Precision for Tooth loss–a New Periodontics

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Abstract

Precision dentistry as the name suggests "precise" meaning, taking care to be exact and accurate, especially about small details is defined as a contemporary, multifaceted, data driven approach to oral health care that uses individual characteristics to stratify similar patients into phenotypic groups. It is a paradigm shift that requires a new way of thinking about diagnostic categories. This approach uses patients' risk factor data (including, but not limited to, genetic, environmental and health behavioural), rather than expert opinion or clinical presentation alone, to redefine traditional categories of health and disease. Precision is based on a combination of clinical parameters and biological markers reflecting the underlying biological processes; this enables highly reliable prediction of periodontal disease susceptibility, early diagnosis, prognosis, and planning of the most effective and safe treatment strategy meeting individual patient needs. This review aims to elaborate the concept of precision periodontics and periodontal biomarkers with future implementation of a role of precision approach in periodontal practice.

Keywords: Data, Personalized medicine, Precision dentistry.

Introduction

Precision dentistry as the name suggest "precise" meaning taking care to be exact and accurate, especially about small details. It is defined as a contemporary, multifaceted, data-driven approach to oral health care that uses individual characteristics to stratify similar patients into phenotypic groups.[1]It is also defined as contemporary, multifaceted approach to care involving the consideration of "individual differences due to people's genetic make- ups, environments and lifestyles".[2] It is a paradigm shift that requires a new way of thinking about diagnostic categories. This approach uses patients' risk factor data (including, but not limited to, genetic, environmental and health behavioural) rather than expert opinion or clinical presentation alone, to redefine traditional categories of health and disease.

The main objective of precision dentistry is to remove the concept of "average treatment" and allow the clinician to improve treatment planning and incorporating two different classification methods unsupervised learning and supervised learning. These two new classification systems divide the disease into grades and stages. They become more serious with each successive step. This new style of classification enable the practitioner to use more signs, symptoms and other associated factors for "precision" while placing them in a diagnostic category. For example unsupervised learning has more superiority than the supervised learning if a 10 year tooth loss and attachment loss progression is to be predicted. Periodontal profile class stages (unsupervised learning approach) has better result between the periodontal phenotypes and systemic disease and condition as the homogeneity and exclusiveness is better associated with this group.[3]

Need for Precision

In general, scaling and root planing (SRP) is the prime management in periodontal diseases. There is no further examination done on lesions and systemic diseases like diabetes mellitus, cardiovascular diseases etc which should be done. There should be more precise method with staged and grade management approach is the need of new era of dentistry.[4]

Building on a deeper understanding of oral conditions and their pathogenesis and trajectories and also the most important- the knowledge and idea of the wider social, behavioural and systemic pathogens of oral health with their corelation with general health is of paramount importance.[5] Focusing primarily on periodontal diseases, the control and modulation of the oral microorganisms with the management of periodontal inflammation is the main concern inperiodontitis.[6] thus the need for precision in dentistry.

What is precision in medicine?

A form of medicine that uses information about a person's own genes or proteins to prevent, diagnose, or treat disease. In cancer, precision

medicine uses specific information about aperson's tumor to help make a diagnosis, plan treatment, find out how well treatment isworking, or make a prognosis, given by national cancer institute (NCI). Precision medicine refers to the tailoring of a therapy to an individual i.e. his or herbiological (genomic, microbiomic, proteomic), social (economic, educational), and behavioural (lifestyle) characteristics or traits, allowing to predict which therapy may be most efficacious, efficient, and safe, but also to prevent the onset and progression of early disease stages.[4]

This concept existed even during the times of Sir William Osler, it is reintroduced in the arm with the project named "Precision Medicine Initiative" launched by Barack Obamain 2015.

