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PERSONALIZED MEDICINE IN CARDIOLOGY: STATE OF THE PROBLEM AND OUTLOOK

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Annotation
Personalized medicine emerged about three decades ago. Even then, it interested many scientists, researchers, doctors. However, only after the complete discovery of the human genome in 2001, personalized medicine began to make it possible for some pathologies (oncology, rheumatology, cardiology) to select the most effective treatment with minimal adverse drug reactions for a particular patient. The ability to own genetic information gives a chance to suspect, predict, predict the onset of the disease. Personalized medicine is able in some cases to tell exactly whether a drug will work for a given patient, bringing us closer to "treating not the disease, but the patient." But doctors to this day, to determine risk factors, are guided by the individual characteristics of the patient, such as age, gender, body weight, concomitant diseases, and, based on this, prescribe drugs, adjust the dose, and change the treatment regimen if ineffective.

Keywords: pharmacogenetics, biomarkers, personalized medicine, genetic information, genetic testing.

INTRODUCTION

The ability to own genetic information made it possible to start introducing personalized medicine into clinical practice. Genetic studies have begun to show that certain drugs under certain conditions are very effective for some patients and ineffective, and sometimes even dangerous, for others. Therefore, at the intersection of pharmacology and genetics, pharmacogenetics arose, a science that studies the role of genetic factors in the formation of the pharmacological response of the human body to a drug [1]. This can enable the doctor to personalize both the drug itself and the dose for a particular patient and ensure maximum efficacy and safety of the drug.

MATERIALS AND METHODS

The role of heredity in the formation of an individual response to drugs has been known for a long time, understanding the mechanisms of the influence of genetic factors on the effectiveness and safety of pharmacotherapy became possible only with

the development of molecular biology methods and the implementation of the international program "Human Genome". The latest data available on the structure of the human genome clearly show that there are many gene variations that explain differences in drug absorption, distribution, metabolism, excretion, and ultimately the body's response to a pharmaceutical drug. Such preliminary successes made it clear that such research would lead to a medicine that would be both individual and accurate.

RESULTS AND DISCUSSION

The terms "genetics" and "genomics" can be used interchangeably [3]. The term "genetics" is often used in relation to the study of heredity, with an emphasis on a specific and limited number of genes with a known function in disease. The term "genomics", in contrast, refers to the totality of an individual's genetic makeup. The main focus will be on “genomics”, although in a given clinical situation for a particular disease or drug, it will be necessary to focus on one or more individual genes or variants within them [4]. If the pharmacogenomics profile is sufficiently predictive of drug response, then this can be used to predict likely side effects and treatment efficacy in an individual prior to drug administration, as well as to identify those patients who should be evaluated more carefully. to ensure that the drug reaches the therapeutic level. For example, variability in response to antiarrhythmic drug therapy, as well as variability in response to other forms of pharmacological therapy, may be associated with controlled drug distribution. Thus, dysfunction of CYP2D6, which codes for hepatic cytochrome P450, responsible for the metabolism of approximately 25% of clinically used drugs, is common. This is especially true for slow metabolizers [5]. Let us consider an example of a change in the pharmacological response in CYP2D6 metabolizers. In the body, the antiarrhythmic propafenone is metabolized to 5-hydroxypropafenone, which has a beta-adrenergic blocking effect. In turn, the inactivation of 5-hydroxypropafenone occurs under the influence of CYP2D6.

The idea that rare hereditary syndromes are accompanied by a high risk of cardiac arrhythmias arose in the middle of the 20th century. Large studies led to the identification of disease genes - long QT syndrome [21], [22], and then in other hereditary types of arrhythmias. These studies have not only identified the disease genes for these rare syndromes, but as a result have identified key molecular components that regulate normal cardiac electrophysiology. Genes for other congenital syndromes have also been identified, such as catecholaminergic polymorphic ventricular tachycardia, Brugada syndrome, short QT syndrome [23].

Recognition of congenital arrhythmia syndromes of this type is especially important for screening relatives and identifying latent forms of these conditions, since knowledge of the main pathophysiological disorders obtained directly from human genetics often informs about a rational approach to therapy [24].

Genetic studies on long QT syndrome have identified increased net current flow during cardiac repolarization as the underlying lesion in congenital long QT syndrome. This situation may arise due to mutations that cause a loss of outward current, in particular in the KCNQ1 and KCNH2 potassium channel genes or their subunits, or mutations that directly cause an increase in current flow through sodium or calcium channels during repolarization process. It should be noted that the identification of these mutations is necessary in order to emphasize and clarify the role of encoded channels in the normal physiology of the heart. Thus, for example, a channel as a result of the expression of KCNQ1 (heart potassium channel gene) with the function of changing the KCNE1 subunit creates outward currents of K ions, an adrenergic sensing current, which probably serves to limit the duration of the action potential under conditions of sympathetic stimulation. Similarly, a channel resulting from KCNH2 expression (called HERG or Kv11.1) plays a key role in the development of cardiac potential from potential plateau to resting potential at the end of phase 3 of the action potential [25].

Despite the fact that personalized medicine has high hopes in the treatment of patients, and research shows good results, there are still too many problems, without which it will remain an unrealized idea for a long time.

One of the biggest challenges is the search for new biomarkers. In the US, only 1-2 new biomarkers have been approved for all diseases, despite huge technical advances in omics. This is due to the fact that the risk of false detection of markers increases with an increase in the number of measured parameters. Thus, the current ability to measure hundreds to thousands of analyzes in a single experiment will lead to potentially false findings. However, this problem can be solved using widely used statistical methods. There are three categories that newly discovered potential biomarkers fall into: randomness, bias, and generality. The only category that can lead to a potentially clinically useful biomarker is generalization. If a sufficient number of new biomarkers associated with diseases are not discovered in the near future, this will mean that personalized medicine will remain out of work for a long time to come.

CONCLUSION

The saying "easier said than done" best describes the current circumstances regarding the implementation of the concept of personalized medicine. At this stage, personalized medicine is an ideal model, part of which is being introduced into medical practice. The success is that now in a number of cases with certain pathologies (oncology, cardiology) it is possible to prescribe the drug in the required dose and be sure that this is exactly what the patient needs. The rest of personalized medicine leaves much to be desired. This is the incompatibility of system data. You need to make sure that the systems will interact with each other. No less important is the fact that doctors themselves do not believe in personalized medicine, are afraid of it and do not want to associate themselves with it, because, as it seems to many, based on their experience and knowledge, they may well decide which drug, which dose to prescribe. patient.

The ability to predict and prevent the disease in advance is probably the key task, but there are many "pitfalls" in this issue. Of all the prerequisites for the implementation of personalized medicine, the most significant are biomarker studies, reliable evidence of pharmacogenetic tests demonstrating clinical utility. The study of biomarkers is a difficult task, because it is currently impossible to find their exact number for a number of diseases. One thing is for sure, the implementation of the concept of personalized medicine requires a coordinated effort of all stakeholders in the field of healthcare.

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