



Review on Personalised medicine

*Amruta P. Umardand, Aniruddha A. Patil, Swarupa D. Shirtode, Sanjivani S. Patil, Tushar A. Mule

Abstract: In this review we discussed about introduction of personalised medicine concept its overall journey from ancient times to today's era. Some examples of it in present and different types of challenges, Benefits and strategies to adopt personalised medicines.

Keywords: Personalised, Customised, Patient, Medicine, Drug

Introduction: In the medical and healthcare industries, personalised medicine (PM) is a relatively new and interesting concept. It's a notion that has the potential to revolutionise medical interventions by providing effective, customised therapeutic solutions based on an individual's genetic, epigenomic, and proteomic profile, while also taking into account the patient's unique circumstances. PM is effective not just in therapy but also in prevention. Increased use of molecular stratification of patients, such as testing for genes that cause drug resistance, will offer medical professionals with solid evidence on which to base treatment options for individual patients. There will no longer be a reliance on the negative effects of trial and error prescribing procedures as a result of this advancement. Currently, when a given drug isn't working, the patient can try a new one. Patients suffer from unpleasant side effects, drug interactions, probable disease progression while appropriate therapy is delayed, and patient unhappiness as a result of this trial and error strategy. [1]

History

Individual targeted medicine was originally documented thousands of years ago. Since then, other therapy approaches have been developed. Conventional remedies, however, do not take into account an individual's idiosyncrasy or genetic make-up, and consequently fail to be beneficial in some circumstances. The need for more precise and effective therapy led to the creation of a scientific branch known as "personalised medicine" throughout time. Personalized medicine has been recognised as the next generation of diagnosis and therapy as a result of significant technical developments in this field. Although personalised medicine has received a lot of attention in recent years, it still faces a number of challenges in clinical practise. The COVID-19 epidemic has brought these limitations to light recently. This review traces the "journey" of personalised medicine over time, highlighting key milestones along the way. Beginning with malaria therapy as a first more individualised therapeutic strategy, it emphasises the need for new diagnostic techniques and therapeutic regimens based on an individual's genetic background. It also intends to raise global awareness about present

constraints and the need for a personalised strategy to overcome healthcare issues and, as a result, the current crisis. [7, 8]

In ancient times, around 1550 BC, the first evidence of treatment tailored to an individual's health was found in Homer's *Odyssey* "Telemachus, Odysseus' son, pays a visit to Menelaus and Helen in search of information about his father, who has yet to come home during the Trojan War. Helen slips a medication (ovo) into the glass of wine, which eases grief or wrath and lets one forget one's woes, while reminiscence of the missing Odysseus leads to tears. This medicine comes from Egypt, according to Homer. Egyptians were regarded "the wisest of men" even by Greek physicians, according to Homer, since they were descended from Paeon, the gods' physician. [9, 10]

The Classical period, when medicine was split into categories and every doctor was a specialist for one ailment, one body part, the adaptation of that old "Egyptian medicine" to an individual's health situation was further described by Herodotus. This is the first example of personalised medicine, since doctors understood that categorising diseases by human body parts may help them gain a better understanding of illness and, as a result, improve therapeutic outcomes. The Greeks were enthralled by this approach to treatment, which is why they frequently praise Egyptian medicine in their treatises. Only after the fifth century, when Hippocratic medicine appeared, did Egyptian medicine begin to be excluded from Greek text. [11, 12]

Although "Hippocratic medicine" resembles Egyptian medicine, the former does not invalidate the latter. Hippocrates, on the other hand, enhanced Egyptian medicine by removing the magical and religious aspects and making it more logical. In reality, in order to have a good therapy during that time, physicians had to consider the patient's wants and beliefs. Hippocrates thought that "diseases can be treated from their source" and that "therapy should be directed towards the disease's cause." As a result, they concentrated on a more customised approach to the condition and dispelled all of the myths that surrounded this period of history. In light of that achievement, Hippocrates was ahead of his time, as he was able to drive the understanding of genetic medicine by arguing that each individual is unique, which has implications for disease prediction and therapy. [13, 14]

Personalized medicine has evolved over the last twenty-five centuries, from the so-called Father of Western Medicine, Hippocrates, to the current physician.