The concept of precision medicine is well known in the field of oncology. Patients having same type of cancer fails to respond to standard treatments, which are attributed to the idea of that particular cancer in one individual and very different from cancer in another individual, Researches are getting carried out to understand in depth why individuals having the samecondition respond differently. Clinical outcomes are associated with molecular subtypes of tumors, irrespective of their organ of origin.[7]

Precision dentistry

Precision dentistry is defined as a multifaceted, data-driven approach to oral and dental healthcare that uses individual genetic data to segregate and stratify individuals with similar genetic makeup into phenotypic groups to deliver preciseor targeted treatment.[8]

The main objective of precision dentistry is to classify the patient based on their risk of tooth loss and disease progression and this new objective requires a different approach. It requires classifying a patient based on the objective of placing each individual into groups where all the members of that group are homogeneous asfar as the condition is concerned.

As far the aim or precision dentistry is considered all the members of one particular groupshould have a same or equal progression, risk of disease development and should respond equally, example1, 2, 3 or A, B, C.[3]

Paradigm shift

A paradigm shift is a fundamental change in the basic concepts and experimental practices of a scientific discipline. This concept was introduced and brought by the American physicist and philosopher Thomas Kuhn in philosophy of science in the year 1962 in his book named "The Structure of Scientific Resolution".[9]

Precision dentistry needs a paradigm shift from what can be the proper diagnostic category for a patient to what is the risk of tooth loss, disease progression to the patient, so that we can classify and assign a patient into a group more homogeneously according to a condition. Homogeneity here means placing each patient into a more unbiased group with mutual exclusiveness which shows the same phenotype of interest. This phenotype should have anequal risk factor for disease progression, development and should similarly respond to thetreatment.[3]

Advantages

According to Bartold, it aligns the field of dentistry with current medical practice, avoiding a tendency to administer an "average" treatment for all patients with a certain condition.[10]

According to Schwendicke this "tailored dentistry" is not only advantageous, but it is necessary for the future of dentistry.[8]

It is cost effective as it is patient centered treatment plan.

Disadvantage

It requires a considerable span of time to determine or classify homogeneity of the group.

Stages and their grades

Tonetti et al [1] has given a multidimensional staging and grading classification system for chronic periodontitis, in which the staging denotes the severity of disease and complexity of case management whereas grading predicts the progression of disease, risk factor at personal level and potential threats to overall health. A new classification structure referred as stage, each stage has an appropriate grade which shows or reflects risk factors like diabetes mellitus, smoking, also indicates the loss of tooth loss. Both the stage and grade are developed with a sole purpose to reflect the complexity of treatment need as well as the prognosis.

WORLD WORKSHOP MODEL 1 is a novel system and is a great example of supervised learning model which has a great prospective for the classification of disease. It uses complex variable to represent an observable trait that the provider considers prognosis and progression of the disease. It also places each individual of patients into a more homogeneous group. After the stage is confirmed for a patient, the grade should be fixed based on an estimate of progression of periodontitis. The first outlook is the longitudinal substantiation of worsening radiographic bone loss or clinical attachment loss

(percentage bone loss/age) over a 5 year period. The direct measures are if there is no progression over 5 years, the individual is classified as grade A- if there is progression <2mm over 5 years they are classified as grade.

B-if the progression is ≥2 mm over 5 years the individual is classified as grade C. the indirect measures which can be used are relationship between the level of biofilm deposits, the level of destruction and bone loss with age.

Another classification is the Periodontal Profile Class model. Fundamentally, this new classification model builds on seven types of periodontal status which are seen around a tooth and also with missing teeth. These seven Tooth Profile Classes include teeth that are: healthy have recession, have crowns, have a high gingival index, have interproximal attachment loss, have a reduced periodontium and have severe disease[11]

Both the classification models have common intent, the World Workshop Model which represents a supervised learning approach, where as the Periodontal Profile Class model is example of an unsupervised model.

Latent class analysis

Latent class analysisis a statistical model of unsupervised learning. The fundamental assumption underlying latent class models is that of local independence, which states that objects (i.e, individuals, cases) in the same latent class share a common joint probability distribution among the observed variables.

