BIOETHICAL PRINCIPLES IN PRENATAL DIAGNOSTICS AND GENETIC COUNSELING

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The field of bioethics, as a new reality in the contemporary world, has left a deep imprint on prenatal diagnosis and genetic consultation through the profound influence of principles and values such as respect for life in general, for human dignity, respect for the patient, for their well-being, and their autonomy within the medical act. The bioethical principles of genetic research, including those referring to prenatal diagnosis, at the current stage of scientific development, continue to deserve special attention, as well as the methodological and clinical aspects as well as those, related to the organizational improvement of genetic assistance. The continuous evolution of society and the rapid development of biomedical technologies and medical genetics bring bioethical aspects to the fore. Specifically, the ethical aspects of medical genetics and genetic technologies have been the object of special attention by the World Health Organization (WHO, 1998) and have been repeatedly reviewed in the specialized literature.

In this context, within genetic consultation and prenatal diagnosis of hereditary diseases in the doctor-patient relationship, bioethical principles must be respected. Practical recommendations are based on the following general principles and foundations of medical bioethics:

1. The principle of justice involves risk assessment, risk minimization, and benefit maximization for the patient and their family.
2. The principle of responsibility and freedom refers to the amount of freedom that is proportional to the responsibility. The more freedom both the doctor and the patient possess, the more responsibility they have. The principle of the patient's and the doctor's responsibility and freedom consists of the patient assuming the risk of giving birth to a child with genetic diseases, a fact that represents inalienable individual freedom but is correlated at the level of each future mother with a responsibility towards society and also towards their family members. The doctor's responsibility is to reduce the risk through information, accurate assessment, and knowledge of the degree of risk.
3. The principle of informed consent requires that the genetic consultation includes full information for the patient regarding the risk, nature of the disease, prophylaxis methods, etc., intending to obtain the patient's consent to be medico-genetically counseled within the genetic consultation. The patient has the right to give their consent voluntarily, without being coerced by anyone, based on full information, for carrying out genetic tests or any other diagnostic method.

4. The principle of morality assumes that the doctor's actions must be moral, following general ethical norms (to be honest, to respect the patient's dignity, interests and autonomy).
5. The principle of accessibility to genetic services refers to involving as many patients as possible who require genetic assistance by reducing the barriers between them and the geneticist.
6. The principle of efficiency and usefulness, for the prevention of the birth of children with genetic diseases, aims at the actions of medical collaborators to obtain an increase in the efficiency of prophylactic measures and reduce the incidence of medical errors in diagnosis through the high degree of qualification of specialists.
7. The principle of the confidentiality of medical and genetic information aims at the comfort of the patient and strengthening their relations both with the geneticist doctor and with the entire genetic assistance system because the data provided by them to the doctor, as well as the information ascertained following the analyzes or regarding the possible risks of genetic diseases in offspring, are confidential.
According to these basic principles, genetic assistance, including prenatal diagnosis, must be provided to those who need it, according to medical indications, regardless of their income level and other social and legal conditions. Prenatal diagnosis (PD) is based on the "benevolent" principle. The essence and value of prenatal diagnosis are determined especially by the information regarding the genotype and phenotypic manifestations in fetuses and avoiding the birth of children with genetic pathologies. These aspects are analyzed from all points of view, taking into account the vital prognosis and the quality of life.
The genetic consultation must anticipate prenatal diagnosis. The geneticist provides the woman (couple) with clinical information related to the condition under discussion, the evolution of the disease, including the terms of manifestation. After confirming the diagnosis, any decision taken by the woman or the couple must be received with respect and protected within the limits of family rights and legal norms, which determine the social and cultural principles of each country. Only the parents, and in no case the medical workers, make decisions about the fate of the fetus. Repeated genetic consultation is performed when indicated in the case of invasive prenatal diagnosis and other non-invasive genetic and laboratory tests. Accordingly, the family receives complete information and signs the "Informed Consent Regarding the Genetic Investigation or Test," and the geneticist in their clinical activity is guided by the basic bioethical principles, and the following information must be provided to the family:
• The exact name and general characteristic of pathologies, which can be diagnosed in the PD result. The influence of the condition on the future child, their parents, and family members will be mentioned.
• Calculating the genetic risk and describing the probability that the child may be ill. Risk can be expressed in percentages, proportions, or in words.

