REVIEW ARTICLE

PRECISION DENTISTRY - A PERSONALIZED APPROACH

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ABSTRACT

Precision medicine is an expanding area in which physicians make use of diagnostic tests in identifying biological markers, often genetic, that aid in planning medical treatments, as well as technique, that works best for each patient. Presently, researches are undertaken related to using diagnostic tests in medical diagnosis based on genomics, proteomics, and metabolomics to enhance and prophesy patient's reactions to targeted therapy. Precision Dentistry is an innovative technique in the field of oral health. It is derived from the concept of precision medicine. Similar to precision medicine, precision dentistry refers to a contemporary, multifaceted, data-driven approach to oral health care that utilizes individual characteristics to stratify similar patients into genotypic groups. This review focuses on an introduction to precision medicine and precision dentistry, its applications and future aspects.

Key words: Precision medicine, precision dentistry, personalised medicine, genomics, biomarkers.

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INTRODUCTION

Precision medicine is an expanding area in which physicians make use of diagnostic tests in identifying biological markers, often genetic, that aid in planning medical treatments, as well as technique, that works best for each patient. Presently, researches are undertaken related to using diagnostic tests in medical diagnosis based on genomics, proteomics, and metabolomics to enhance and prophesy patient's reactions to targeted therapy. This area is designated as precision medicine. It conglomerates the human genome, information technology, and biotechnology with nanotechnology to provide specific and personalized cures based on specific differences set against population trends. This approach will allow doctors and researchers to predict treatment and prevention strategies for a particular disease, more accurately.[1]

This evolving discipline is resulting in a much-needed change in the approach towards health care delivery by a transition towards disease prevention, early intervention, and risk assessment.[2] In this new form of treatment, a thorough analysis of the genomic profile of the patient and environmental and cultural influences that impact the risk of disease are considered. Given dentistry's historical commitment to disease prevention, the dental profession must position itself to embrace this innovative approach to patient care.[3,4]

Precision Medicine Vs Personalized Medicine

There is considerable overlap between the terms 'precision medicine' and 'personalized medicine.' The word 'personalized' could be misinterpreted as prevention and treatment modalities developed uniquely for each individual, whereas in reality, it is based on the genetic, environmental, and lifestyle factors of the patient.[5] Personalized medicine is an approach that considers patient's genetic make-up but with attention to their preferences, beliefs, attitudes, knowledge, and social context. In a broader contextprecision medicine describes a model for health care delivery that relies heavily on data, analytics, and information. This model is beyond genomics and has broader implications for our nation's research agenda and its implementation and adoption into health care.[6] Hence the term 'precision medicine' is preferred. However, both terms are used interchangeably.[5]

Precision Medicine- Definition

The National Research Council's Toward Precision Medicine adopted the definition of precision medicine from the President's Council of Advisors on Science and Technology in 2008 as: "The tailoring of medical treatment to the individual characteristics of each patient…to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment. Preventative or therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effects for those who will not". As this definition suggests, the power of precision medicine lies in its ability to guide health care decisions toward the most effective treatment for a given patient, and thereby improving quality of care, while reducing the need for unnecessary diagnostic testing and therapies.[6]

Precision Medicine Ecosystem

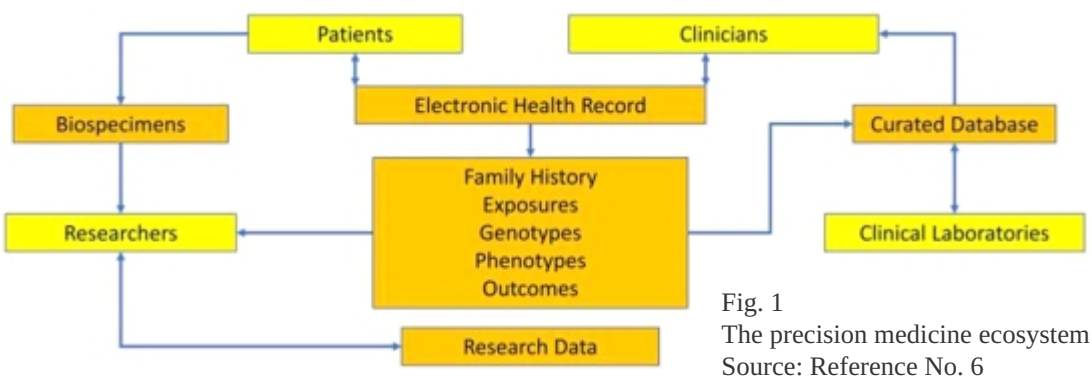

Fig. 1
The precision medicine ecosystem
Source: Reference No. 6

Role of Biomarkers

A biomarker is a defining characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions. The three types of biomarkers include diagnostic biomarkers, prognostic biomarkers, and predictive biomarkers.[7]

