve patient care. Another challenge is needed to integrate genomic and proteomic profiles with clinical and health history data.

Application of customized oral health care in dental practice:

Dental caries

An individualized caries risk assessment will help to identify and understand the factors associated, so that a prospective oral health care plan can be developed.

The specific information gained from a systematic assessment of caries risk guides the dentist in the decision-making process to establish treatment and preventive protocols for the individual with oral disease and for those at risk.[18]

Risk assessment tools help in identifying the individuals at risk and also the type of risk low, medium or high risk. Several reports have shown that prevention of caries is more cost effective when compared to treatment of caries. Patient management protocols should be based on individuals risk level, age and compliance.[19,20] Evidence based dentistry suggests that examination for the development of carious lesions should be done once in a year. If there is any increase in risk such patients require frequent visits.[21,22]

Oral cancer

The common medical diseases underlying pathogenesis is not fully understood but involves multiple factors with the influence of genetic polymorphisms and single nucleotide polymorphism. Genomic research is very useful in identification of the biologic factors involved and designing various new diagnostic tools, thereby modifying the approaches.[23,24]

The incidence of Oral Cancer is increasing in the population. Research has revealed that many of the cancers have its own genomic signature, with some tumor-specific features and some features common to multiple types.[25] Many targeted therapies have been developed, and shown to be great benefit. In addition, Individualized approaches have recently produced some profound responses, with signs that molecular signatures may be strong predictors of benefit. Customizing cancer treatment based on specific molecular arrangements of an individual tumor offers a much better chance of delivering effective and long-lasting therapies.[26,27]The Indian Dental Association recommends an oral examination once annually to screen for early signs of oral cancer

Periodontal disease

Periodontal diseases are chronic inflammatory infections which affects both soft and hard tissues.[28] Local and systemic factors play important role in disease expression. Systemic

diseases like Diabetes, Cardiovascular diseases are associated with periodontal disease. Current periodontal disease assessment cannot determine the disease activity. These methods cannot predict future risk for disease. Personalized preventive methods will help to identify specific genotypes susceptibility and risk which further improves treatment modalities.[29,30]

Authors suggested in a study that the association between the frequency of preventive services and tooth loss events was not significant in low risk individuals weather the frequency of dental visits was once or twice annually. Preventive approaches should be planned for patients with high risk factors.[31]

Current scientific and technologic gaps for customized oral health care include[32,33]

1. Definitive linkages between both biomarkers and genotypes and clinical outcomes
2. Cost effective and non invasive imaging technologies for detection of pathologies of oral-craniofacial complex.
3. Clarification of the association between and among the environment microbiome and genetics
4. More accurate disease risk and drug response prediction
5. Improved drug design and delivery

Public awareness and acceptance of the benefits and risks of personal genomic sequencing are the critical elements in success of Customized oral health care.

Future directions for customized oral health care are Promotion of the concept of Participatory "Nothing about me without me" where patient is involved in all aspects. A number of evidence based studies strongly depends on doctor patient collaboration.[34]

Conclusion:

Customized oral health care improves our approach towards treatment of oral diseases. Individualised methods focuses on the shift in reactive treatment based clinical approach to predictive methods which shows importance of oral and systemic health. Application of scientific knowledge into clinical practice will have extensive effects on oral care.

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