Importance of latent class-

(a) Latent class analysis can take into account multiple characteristics of the phenotype, rather than just one or two as in other approaches.

(b) Latent class analysis classification is based on individuals who are placed together in mutually exclusive classes based on multiple, similar characteristics, rather than in predefinedgroups;

(c) The individuals in each class are more homogeneous than in most other approaches.

(d) Latent class analysis modelling creates latent (hidden) classes that may not be obvious from looking at the clinical signs themselves and the probability of being placed in a specific class based on characteristics is extremely high eg, misclassification is extremely low.[13]

Need for precisionin Periodontology

Precision is based on a combination of clinical parameters and biological markers reflecting the underlying biological processes; this enables highly reliable prediction of periodontal disease susceptibility, early diagnosis, prognosis, and planning of the most effective and safe treatment strategy meeting individual patient needs. [3]

Single biomarker will not able to predict periodontal disease activity and severity, so combinations of biomarkers are used to predict the disease activity. In 'OMICS' technologies including epigenomics, genomics, exomics, transcriptomics, proteomics, metabolomics, salivomics and nascent fields such as viromics coupled with bioinformatics and biostatistics, generated and processed massive biological data hence combination of data is used to predict the disease activity.

Biomarkers in periodontology

Biomarkers in periodontology include;

•Predictive markers measured in healthy individuals in the disease prevention stage;

•Diagnostic markers of disease onset;

•Prognostic markers for the assessment of disease progression, stage, and grade in the treatment planning phase.

Yusuke kamagate et al conducted a study on cytokine production in inflamed human gingival tissue in periodontitis (TNFαandIL1α,β). Twelve periodontitis patients were included in this study. Control subjects with healthy periodontium consisted of nine individuals. Gingival samples were biopsied from inflamed and from healthy gingival tissues. Results suggest thatIL-1 may play a critical role in inflammatory destruction, such as alteration of gingival connective tissue and loss of alveolar bone in periodontitis.[15]

Offenbacher S et al conducted a study between two groups having periodontitis and did scaling and root planing. One group with no further attachment loss had a mean GCF PGE2 level significantly lower comparing to another group with one or more sites of 3mm or more of attachment loss. Authors concluded that on the basis of the GCF PGE2 level it can be claimed that it is a predictive marker of periodontal disease activity.[16]

Collagenase are part of matrix metalloproteinase family which degrade collagen. The two important collagenase are MMP-8 derived from PMN' and macrophages which in predominant in

GCF, MMP-1 found in fibroblast. In untreated chronic periodontitis patients GCF levels of MMP-8 are significantly higher compared to healthy individuals. GCF MMP-8 levels are shown to be reduced significantly after periodontal treatment.[16]

Elastase which degrades proteoglycans and activates latent collagenase are found in GCF which significantly correlate with the increasing probing depth, gingival inflammation, attachment level and boneloss.[16]

Glucoronidase are lysosomal enzymes found in PMN's. β Glucoronidase is an acid hydrolase which is considered to be a marker release by these cells. Kennett CN conducted across sectional studies and found that both these enzymes in GCF have significant correlation with gingival inflammation, pocket depth and bone loss. These markers (collagenase, elastase glucuronidase) are helpful for diagnosis of the disease onset.[16]

Osteonectin and bone phosphoprotein both the proteins have been detected in GCF of periodontitis patients. The total amount of both proteins have shown to increase with increasing probing depth. [16]

Role of genomics in periodontal disease

Periodontal disease is a polymicrobial in origin which is highly governed by host response, environmental factors, and genetic factors. There are chromosome regions that potentially harbor susceptibility genes for periodontal diseases. An interaction of IL-1 positive genotype with age, smoking, and Porphyromonas gingivalis which suggests that IL-1 genotype is a contributory but non essential risk factor for periodontal disease progression in this population.

