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Letter

"Multiomic" Studies as a Promising Clinical Pharmacological Tool for Personalization of Socially Significant Diseases Pharmacotherapy in Russia

Dmitry A. Sychev

Russian Medical Academy of Continuous Professional Education, Moscow, Russian Federation;
* Correspondence: rmapo@rmapo.ru; Tel.: +7-495-680-05-99 (D.A.S.)

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Currently, after a patient has been diagnosed (based on clinical, laboratory and instrumental data), doctors prescribe medications, the use of which is regulated by the relevant clinical guidelines for the treatment of a particular disease, developed by experts from professional organizations based on the principles of evidence-based medicine, based on the results of randomized clinical research. At the present time, within the framework of clinical recommendations, several options for pharmacotherapy can be provided. At the same time, the most important task of clinical pharmacology is to develop approaches to personalizing the choice of drugs and their dosing regimens, which should ensure maximum efficiency and safety of treatment in a particular patient. In the same time, pharmacogenetic / pharmacogenomic, pharmacoepigenomic and pharmacometabolomic biomarkers are being actively studied, which reflect the individual characteristics of pharmacokinetics and pharmacodynamics in a particular patient at different levels: from the genome and regulation of the corresponding genes' expression to the "implementation" of the work of their products (biotransformation enzymes, drug transporters) in the form of values of concentrations of drugs and their metabolites in biological fluids. At the same time, pharmacogenetic / pharmacogenomic biomarkers can be referred to as "apriori" biomarkers (i.e., predicting individual characteristics of pharmacokinetics and pharmacodynamics before prescribing a drug), and pharmacoepigenomic and pharmacometabolomic biomarkers can be referred to as "posterior" biomarkers (i.e., reflecting "current" individual features of pharmacokinetics and pharmacodynamics against the

background of the prescription of the drug). Development and implementation of algorithms for personalizing the pharmacotherapy of patients with a number of common socially significant diseases based on pharmacogenetic/pharmacogenomic, pharmacoepigenomic and pharmacometabolomic biomarkers in clinical practice looks promising.

The developed personalization algorithms, "packed" for the convenience of the doctor in the form of computerized clinical decision support systems, have been tested in real clinical practice ("clinical validation") and allow to increase the effectiveness of treatment, reduce the frequency of adverse reactions, and also reduce the economic costs of ineffective treatment and correction of medical complications. The most important conditions for the translation of such approaches are the development and implementation of educational programs for advanced training and educational events and schools for young scientists to form competencies among doctors, researchers and other healthcare professionals in the development and use of new biomarkers for the personalization of pharmacotherapy for their successful implementation in clinical practice.

It is important that in Russia a number of research teams have created and successfully applied a unique methodology for creating and implementing this kind of algorithms for personalizing drug prescriptions in patients with various diseases, from studying the problem of pharmacotherapy in the clinic and selecting candidate biomarkers (including through research *in silico* and *in vitro*) before their introduction into clinical practice within the framework of the so-called translation cycle. According to this methodology, algorithms for the personalization of pharmacotherapy based on pharmacogenetic/pharmacogenomic, pharmacoepigenomic and pharmacometabolomic biomarkers in patients taking antithrombotic, psychotropic, antihypertensive, analgesic, anti-secretory, anti-tuberculosis, antiviral (for COVID-19), antiglaucoma drugs have already been developed and are being implemented in Russia, as well as drugs used in diseases of the gastrointestinal tract and bronchial asthma and in oncological practice, etc. Developments of this kind are undoubtedly promising and correspond to the priority for the development of domestic healthcare, regulated in the Strategy for Scientific and Technological Development of Russia: “transition to personalized medicine ... through the rational use of drugs”.

Dmitry A. Sychev, MD, Prof.

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