Even in recent decades, medical therapy used a wide strategy based on clinical and genetic/genomic data from various populations rather than focusing on each patient, despite the ancient vision and prescriptions (National Institutes of Health, 2007). To choose a therapy regimen, doctors used standardised procedures based on data and understanding of previous patients/diseases. Clinical studies were only designed to identify 20% of the population that would not react to treatment or, worse, incur harmful consequences due to genetic variations. This meant that idiosyncrasy (from ancient Greek *ioi/idiosynkrasia*, "a distinctive temperament, habit of the body, e.g., blend of humours") had no place in medicine. In the nineteenth century, idiosyncrasy defined the way physicians thought about diseases.1) this mindset began to shift in the 1870s, when discoveries made by European academics enabled the emergence of "scientific medicine," a predecessor to evidence-based medicine. [15]

Scientists began to recognise the need for "evidence-based medicine" in the early 1950s. The discipline of today's "personalised medicine" arose from the prediction of drug response in order to assure the patient's safety as well as a better outcome. The field of molecular biology has helped to improve our understanding of drug response. Human genome mapping was a breakthrough in this area, allowing researchers to gain a deeper grasp of people's genetic makeup. Individuals are 99.1% identical, but the remaining 0.9 percent of interindividual genetic diversity is what causes the apparent heterogeneity in humans. [16]

Overall, researchers and physicians still face an enormous problem today. The goal of personalised medicine is to combine modern medicine with molecular advances in order to target patients individually and increase the therapeutic approach's efficacy and effectiveness (Mini and Nobili, 2009). The understanding that using candidate genes alone is insufficient to explain differences in disease risks between ethnic groups and within individuals led to whole genome approaches. With the advancement of genotyping technologies, it is now possible to focus on specific sections of the genome, allowing for greater coverage and knowledge of variants. As a result, medical professionals were able to identify and treat individuals based on their distinct traits. [17]

Today, Hippocrates' four humours, blood, phlegm, yellow bile, and black bile, which defined each individual's treatment (Hippocrates, 1543), have been replaced with the four building blocks (A, T, G, C), allowing for better medical forecasts.

Personalized medicine has become a reality thanks to cutting-edge biochemical discoveries such as single-nucleotide polymorphisms (SNPs), genotyping, and biochips, supporting the term's use in recent decades.

Indeed, the genome's unique identity gives vital information about disease development and progression, as well as responsiveness to various therapy regimens (Agyeman and Ofori-Asenso, 2015). Variations in the human genome such as SNPs, insertions and deletions, structural variants, and copy number variations all play a role in the onset and progression of diseases like cancer, diabetes, and neurodegenerative and cardiovascular disorders (Agyeman and Ofori-Asenso, 2015). As a result, biomarkers are being studied as a means of forecasting certain diseases as well as identifying patient subgroups who only respond to specific treatments. Environmental factors, on the other hand, can operate as triggers and/or cofactors. As a result, predicting drug response and therapy based solely on genetic information without taking environmental variables into consideration can lead to poor or incorrect findings. [18]

The exact vision of personalised medicine is to combine the human DNA, environmental factors, disease assessments, and medication in order to obtain a superior therapeutic outcome. For the reasons stated above, it is clear that the customised medicine journey, as outlined in our previous article (Visvikis-Siest et al., 2018), has not yet reached its conclusion. A slew of issues still revolve around the patient's requirements, which is a difficulty for personalised medicine today [2].