Biomarker testing is a way to look for genes, proteins, and other substances that can provide information about the disease. Each person's disease has a unique pattern of biomarkers. Some biomarkers affect how certain treatments work. Hence, biomarkers are an integral component of precision medicine.[8]

Precision Medicine - Potential Applications

The general goal of present-day disease management is demand-orientated, and to reduce morbidity, mortality, and disability, precision medicine is a technical innovation.[9] Precision medicine has its role to play at many points during the entire life span of an individual. Before conception, genetic screening can be used in identifying genetic disorders in the offspring.[6,10,11] During pregnancy, the mother can have genetic testing to assess the fetus for any chromosomal abnormalities. The genome sequencing of the fetus can also be performed.[6,12] At birth, genome sequencing can be done to diagnose many critical conditions.[6,13] Later in life, it can be applied to diagnosing a large number of diseases especially chronic diseases and cancer.[6] Currently, the applications of this approach have been documented in the literature in different clinical specialties including oncology, pulmonology, cardiology, pathology, clinical neurology, nuclear medicine, medical imaging, urology and nephrology, endocrinology, and psychiatry.[14] The following is a summary of potential applications of precision medicine.[9]

Examples of diseases presently managed by precision medicine include (bio-markers for each disease is provided within brackets) cancers - chronic myeloid leukemia (BCR+ABL) and lung cancer (EML4-ALK); infections – HIV/AIDS (CD4+ T cells, HIV viral load), hepatitis C (hepatitis C viral load); hematology - thrombosis (factor V leiden); cardio-vascular disease - coronary artery disease (CYP2C19); pulmonary disease - cystic fibrosis (G551D); renal disease - transplant rejection (urinary gene signature); endocrine disease - multiple endocrine neoplasis - type 2 (RET); metabolic disease - hyperlipedemia (LDL cholesterol); neurological disease - autoimmune encephalitis (CXCL13); psychiatry - alcohol use disorder (GRIK1); pharmacogenomics - smoking cessation (CYP2A6), ophthalmology - Leber's congenital amaurosis (RPE65).[9]

Precision Dentistry

Precision Dentistry is an innovative technique in the field of oral health. It is derived from the concept of precision medicine. Similar to precision medicine, precision dentistry refers to a contemporary, multifaceted, data-driven approach to oral health care that utilizes individual characteristics to stratify similar patients into genotypic groups.[15]

Precision dentistry, thus, is a dental management model that proposes the customization of dental/oral care, with clinical decisions, practices, and/or products being tailored to the individual patient. This approach will bring dentistry in line with current medical practice whereby individuals are assessed, and targeted treatments are developed, based on specific data gathered during the examination and treatment phases of patient management. At present dentistry falls way behind medicine in this model of management.[16]

Complex dental diseases such as dental caries, gingivitis, and chronic periodontitis, orofacial pain, and oral cancer, are conditions where, the application of precision medicine can mitigate the chronic and often destructive nature of these conditions and aid in taking a more proactive approach to diagnosis and treatment of these diseases, compared to our present reactive, wait and see approach.[17] Despite these complexities, evidence suggests identification of biomarkers can be of use in precision treatment. Thus, the cornerstone for successful precision

depends on the identification of clinically validated biomarkers, which can be reliably linked to a specific disease and provide reliable targets for therapy. These biomarkers will also enable more precision drug manufacturing.[17]

Precision Dentistry - Potential Applications

Periodontal diseases: Periodontitis is a polymicrobial infection. Research has the variability in the disease could well be clarified through genetic factors. Genes can affect host-bacterial interactions in the periodontal tissues due to elevated levels of proinflammatory cytokines, such as interleukin-1 (IL-1). IL-1 plays a dynamic role in the pathogenesis of periodontitis, by host inflammatory response regulation. The genes that encrypt IL-1 production in recent times received utmost attention as likely predictors for periodontal disease progression. Promising results have been shown with IL-1, which is the pro-inflammatory cytokine, and the presence of the IL-1 positive gene is associated with the increased inflammatory response. Although presently, the studies have identified IL 1, in the future, further genetic markers may be recognized in due course of time.[1]

Dental caries: Dental caries is regarded as a public health problem worldwide. With the multifactorial etiology, various factors influence the disease process, which can be broadly categorized into environmental and host factors. [18]

Various researches have reported that 40-60% of dental caries susceptibility is genetically determined. It is also reported that dental caries is, infact, influenced by numerous genomic and loci factors, like a mutation in the single-nucleotide polymorphism of Amel X gene responsible for normal enamel development, defect in KLK4 gene responsible for enamel maturation, LYZL2 that involves in antibacterial defenses, and AJAP1 that may influence tooth development.[1,19,20] Hence, early detection of these specific genes benefits the patient but and the dentist, who can render better treatment to the patient with thorough knowledge concerning its diagnosis and prognosis.[1]

