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ETHICAL ISSUES IN RARE DISEASES

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Abstract

Scientific, technical and medical advances continue to raise consequential ethical questions and dilemmas also in the field of rare diseases. Difficult and complex issues of medical ethics in rare diseases are presented and several different ethical problems, like those regarding inborn errors of metabolism, are discussed.

Key words: rare diseases, ethical aspects

Streszczenie

Ogromny postęp naukowy i techniczny prowadzi równocześnie do narastania skomplikowanych, trudnych do rozwiązania problemów i dylematów moralnych oraz etycznych także w zakresie chorób rzadkich. W pracy przedstawiono różne aspekty etyczne chorób rzadkich tj. dotyczące: diagnostyki, prowadzonego leczenia, ich finansowania itp.

Słowa kluczowe: choroby rzadkie, aspekty etyczne

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The quality of society and civilization is measured by the respect which they show the weakest of its members (Document of the Holy See issued on the occasion of the International Year of Disabled People 1981).

The issues related to the ethical aspects that concern the topic of rare diseases, are primarily the marginalization or exclusion of patients and their families from a full social life on the one hand, and on the other hand a number of other issues, such as the failure or only partially addressing the needs of this group of patients in health and drug programs, even in the richest and most developed countries and the range of medical and therapeutic issues such as those resulting from chronic and progressive course, and in most cases, poor prognosis, diagnostics, treatment and rehabilitation [1]. The complexity of a number of other, previously described, subjects causes that each of them can be, and should be also considered in terms of relating to ethics, philosophy and generally philosophical and moral views. For example, the concept of justice, solidarity, honesty, being part of any ethical system should be considered when discussing a number of issues relating to rare diseases [2].

Many rare diseases like inborn errors of metabolism are diagnosed using newborn screening tests. Among classical criteria for screening, developed for WHO by Wilson and Jungner, ethical aspects concern the criteria of public support for the screening program and the common recognition who should be treated as patients. Among the updated and modified criteria – published by Andermann in 2008 [3] an increased number of criteria is connected with ethical aspects, i.e. a screening test answering identified needs, assurance of conscious consent, confidentiality of results and respect for the autonomy of families, promotion of equality and access to screening for the entire target population. Ethical aspects in the field of newborn screening include the risk of discrimination or stigmatization of children included in the screening test as well as their families, and inflicting fears in their parents as a result of false positive results, detection of incurable congenital metabolic diseases, which is sometimes referred to as medicalization of the neonatal period [4, 5, 6].

Difficult decisions and moral dilemmas and problems of responsibility arise in the activities of all those who in

any way have to deal with patients with rare diseases and can actually affect their situation. This includes doctors, specialists and experts in various fields of medicine – clinicians, scientists, academics, psychologists, teachers, speech therapists and physiotherapists as well as officials from the Ministry of Health, the National Health Fund, Agency for Medical Technology Assessment, employees of pharmaceutical companies, insurance companies, local and central government and the media, patient and professional organizations, foundations, charities, etc.

Bioethical issues are related to clinical trials in rare diseases. Randomized clinical trials are the gold standard in research, confirming safety and effectiveness of new medical products: however, for the evaluation of orphan medical products (OMP), for which it is difficult to run an extensive clinical trial, it is crucial to estimate the risk-benefit ratio, rather than results of conventional or unconventional clinical trial methodology. The uniqueness of clinical trials in rare diseases result from the small number of patients and their sparsity, the unknown natural history of many rare diseases and limited interest in investments in new orphan drugs observed on the part of the pharmaceutical industry. For this reason in case of rare diseases special legal solutions seem necessary for clinical trials and research, registration, rules of launching new products and their reimbursement (e.g. simplified registration procedures, support for research, tax relief, etc.).

Among others, bioethical aspects refer to scientific research (eg, conducted in children, studies with placebo, using modern genetic techniques, biological samples and their banks), with the type of treatment used, for example, organ transplantation, also with palliative care, persistent treatment and life support, euthanasia (for example, in the case of progressive neurodegenerative diseases of the brain), with the diagnosis on neonatal mass screening and selective screening, prenatal diagnostics, with the equal access of patients to specialized centers comprehensively dealing with rare diseases – where they would be properly, according to the standards, diagnosed (early detection of a number of diseases and early introduction of appropriate treatment prevents dangerous consequences and allows normal life to patients) and would achieve complete currently available treatment, the possibility of rehabilitation and broader protection. Further elements of aid-social, educational and psychological assistance – and all the activities of the institutions and their staff, politicians and decision makers involved in matters relating to rare diseases also require high standards of ethical behavior.

A key theme is the issue of orphan drugs in relation to their availability to patients, pricing, practices and strategies of pharmaceutical companies and the sale and financing of treatment programs both in rich, developed countries and in developing countries.

