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REVIEW ARTICLE

THE GENESE OF PREDICTIVE-PERSONIFIED MEDICINE AND THE PROBLEMS OF ITS IMPLEMENTATION IN UKRAINE

POWSTANIE PREDYKCYJNO-SPERSONALIZOWANEJ MEDYCYNY I PROBLEMY Z JEJ WDROŻENIEM NA UKRAINIE

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ABSTRACT

The concepts, content and significance of predictive-personified medicine that are able to improve the quality of treatment, using genetic information when choosing the medical procedures that are necessary for a particular person are considered. Characteristic of the principles of predictive-personified medicine and its fundamental foundations are carried out: genomics; proteomics; metabolism; bioinformatics The history of the formation and development of predictive-personified medicine in the world is investigated, the relevant legal documents are analyzed.

The main advantages of predictive-personified medicine are determined: detection of an illness at an earlier stage, when its treatment is more efficient and cheaper; division of patients into similar groups for the choice of optimal therapy; reduction of adverse reactions to drugs by more effective early assessment of individual negative reactions; improvement of the selection of new biochemical indicators, allowing to control the action of medicinal products; reducing the time, cost, and the number of failures in clinical trials of new treatments.

It is noted that in Ukraine none of the well-known projects approved by the American and European committees on gene therapy are implemented. However, the priority direction of research in the field of genetics is chosen annually by more and more medical institutions of Ukraine. Examples of the introduction of predictive-personified medicine into medical institutions and scientific institutes in Ukraine are presented.

It is concluded that ensuring the effectiveness of this direction of modern medicine depends on the elimination of many problems of socio-managerial and regulatory nature. In addition to their solution, the priority tasks in this area include the carrying out of significant informational and enlightening work with the population; increase of state funding for the development of preventive medicine; creation of public-private partnership of base centers.

KEY WORDS: predictive-personified medicine, genetic predisposition of a person, molecular-genetic level, social-managerial and regulatory-legal problems

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INTRODUCTION

The concept of predictive-personified medicine is actively discussed in many countries around the world, including in Ukraine. According to most scholars, predictive-personified medicine can add to substantially improve the quality of treatment. On the basis of genetic information, the physician should identify at the molecular-genetic level the patient's individual inclination to the disease and identify the pathways for early prophylaxis and, by correction, mitigate the adverse effects of functionally defective products of polymorphic genes. Predictive medicine can forecast the disease [1]. As for personified medicine, this fact proves its significance. According to numerous pharmacological studies, 40% of medications are not effective enough because they are aimed at a standard approach to the patient. At the same time, knowing about the genetic features of a person, the doctor will be able to choose the most effective medication and optimal, effective, safe dosage for the organism of a specific person. The effectiveness of the implementation of theoretical developments of predictive-personified medicine in practical medical activities is hampered not by solving a number of issues of an organizational-a managerial, organizational, medical, legal, social, moral and ethical nature.

THE AIM

The aim of the article is a consideration the essence of predictive-personified medicine in relation to its effectiveness, as well as to identify socio-management and legal-regulatory problems of its implementation.

MATERIALS AND METHODS

Methods of research selected based on the purpose of the study. In order to establish the objectivity and validity of scientific statements and conclusions, during the conducted research a complex of general scientific and special scientific methods was used, in particular such as: the formal legal method, comparative legal method, analyt-

ical, etc. The formal legal method was used to clarify the content and essence of European legal documents in this area; with the help of the comparative legal method the approaches to the introduction of predictive-personified medicine in the world and in Ukraine were elucidated; the analytical method contributed to the study of problems and disadvantages of the introduction of predictive-personified medicine in order to eliminate them.

Also the scientific-heuristic potential of such philosophical methods of research as synthesis, deduction, induction, abstraction is used.

REVIEW AND DISCUSSION

The only and unequivocal term for the definition of predictive-personified medicine has not yet acquired its final form, in the USA and European countries, for the most part, use the term predictive-preventive and personified medicine (PPPM). Its meaning is seen in determining the individual inclination to the development of diseases at the molecular genetic level, resulting from a mutation and genetic polymorphisms. The main tasks of the PPPM include: 1) the detection of signs of the disease at the stage of preclinical pathology with the identification of targets adequate for pharmaco-prevention; 2) pharmaco-correction of the revealed violations for the purpose of pharmaco-prevention, which belongs to the category of preventive measures that contribute to suppressing the pathological process at the preclinical stage [2].

The PPPM is based on the following principles:

- predictability (prediction), which allows predicting the disease based on the individual features of the genome and create a probable health outlook based on genetic research;
- prevention (prophylaxis), which at the preclinical level helps to prevent the emergence of diseases through their prevention, as well as vaccines and drugs for «repair» of damaged genes;
- personalization, based on an individual approach to each person (creation of a unique genetic passport for patient treatment and control of the health);
- wide collaboration of various doctors-specialists and patients, and also on the transformation of the patient from the subject of treatment into the object of the medical process.