• The possibility of unwanted test results and sporadic (happening) cases, “de novo” mutations. The probability of obtaining informative laboratory and ultrasound data for the diagnosis and prophylaxis of hereditary diseases.
• Resources to improve the development of the child born with genetic pathology, including drug treatment and social support, from which parents can benefit.
• Possible ways to solve the problem if the child is sick. For example, the birth and education of the child in the family or the state medical institution, the refusal and granting of the right to adoption, the termination of the pregnancy, and the treatment of the fetus during pregnancy, or immediately after birth.
• Explanation of certain laws of transmission of hereditary diseases (Mendelian, multifactorial, “de novo” mutations), some principles of treatment, and resistance to symptomatic therapy of hereditary diseases, since most of the diagnoses and fetal malformations are not treated prenatally.
• No genetic test can give a full guarantee regarding the child’s health because there are many monogenic pathologies, that do not manifest themselves until birth or have a late onset of clinical manifestations (Huntington’s chorea, Marfan’s syndrome, Reklinhausen’s neurofibromatosis). Moreover, specialists may be incompletely informed if this family has a certain risk for a certain condition (there are situations when both spouses can be carriers of the same genetic mutation in a heterozygous state and are at risk of transmitting a serious autosomal-recessive genetic condition).
• Information about the existence of non-invasive screening programs, such as biochemical screening, which is the first stage of prenatal diagnosis that does not allow for establishing a concrete definitive diagnosis.
• The name and address of specialized organizations for people with pathologies diagnosed in fetuses, which can be contacted if necessary.

The bioethical principles listed above and the aspects that regulate medico-genetic consultation, including prenatal diagnosis, are general and, by all their scope, they cannot foresee all the organizational and clinical complications that the geneticist constantly faces. Of course, the possibilities of genetic testing, which are changing and developing so quickly, must also be taken into account. In some situations, and cases when serious fetal pathologies incompatible with life are diagnosed, therapeutic abortion, up to the term of 22 weeks gestation, can and must become a saving solution, because it is important to live a healthy life. The decision to keep the pregnancy or not rests with the couple, the parents and/or the expectant mother. Sometimes, for religious or other reasons, the family does not want to terminate the pregnancy even in the presence of serious congenital or hereditary pathology in the fetus. Much depends on the social and cultural status and the nationality of the future parents. In the Republic of Moldova, prenatal genetic diagnosis is increasingly used, and its possibilities in the prophylaxis of hereditary and congenital diseases are growing rapidly, enjoying remarkable successes. Thus, prenatal diagnosis for chromosomal anomalies and congenital malformations is carried out at the population level through biochemical and ultrasound screening tests, as well as prenatal cytogenetic diagnosis technologies. As non-invasive methods of prenatal diagnosis of

genetic disorders, including congenital malformations, we mention the biochemical screening (triple test), which involves examining the level of alpha-fetoprotein, chorionic gonadotropin, and unconjugated estriol. Among the invasive methods of prenatal diagnosis, amniocentesis is most frequently indicated, with the study of the fetal karyotype at the 16th - 18th week of gestation. Knowing about and performing prenatal testing in the 1st and 2nd trimesters of pregnancy must become a priority. Anyone can fall into the category of increased genetic risk, and the involvement of a specialist and compliance with his indications by the pregnant woman justifies the need to perform prenatal tests. Prenatal screening offers the possibility of early diagnosis of serious fetal conditions at early stages of pregnancy. At the same time, it allows the selection of a group of pregnant women for invasive prenatal diagnosis - amniocentesis, through cytogenetic or molecular genetic research of fetal amniocyte cultures. Conclusions:

1. Bioethical principles and values become mandatory recommendations and postulates to be followed in the daily activity of prenatal genetic diagnosis and medico-genetic consultation to streamline and modernize curative relationships as well as due to the need to connect the local medical system to international provisions.
2. The diagnosis of genetic diseases, using the entire spectrum of biotechnologies, is carried out during the prenatal period. Thanks to ultrasonographic and biochemical screening, cytogenetic and molecular-genetic analyses, it has become applicable in the case of hundreds of hereditary pathologies and congenital malformations.
3. The methods of prenatal diagnosis are considered to be safe tests, applied on a large scale, and the specialist, the geneticist within the medico-genetic counseling, following the bioethical imperatives, informs correctly and completely, in the understanding of the proband, the role, the advantages, the degree of risk, the indications and contraindications of these investigations.

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