PRECISION MEDICINE IN STROKE: AN IDEAL MODEL FOR STROKE TREATMENT

PRECISION MEDICINE
www.e-precisionmed.com/pmj

ISSN 2456-2254

COMMENTARY

HIGHLIGHTS

This article provides an insight on ischemic stroke associated precision medicine.

An initiative by
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ABSTRACT

Ischemic stroke is one of the second largest cause of mortality and there is an urgent need to develop precision medicine in stroke treatment. Ischemic stroke is the result of undesirable interaction between multiple environmental, physical, social, and genetic risk factors. Precise medicine has recently capativated the attention of clinicians and researchers in the area of stroke. Innovative imaging-intensive registries of interventional therapies have provided an ideal platform to kickstart the precision medicine of cerebrovascular disorders, from acute stroke to more chronic management of intracranial and extracranial atherosclerotic stroke. Evidence based medicine or pharmacogenomics has helped in rethinking the therapeutic regimen of stroke by identifying the clinical outcome and subtypes in treatment with statins, antiplatelet agents and other pharmacological agents used in the management of stroke. Precision Medicine would help in revealing the accurate pathogenesis of the disease and to establish the novel target oriented therapy and eventually will work for the betterment of human beings.

KEY WORDS

Precise medicine; ischemic stroke; pharmacogenomics; pharmacological agents; omics

Received 10 July 2016; **Revised** 12 July 2016; **Accepted** 14 July 2016; **Published** 18 July 2016

Anjana Munshi[1]*, Vandana Sharma[2]
[1]Centre for Human Genetics, School of Health Sciences, Central University of Punjab, Bathinda, Punjab, INDIA
[2]Institute of Genetics and Hospital for Genetic Diseases, Hyderabad 500016, INDIA

***Corresponding author:** anjanadurani@yahoo.co.in, **Tel.:** +91- 9872694373

ISSN: 2456-2254
PRECISION MEDICINE

INTRODUCTION

Stroke is highly prevalent and second largest cause of mortality and chronic disability worldwide [1]. The ischemic stroke results from thrombotic or embolic occlusion of a blood vessel. Since thrmboembolic ischemic stroke is the major health issue, researchers and clinicians are trying to find adequate treatment based on an individualized patient centred precision medicine approach [2]. A vast variety of risk factors such as social, environmental, and genetic are responsible for the pathogenesis of stroke. An innovative approach of treatment taking care of all the concerns such as avoiding drug related side effects, adverse effects along with the right dosage to the right patient in the right amount is required. This will bypass the commonly practiced traditional drug prescribing method/system in which one dose fits for all patients with the same disease and the same age group. Certainly, the system developed using precise medicine will benefit the current clinical practice of saving lives and improving recovery rates. The accuracy and efficacy of stroke treatment is highly time dependant. Clinical techniques involving a combination of viscoelastic methodologies may be used in a personalized patient-centered regime, including thromboelastography (TEG®) and the lesser used scanning electron microscopy approach (SEM). Thromboelastography is used to provide a dynamic measure of clot formation, strength, and lysis, whereas SEM is a visual structural tool to study the detailed fibrin structure of a patient. Neurosurgeons, neurologists and researchers agree that since there is a delicate relation between thrombotic and bleeding events, it is utmost important to understand the patients baseline risk factors and clinical complications which have to be managed to achieve the perfect management of ischemic stroke. The SEM and TEG®are the perfect examples of unique techniques to confirm stroke diagnosis, to screen at risk patients and to monitor treatment efficacy [1].

The main root of precision medicine is the ability to develop target specific health care decisions on individual's risk basis. This has been established by assessing genetic variability determining the susceptibility to develop a disease and likely response of medicines. Another approach is of big data movement which offers a potentially powerful complement to genome based precision medicine [3]. The big data in the form of administrative claim datasets and large clinical trial data sets have generated a precise huge amount of clinical subtypes which can help in clinical decision making.

According to a study conducted by a company, 'Constant Therapy', which provides a customized brain rehabilitation software program, big data and mobile technology are playing an important role in stroke related language and cognitive impairment. This company found that the stroke patients engaged in at home treatment received more therapy and experienced greater improvement in both cognitive and speech accuracy and processing speed during their recovery. The company analyzed around 100 million points [4] (http://www.mobilehealthtimes.com/big-data-and-mobile-technology).

Numerous genetic studies correlating genetic variants with the risk of stroke have already been established in different geographical areas [5, 6]. Microaray and next generation sequencing have enabled to collect large amounts of digital genetic data. The novel technological advances have made it possible to provide immediate molecular information from the genome, transcriptome, epigenome and proteome, and have attracted researchers and clinicians for the treatments of neurological diseases including epilepsy and stroke [7].