The fundamental basis of the PPPM include:

- genomics (a chapter of genetics that investigates the genomes of living organisms and the principles of coding proteins; genomics provides scientific information about individual genetic features of the patient, thus determines the charecter of the disease and reaction to certain types of treatment);
- proteomics (the branch of molecular biology, which defines a complete set of proteins that are associated with a specific physiological or pathological state; its main task is to quantitatively analyze the expression of proteins in cells, depending on their type, state or influence of external conditions);
- metabolomics (engaged in the study and analysis of metabolism - a collection of all low molecular weight metabolites of biological fluids, tissues and cells of the body; some of the low molecular weight metabolites can become indicators of pathological conditions);
- bioinformatics (creates informative information bases in the sphere of PPPM).

Predictive medicine was initiated in the 80's and 90's of the twentieth century and formulated by the Nobel Prize winner Jean Dausset, whose the innovative work outlines the main principles that have contributed to the development of key ideas by the description of systems of antigenic tissue compatibility (HLA, human antigens of leukocytes) in predictive, preventive, personalized, and participative medicine (4P medicine) and subsequently reflected in the human genome project.

Today, the concept of PPPM is thoroughly discussed at international conferences, including the Cambridge, Oxford University (2010-2012), the International Symposium on Biopredictors (Dresden, Germany, 2011), the First European Congress on the PPPM (September 2011) , which founded the European Association of PPPM (EPMA). The Association has a clear structure for achieving the best coordination of multiaspecting activities related to the principles of the PPPM throughout Europe, which includes National Representatives of all 27 EU Member States and Associate Members (eg Israel, Serbia, etc.). Note that on July 1, 2011, the Board of Directors of EPMA approved the National Representative in Ukraine.

To the basic European legal documents, we will attribute the Universal Declaration on the Human Genome and Human Rights dated 11.11.1997 (UN, UNESCO), the International Declaration on Human Genetic Data of 16.10.2003 (adopted by the resolution of the General Conference of UNESCO on the report of the Commission III on 20th plenary meeting), the Resolution of the Inter-Parliamentary Assembly of the CIS member-states 329-12 "On the ethical and legal regulation and safety of genetic medical technologies in the CIS member states", the Explanatory report to the Additional Protocol to the Convention on Human Rights and biomedicine concerning genetic testing for medical purposes.

The modern concept of the PPPM provides for a complex integrative function of scientific, medical, preventive and educational institutions, requires the use of not only modern diagnostic tests and equipment, but also appropriate modernization of the system of state guarantees, financing, with the possible involvement of private sources, and legal norms of interaction between the physician and the patient [3,]. The main advantages of PPPM include: identifying a disease at an earlier stage, when its treatment is more efficient and cheaper; division of patients into similar groups for the choice of optimal therapy; reduction of adverse reactions to drugs by more effective early assessment of individual negative reactions; improvement of the selection of new biochemical indicators, allowing to control the action of medicinal products; reduction of time, cost and number of failures in clinical trials of new treatment methods [4, 17].

Experts have proved the genetic predisposition to such diseases as: hereditary thrombophilia, cardiovascular diseases, respiratory diseases (bronchial asthma), joint pain, miscarriage, gastrointestinal tract (celiac disease), endocrine diseases (diabetes mellitus), oncological diseases (breast cancer).

In Ukraine, none of the well-known projects approved by the American and European Gene Therapy Committees are being implemented. However, the priority direction of research in the branch of genetics is chosen annually by more and more medical institutions of Ukraine [5, p. 35]. Here are some examples.

The major research center is the Institute of Genetic and Regenerative Medicine of the National Academy of Medical Sciences of Ukraine, which has departments of cell and tissue technologies with laboratories of immunology; of cell and tissue cultures, experimental modeling; genetic technologies with laboratories of genetic-engineering biotechnologies; of gene-cell modifications; of genetic diagnostics with laboratories of DNA-diagnostics, cytogenetics, metabolomics.

The concept of strategic development of the Odessa National Medical University for the period 2017 - 2019 as one of the main tasks of the introduction of the work of the departments provides a new scientific direction, taking into account predictive medicine, neurology, NBIC-technologies.

Scientific researches related to molecular genetic markers in sports are conducted jointly by the Department of Human Biology of the National University of Physical Education and Sports of Ukraine and the Laboratory of Theory of Methodology of Sport Training and Reserve Opportunities of athletes at the Research Institute of the National University of Physical Education and Sports of Ukraine.

Today, person-based research can be conducted in selected regions of Ukraine. So, at the Interregional Center for Medical Genetics and Prenatal Diagnostics in Kryvyi Rih (Dnipropetrovsk Region), a laboratory of molecular genetics "Genomics", which equipped with the latest unique equipmentwas, opened.