In fact, the answer to the crucial and difficult question of how much a human life is worth, should be given.

Lack of or inadequate meeting of the existing needs of a specific consumer of medical services, who is a patient with a rare disease, raises a number of consequences of the economic, social and ethical nature. Often, especially in the media, there are visible emotional and social pressures (on the decision makers) in order to ensure that individual patients or groups of patients obtain funding for possible and existing, very expensive treatment. The noble idea of egalitarianism in relation to this, in the face of shortages or lack of appropriate measures, cannot be fully implemented for execution. The main problem is that the needs to make an effort and expenditure for the treatment procedure for patients with rare diseases are growing very quickly and do not have full coverage and financial security by the payer (in Poland: National Health Fund and the Ministry of Health). Choices are therefore necessary, to whom to allocate resources from a limited pool of money, based on a subjective sense of justice and solidarity and look for more objective methods remaining the responsibility of pharmacoeconomics. In these cases, decisions related to management of health or medical programs, in particular to define clear criteria for taking on or off of the program and its funding must be fully transparent. These activities must be in accordance with applicable law, which, through the procedures, gives patients and families the ability to report and enforce the claims in this regard.

There is no uniform system of ethical values, which clearly could be made for funding the treatment of patients with rare diseases, especially for the most expensive therapies and types of diseases. In making these decisions, medical technology agencies (HTA) help evaluating the efficacy, safety and cost-effectiveness in relation to the data of the treatment. However, the criteria applied for pricing and reimbursement decisions in the case of rare diseases are objectionable in view of economic and ethical dilemmas. On the one hand, we face low profitability of the development of new therapies in rare diseases (measured by their health effects for the whole population), while on the other hand they frequently offer the only chance for the patients to recover. For this reason the use of placebo in research concerning rare diseases is frequently questioned. In the case of some diseases, particularly progressive conditions, the length of randomization tests is limited to a relatively short period to avoid ethical concerns, related with a conscious decision to leave patients without the only therapeutic option.

Another issue, having a relationship with ethics, is responsibility for decisions made (eg political) on the current activities and the use of public funds in financing the treatment of patients with rare diseases and providing them with appropriate social support. The problem connected with the dynamically increasing number of orphan drugs and high costs of these therapies constitute a challenge for state budgets with limited funds. A question arises whether financing treatment of rare diseases grants a special status to orphan drugs and products or whether it is rather a handicap for patients with rare diseases in comparison to those with common conditions [7]. This results in a different approach to pharmacoeconomic analyses, including indexes of therapy profitability such as e.g. QALY, i.e. the threshold cost of receiving an additional year of life, adjusted by its life, which in accordance with the law binding in Poland is established at three-fold

Gross Domestic Product per capita. From the point of view of the patient the adoption of such an index is a limitation of treatment availability.

Most rare diseases affect children, and a large proportion of cases occurs with central nervous system involvement, resulting in mental retardation and many of its consequences. Also the issue of research on this age group [8], and people with different disabilities, creates additional problems, including ethical issues.

Further, equally important, ethical issues regarding rare diseases are related to biotechnology and pharmacogenetics, carrying out some research, for example on genetic engineering, cloning and use of stem cells and gene therapy, which can highly expand treatment possibilities, however, bringing about different threats.

Other issues are: – the use of and access to customized therapies – relationship between doctor and patient – information about the disease, treatment, etc., also confidentiality of certain data - the use of conscience clause by a doctor and nurse (pharmacist ?).

Monitoring and evaluating these issues, the dispute, should be left to the special bodies, which are the ethics committees at various levels.

REFERENCES

1. Barrera LA, Galindo GC. Ethical aspects on rare diseases. Adv Exp Med Biol. 2010;686:493-511.
2. Cookson R, Dolan P. Principles of justice in health care rationing. J Med Ethics.2000;26:323-329.
3. Andermann A, Blancquaert I, Beauchamp S, Dery V. Revisiting Wilson and Jungner in the genomic age: a review of screening criteria over the past 40 years. Bull World Health Organ. 2008;86(4):317-319.
4. Wilcken B. Evaluating outcomes of newborn screening programs. Southeast Asian J Trop Med Public Health. 2003;34(3):13-18.
5. Levy HL. Newborn screening conditions: What we know, what we do not know, and how we will know it. Genet Med. 2010;12(Suppl):S213-214.
6. Dhondt JL. Expanded newborn screening: social and ethical issues. J Inherit Metab Dis. 2010;33(Suppl 2):S211-217.
7. McCabe ER. Newborn screening: A complex system that requires a culture of safety. Mol Genet Metab. 2014;113(1-2):6-7.
8. Helseth S, Slettebo A. Research involving children; some ethical issues. Nursing ethics 2004;11:298-308.

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