Several studies have well established that rare single gene stroke syndrome, e.g. Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL), is the result of mutations in *NOTCH3* gene. The mutations in *NOTCH3* gene result in abnormal receptor protein, which impairs the survival and function of vascular smooth muscles thereby damaging the blood vessels. Genome wide studies can establish the perfect diagnosis of certain diseases, and can help in planning selective treatment. Although the treatment is still not available for CADASIL but enzyme replacement therapy has been established for Fabry's disease, another well known single gene disorder leading to stroke [3].

Exome sequencing, epigenetics, and other genetic advances offer novel mechanisms to treat the complex cerebrovascular disorders like stroke. Precision in phenotype description via big data, and the addition of advanced imaging state data, promises to complement advances in health sciences to reduce the chances of error in secondary stroke treatment of cryptogenic origin with more perfection. The first large-scale exome wide sequencing study has identified protein-coding variants in two new genes phosphodiesterase 4D-interacting protein (*PDE4DIP*) (rs1778155) and acyl-coenzyme A thioesterase 4 (*ACOT4*) (rs35724886) significantly associated with ischemic stroke [8].

ISSN: 2456-2254
PRECISION MEDICINE

A few examples are already available where genetic studies have been in use to influence the medication use in associations between drug and genetic variants and are included in prescription guidelines for clopidogrel, metoprolol, and warfarin [9]. Biomarkers have been established and are being actively found to influence the drugs prescribed in stroke, e.g. antiplatelet agents aspirin and clopidogrel. Gene expression profiling have been undertaken to identify the role of genetic markers in relation with stroke and its subtypes and to differentiate between ischemic stroke and transient ischemic stroke [3] . Animal studies and translational observational human studies are underway to identify the role of a single gene as a biomarker which controls 80% of the variation of the arterial collaterals [10]. If these studies provided expected results, a patient's collateral genetics could be used in the selection of endovascular therapy [3].

CONCLUSION

Precision medicine is an emerging area integrating scientific research and current clinical practice to develop a platform which can precisely guide tailor made medical practice and can improve patient care. This will result in targeted therapy according to the needs of individual patients fitting to their genetic, biomarker characteristics and bioinformatics determining better clinical outcome. The prospect of applying the concept of precision medicine has been favoured and improved by the recent development of large-scale biological databases (such as the human genome sequence), proteomics, metabolomics, genomics, drug designing and protein modeling and even with mobile health technology. The ischemic stroke is a multifactorial disease with complex genetic, lifestyle and environmental factors. The precision medicine in stroke will not only aid to the perfect diagnosis and therapeutic measures but to the improvement in quality of life in post stroke rehabilitation.

CONFLICT OF INTEREST
The authors declare no competing interests.

ACKNOWLEDGEMENT
None.

FINANCIAL DISCLOSURE
None.

REFERENCES

[1] *de Villiers S, Swanepoel A, Bester J, et al. Novel Diagnostic and Monitoring Tools in Stroke: an Individualized Patient-Centered Precision Medicine Approach. J Atheroscler Thromb. 2016; 23(5): 493-504.*
[2] *Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med. 2015: 26; 372(9): 793-795.*
[3] *Rostanski SK, Marshall RS. Precision Medicine for Ischemic Stroke. JAMA Neurol. 2016:1; 73(7): 773-774.*
[4] *http://www.mobilehealthtimes.com/big-data-and-mobile-technology.*
[5] *Maasz A, Melegh B. Three periods of one and a half decade of ischemic stroke susceptibility gene research: lessons we have learned. Genome Med. 2010; 2(9): 64.*
[6] *Munshi A, Das S, Kaul S. Genetic determinants in ischaemic stroke subtypes: seven year findings and a review. Gene. 2015: 25; 555(2): 250-259.*
[7] *Tan L, Jiang T, Tan L, et al. Toward precision medicine in neurological diseases. Ann. Transl. Med. 2016; 4(6): 104.*
[8] *Auer PL, Nalls M, Meschia JF, et al. Rare and coding region genetic variants associated with risk of ischemic stroke: the NHLBI Exome Sequence Project. JAMA Neurol. 2015; 72(7): 781-788.*
[9] *Kaufman AL, Spitz J, Jacobs M, et al. Evidence for clinical implementation of pharmacogenomics in cardiac drugs. Mayo Clin. Proc. 2015; 90(6): 716-729.*
[10] *Sealock R, Zhang H, Lucitti JL, et al. Congenic fine-mapping identifies a major causal locus for variation in the native collateral circulation and ischemic injury in brain and lower extremity. Circ. Res. 2014; 114(4): 660-671.*