The role of genomics has also been researched about Early Childhood Caries (ECC).The first-ever genome-wide association study (GWAS) of primary dentition caries (children ages 3-12) discovered suggestive evidence of association for 7 genetic loci, two of which (MPPED2 and ACTN2) were replicated in a subsequent investigation. Additional key findings from this new line of research utilizing the GWAS methodology is that genetic influences on dental caries may differ between the primary and the permanent dentition, as well as between tooth surfaces (i.e., smooth versus pits and fissures).[21]

Oral cancer: Oral squamous cell carcinoma (OSCC) is one of the leading cancers in the world. OSCC patients are currently managed mostly, with surgery and/or chemoradiation. Prognoses and survival rates are dismal, however, and have not improved for more than 20 years. Recently, the concept of precision medicine was introduced in the management of oral cancer, with promising outcomes.[22]

Recent developments in the influential omics tools, which include genomics, epigenomics, transcriptomics, proteomics, metabolomics, and lipidomics are initiating novel paths in the direction of biomarker detection for prompt diagnosis of oral cancer. The detection of these biomarkers facilitates in determining and discriminating the behavior of oral cancer in each of the affected patients thus, providing personalized therapies for these patients.[1,23]

Orthodontics: Genetics has a very important role to play in the field of orthodontics. Genetics has a pivotal contribution in understanding the etiology of malocclusion. The comparative influence of genetics and environmental factors in the etiology of malocclusion has been a matter of debate.[24]

The present researches in this field focus onthe genomic basis of craniofacial growth and genetic variants of dentofacial abnormalities. In orthodontics, for instance, mandibular prognathism (Class III) and cleft lip and palate are primarily genetic in origin, and also a certain number of them are environmental in origin.[1]

Class III malocclusion mandibular protrusion obvious in Spain Charles royal families, also called as Hapsburg jaw is considered as a monogenic dominant phenotype, and is also an expression of certain genes that encode specific growth factors (Indian hedgehog homolog, parathyroid-hormone like hormone, insulin-like growth factor-1, vascular endothelial growth factor, harbor genes [chromosomal loci 1p36, 12q23, and 12q13], etc.) accountable for Class III malocclusion.[1,25]

Certain genes transmembrane protein 1 and GAD1 are responsible for the occurrence of cleft lip and cleft palate and also certain genetic variants REF IRF6, PVRL1, and MSX1 are involved in the formation of syndromic-associated cleft lip and palate.[1]

Precision Dentistry and Dental Public Health

On the surface, the precision oral health movement seems to be at odds with dental public health. While Precision dentistry focuses on the individual patient, dental public health addresses the oral health needs of populations. Thus, the concept of precision public health will have a profound impact on the future of health care and how dental public health will be practiced. With the opportunity for epidemiological methods to be applied to big data sets, dental public health specialists can look at these "omic" biomarkers and demonstrate generalizable, potential causal relationships between oral disease and certain factors observed in our genome.Precision public health literature about oral health identifies possible threats that could inadvertently increase health inequities and proposes potential opportunities that precision public health could utilize to reduce oral health inequities. Precision public health is a recently evolving field that proposes synergistically integrating public health data with other health information sources to improve health status and reduce costs. Precision public health expands precision medicine's recent call for a new taxonomy of disease and a knowledge network of integrated biomedical research, from an emphasis on diagnosis and curative medical treatment to also include prevention and health promotion.[26]

PRECISION DENTISTRY – THE FUTURE

If the dental professionals can successfully implement personalized medicine in their practice, dental professionals will have a deeper understanding of oral and systemic health, a working knowledge of genomic medicine - its strengths and weaknesses, proficiency in the use of newer diagnostic tools such as salivary diagnostics. As with any emerging field, dentistry has to overcome a few challenges such as gaps in knowledge, lack of an integrated health record, lack of motivation to adopt the new technique. Despite these transient challenges, the dental profession is in a strategic position to embrace and adopt precision medicine.[17]

Opportunity, challenges, and feature of personalized medicine that could be implemented to personalized dentistry are the following:

- Directing targeted therapy and reducing trial-and-error procedures
- Decreasing adverse drug reactions
- Increasing patient willingness to treatment
- Reducing high-risk invasive testing procedures
- Facilitating to control the overall cost of health care[1]

CONCLUSIONS

As the science of personalized medicine continues to advance, there will be better tailor made treatment options available for the management of diseases. The advent of personalized medicine marks a transition from the traditional 'One size fits all approach. With an in-depth understanding of the disease process through genomics and biomarkers, precision medicine has a huge potential in the prevention and treatment of disease in a customized way. As personalized medicine becomes more widely implemented within our healthcare environment,the dental profession must demonstrate its leadership in advancing personalized medicine into the practice environment as there are potential applications of precision medicine in oral health care.

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