Specialists have developed and successfully implement such areas as diagnosing the genetic causes of male, female infertility and other reproductive disorders; detection of predisposition to oncopathology (breast and ovarian cancer); cardiovascular diseases (heart attacks, stroke, hypertonic disease); diabetes mellitus (type I, type II); individual selection of medicaments (medication against hypertension, allergies, antitumour, etc.). In addition, thanks to unique equipment for the first time in Ukraine is introduced the most complete and quick diagnosis of cystic fibrosis - a widespread hereditary disease that can manifest itself in the form of pathology of the respiratory, gastrointestinal and reproductive systems, and without timely treatment it leads to the death of the patient and can not be diagnosed with general clinical methods. Furthemore, the mild form of this disease manifests itself in the form of male infertility of unclear origin [6].

The formation and development of the PPPM requires solving many tasks. S.Suchkov, M.Legg, M.Paltsev, O.Golubnichna among tasks allocate, first of all, the creation of a regulatory and legal framework that would meet all the requirements for the protection of individual health (rules of state guarantees of the system of PPPM; channels of financing of the industry, which include both state and private sources, the rules for regulating the relationship between a doctor and a patient, a system for familiarizing the population with a new approach to health care); secondly, the novelty of the task requires radical retraining of medical personnel, qualitative changes in their level of qualification, the range of services provided by them to the population, etc. [2].

The professional literature identifies such problems in these and other areas. To socio-managerial problems D. Horin [7] includes:

1) the problem of social inequality and the spread of predictive-personified medicine. It is that low-income groups of the population can not afford high-quality medical care. The introduction of predictive-personified medicine should be carried out in compliance with the principle of social justice and contribute to reducing the social gap in access to new genetic services;

2) the proliferation of predictive-personified medicine and the problem of aging population. Increasing the life expectancy inevitably leads to an increase in illnesses of the elderly, the need to seek additional resources to provide them with comprehensive, well-qualified care and the limiting the capacity of the health care system to provide predictive-personified health services;

3) the principle of social justice in the dissemination of predictive-personified medicine is that health workers should not be motivated to profit and use patients to receive it. They should focus on the needs of patients, not on their solvency, while adhering to the equally high standard of provision of medical genetic services for all.

A team of foreign scholars highlights a wide range of organizational, legal, economic, and moral-ethical aspects during the introduction of predictive medicine [8, p.6-12]. Organizational problems are connected with the necessity of carrying out significant researches, lack of necessary organizational resource for this, adequate state financing, and the lack of interest of public healthcare authorities and medical institutions in their conduct. Economic problems are caused by the lack of proper and necessary funding of projects for predictive medicine and personified prevention. Legal problems arise when obtaining permits for the use of new methods of prevention, diagnosis and treatment of diseases (examination of documents and decision on granting such permission takes place over a long period of time, and also a long period of registration of a patent). To moral-ethical issues include the need to address the following issues: at what age should genetic testing? Who should have access to its results? Should close relatives know about the research results? Where and how should results from genetic research be stored? etc.

To organizational and medical measures, we also include: 1) an active detail of the history of the patient; 2) deter-

mining the risk factors for the patient and his relatives; 3) referral to the cabinet of oncological counseling; 4) compilation of the genetic map + genotyping of the patient patient, as well as his relatives (in the case of diagnosis of mutations); 5) blood collection from relatives who are in the risk group; 6) discussion of the results obtained by the oncologist and geneticist; 7) statement of the genetic diagnosis and determination of the principles of prevention and follow-up monitoring to protocol. After obtaining the necessary results an individual map of prevention, routing and detected chronic pathology is taken into account taking into account the established risks [3].

O. Minczer and V. Vishnevsky also called such problems of the introduction of personalized medicine - its high cost (however, if eight hundred years ago genome sequencing cost hundreds of thousands of dollars, today this amount does not exceed one thousand dollars); undevelopment of the correct methods for assessing the dynamics of risk factors in time suitable for clinical practice, due to their large number; the ambiguity of the interpretation of the concept of "risk factor dynamics", etc. [9].

Specialists express the following proposals for the development of the Ukrainian health care system of the innovative concept of predictive medicine: to create and test a pilot model of predictive help on the example of one of the regions of Ukraine; to develop and implement training programs for the training of relevant specialists; to open departments and faculties of predictive medicine on the basis of leading educational institutions of Ukraine [10].

CONCLUSIONS

The formation of predictive-personified medicine is due to the development of genomics, proteomics, metabolomics, bioinformatics. In Ukraine, predictive-personified medicine is still at the initial stage of its development. At the same time, in this area, projects are being developed that involve the transition from studying the genetic predisposition of a person to the diagnosis and prevention of its diseases, individual treatment. Ensuring the effectiveness of this direction of modern medicine depends on the elimination of many problems of socio-managerial and regulatory nature. In addition to solving them, to the priority tasks in this area include conducting significant info-sensitization with the population; increase of state funding for the development of preventive medicine; creation of public-private partnership of base centers.

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Conflict of interest:
The Author declare no conflict of interest.

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