Examples of Personalized Medicine in the Present

Drugs like warfarin, PQ, and imatinib, which appear to only work – or only work without side effects – when a patient has a specific genetic profile, have sparked a lot of interest in figuring out what factors, like genetic variants, influence a patient's response to a variety of drugs and

interventions. This fascination with developing individualised medicines to treat diseases has grown to include personalised disease surveillance (i.e., early detection techniques) and personalised disease prevention strategies. A few recent examples of this action are briefly described. [19]

Challenges

PM is a healthcare system innovation since it is preventative, coordinated, and proven. Stakeholders and consumers in the present healthcare system are still unaware of the benefits of PM. Recent research has revealed the following obstacles to PM development: Scientific challenges (with a poor understanding of the molecular mechanisms of certain diseases, genetic markers are the most clinically significant); economic challenges; operational issues (difficulty identifying technology and operational systems that will save costs); and protection of private information during the investigation and development stages. There are also policy issues with the relationship between government research and regulatory agencies. [4,5]

Benefits

By approving novel therapeutic strategies and changing the perception of medicine in the healthcare system, PM has the potential to improve medication selection and targeted therapy, reduce adverse effects, increase patient compliance, shift the goal of medicine from reaction to prevention, improve cost effectiveness, and increase patient confidence post-marketing.[3]

Strategy

Pharmaceutical corporations must invest in these new technologies and demonstrate a willingness to collaborate with academic research teams if PM is to be developed and adopted quickly. More stringent biomarkers must be identified in order to inform a proactive strategy to PM. The recent discovery of liquid biopsies, which may detect DNA circulating in the blood, is one example. This sort of biopsy is less intrusive than regular biopsy and has been used to diagnose disease at an early stage. One of the early applications of liquid biopsy was as a Down syndrome screening for pregnant women. TRACERx is a study that uses circulating tumour DNA (ctDNA) to analyse and predict the progression of lung cancer tumours. Medical personnel will be able to use PM in a proactive manner by anticipating the course of tumour evolution and switching patients to various therapies as soon as indicators of drug resistance are found. This could help to postpone the emergence of resistance. Pharmaceutical businesses must educate themselves in order to be profitable employing revolutionary diagnostic and treatment technologies in significantly reduced quantities in the long run. Because developing new treatments is excessively expensive, pharmaceutical corporations are increasingly interested in repurposing current ones. PM enables treatment regimen optimization, hence increasing the efficacy of existing medications. [2]

All pharmaceutical businesses use the following strategies to adopt PM: i) Moving from traditional drug approaches to PM is not an option, but a requirement. Accept that each molecule in the pipeline will be tailored to specific patient populations rather than being sold to the general public. ii) PM is a novel way to providing better healthcare while lowering total healthcare expenses. This will be accomplished by implementing healthcare digitalization,

upgrading the healthcare IT system, and developing breakthrough technologies, such as single-cell omics, which allows for high-throughput research of diverse cells. iii) Integrating project management abilities into the existing healthcare system PM adoption necessitates a collaborative effort from a wide range of stakeholders, all with the same objective of leveraging scientific breakthroughs to improve patient care. iv) Biomarkers (indicators of biological condition) are assisting research and development (R&D) in the healthcare industry. Reduced trial sizes and faster time to market help to boost R&D. Support therapeutic drugs with a smaller market that are more likely to succeed. v) Form partnerships to gain access to new capabilities; for example, firms with assay developers and other industries can gain access to world-class diagnostics. vi) Astute sales teams with the most up-to-date knowledge. Patients' histories, as well as diagnostic and treatment approaches, will be needed of sales teams. Furthermore, salespeople must be familiar with molecular biology and illness mechanisms. vii) In PM, post-market surveillance is critical in order to conduct more focused clinical trials of pharmaceutical products. Furthermore, as customers become more knowledgeable about this unique therapeutic strategy, demand for PM will rise in the future decades. This will encourage a shift away from traditional medicine and toward novel diagnostic and treatment methods. Furthermore, clinical studies are currently time-consuming and labour-intensive; but, with regulatory approval, clinical trials will become more advanced and easier to accommodate PM in the future. The improvement of public/private sector collaboration in PM R&D. Create a straightforward technique for identifying and prioritising diseases that could benefit from the use of innovative technology. In addition, collaborative venture programmes for research design validation and biomarker standardisation are being developed. [1]