Diehl et al. analyzed linkage disequilibrium of IL-1 genetic polymorphism with aggressive periodontitis. They selected 28 African-American families and seven Caucasian American families with two or more affected members. IL-1α and IL-1β polymorphism were in strong disequilibrium with each other in Caucasians but not in African-Americans. Results showed that aggressive periodontitis as a complex, oligogenic disorder, with IL-1 genetic variation contributing an important but not exclusive influence on disease risk.[13]

The stepwise manner or stratification of the whole process has gained recognition and momentum in recent years leading to the emergence of "stratified medicine," an umbrella term to encompass multi-disciplinary physicians, clinical scientists, and healthcare professionals. The core aim of these emerging concepts remains "precision diagnosis and management tailored to individual's needs." Thus, fundamentally the stratified medicine offers the system for precision medicine, which implies that an individual patient's clinical care is based on specific risk of disease or response to therapy by using diagnostic tests or techniques, whether conventional or genetic.[13]

The whole model is set in the background of personal lifestyles, the structure and function of the family, sociocultural variation, ethnicity, and the community at large. This model is beginning to yield dividends for patients and healthcare providers from targeted and effective treatments, where as industry benefits from the potential form or efficient therapeutic developments as well as the market expansion for novel therapeutic drugs and devices.(Figure-1).[4]

Shift to Precision Periodontics: Where Are We Stuck?

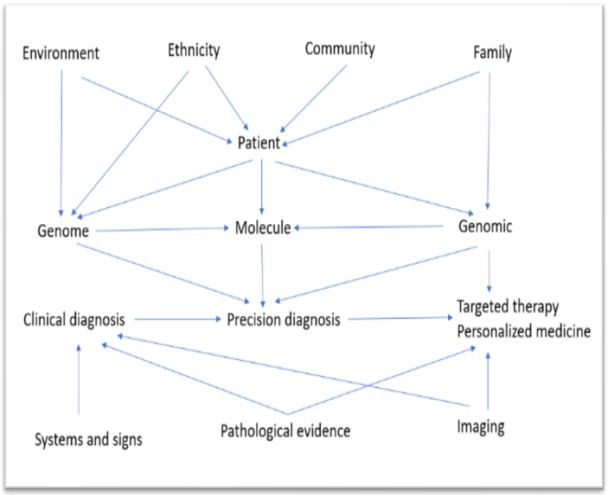
The confusing aspect of the lack of diagnostic markers in periodontology and implantology, despites so many reported biomarker studies, relates to a frequent misinterpretation of biomarkers specifically validated for diagnostic use. Although a biomarker as an indicator of a biological process can be used to study the characteristics of physiological or pathological conditions and their respective responses to different factors (such as treatment), biomarkers validated for diagnostic use need to comply with specific diagnostic requests defined in rigorous guidelines for biomarker validation, varying for each biomarker subgroup causing 'economic burden' as patient is clinical practice.[3]

Precision periodontics undoubtedly represents the future of high-quality periodontal care, so it is of paramount importance that future research studies strictly adhere to the recommendations for the validation of biomarkers in order to accelerate the process of their implementation in routine clinical practice. The coordinated collaborative work of an interdisciplinary and international consortium could substantially accelerate the implementation process of precision periodontics, assuring high-quality, reproducible research in larger pooled samples and subsequent fast implementation in clinical practice.[3]

Conclusion

The move to precision periodontology is a new way of approaching health care that should be thought of as a paradigm shift, because precision in periodontology is not just placing an individual into a diagnostic category. Instead, it includes

placing similar individuals into mutually exclusive, homogeneous categories of risk, specific to a particular disease or condition. This means that instead of using an "average treatment" for all individuals with a particular diagnosis, precision requires that the individuals in each diagnostic subgroup are homogeneous so that a specific treatment will be more effective for the individuals in that subgroup.



(Figure-1)[4]

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