References

1. Sunil Mathur et al, Personalized medicine could transform healthcare (Review), Biomedical reports, July-2017, Volume 7 Issue 1, Pg. no. 1-2
2. Vogenberg FR, Barash C Isaacson, Pursel M. Personalized medicine: Part 1: Evolution and development into theranostics. P T. 2010; 35:560–576. [PMC free article] [PubMed] [Google Scholar]
3. 2. Vogenberg FR, Barash CI, Pursel M. Personalized medicine: Part 2: Ethical, legal, and regulatory issues. P T. 2010; 35:624–642. [PMC free article] [PubMed] [Google Scholar]
4. 3. Sairamesh J, Rossbach M. An economic perspective on personalized medicine. HUGO J. 2013; 7:1. doi: 10.1186/1877-6566-7-1. [CrossRef] [Google Scholar]
5. 4. Sadée W, Dai Z. Pharmacogenetics/genomics and personalized medicine. Hum Mol Genet. 2005; 14:R207–R214. Doi: 10.1093/hmg/ddi261. [PubMed] [CrossRef] [Google Scholar]
6. Sophie Visvikis-Siest et al, Milestones in Personalized Medicine: From the Ancient Time to Nowadays—the Provocation of COVID-19, Front. Genet, 30 November 2020, pg. no. 1
7. Agyeman, A. A., and Ofori-Asenso, R. (2015). Perspective: does personalized medicine hold the future for medicine? J. Pharm. Bioallied. Sci. 7, 239–244. doi: 10.4103/0975-7406.160040
8. Ai, T., Yang, Z., Hou, H., Zhan, C., Chen, C., Lv, W., et al. (2020). Correlation of chest CT and RT-pcr testing for coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology 2020:200642. doi: 10.1148/radiol.202020064
9. Albert, M. A. (2011). Biomarkers and heart disease. J. Clin. Sleep Med. 7, S9–S11. doi: 10.5664/JCSM.1342

10. Ashley, E. A., Recht, J., and White, N. J. (2014). Primaquine: the risks and the benefits. *Malar J.* 13:418. doi: 10.1186/1475-2875-13-418
11. Beutler, E. (1959). The hemolytic effect of primaquine and related compounds: a review. *Blood* 14, 103–139. doi: 10.1182/blood.V14.2.103.10
12. Burstein, H. J. (2005). The distinctive nature of HER2-positive breast cancers. *N. Engl. J. Med.* 353, 1652–1654. doi: 10.1056/NEJMp05819
13. Cascella, M., Rajnik, M., Cuomo, A., Dulebohn, S. C., and Di Napoli, R. (2020). “Features, evaluation and treatment coronavirus (COVID-19),” in *StatPearls*. (Treasure Island, FL: StatPearls Publishing) Available online at: <https://www.ncbi.nlm.nih.gov/books/NBK55>
14. Chasioti, D., Yan, J., Nho, K., and Saykin, A. J. (2019). Progress in polygenic composite scores in alzheimer's and other complex diseases. *Trends Genet.* 35, 371–382. doi: 10.1016/j.tig.2019.02.005
15. Conti, R., Veenstra, D. L., Armstrong, K., Lesko, L. J., and Grosse, S. D. (2009). Personalized therapy and pharmacogenomics: future perspective. *Pharmacogenomics* 10, 927–930. doi: 10.2217/pgs.09.45
16. Cortegiani, A., Ingoglia, G., Ippolito, M., Giarratano, A., and Einav, S. (2020). A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. *J. Crit. Care* 57, 279–283. doi: 10.1016/j.jcrc.2020.03.005
17. Dong, L., and Hu, S. Gao, J. (2020). Discovering drugs to treat coronavirus disease (2019). (COVID-19). *Drug Discov. Ther.* 14, 58–60. doi: 10.5582/ddt.2020.01012
18. Ellinghaus, D., Degenhardt, F., Bujanda, L., Buti, M., Albillos, A., Invernizzi, P., et al. (2020). Genomewide association study of severe covid-19 with respiratory failure. *N. Engl. J. Med.* 383, 1522–1534. doi: 10.1056/NEJMoa2020283
19. Laura H. Goetz et al, Personalized Medicine: Motivation, Challenges and Progress, *Fertil Steril.* 2018 Jun; 109(6): 952–963.