The meaning of patient informed consent in prenatal diagnostics and reproductive technologies

Danielius Serapinas[1,2], Andrius Narbekovas[3], Kazys Meilius[2], Jonas Juskevicius[2]

[1]Department of Pulmonology and Immunology, Medical Academy, Lithuanian University of Health Sciences

[2]Mykolas Romeris University

[3]Vytautas Magnus university

Corresponding author:
Dr. Danielius Serapinas

Abstract

Embryo genetics and epigenetics analyzes genes and their associations with environment that has impact on prenatal human development. In prenatal diagnostics informed patient consent is necessary, especially if the pregnancy has occurred after in vitro fertilization. Doctors knowledge about fetal physiology is mandatory applying reproductive technologies. During 2007 – 2011 years 1156 patients were examined and 49 (4.2%) alterations of karyotype were determined, out of which 30 (61%) are related to Down syndrome, 14 (29%) to Edwards syndrome and 5 (10%) are related to Patau syndrome. After studying the data of the questionnaire and case records, on the basis of the statistical reliability of data analysis, the influence of the main reproductive factors (abortions, contraceptives) and other risk or environmental factors (smoking, genetic diseases and the use of medicines) to fetal anomalies was determined.

Having regard to Recommendation 934 (1982) on genetic engineering of the Parliamentary Assembly of the Council of Europe as well as the World Medical Association's Madrid Statement (1987) on genetic counselling and genetic engineering we convinced that the genetic diagnosis and screening must always be accompanied by appropriate genetic counselling but that such counselling should in no case be of a directive nature.

Key words: in vitro fertilization, informed consent, patient

1. Introduction

In vitro fertilization (IVF) and other assisted reproductive technologies (ART) are effective treatments for infertility and are widely provided at infertility clinics. Although IVF and related ART procedures are generally considered safe, some studies have suggested an excess occurrence of major malformations, low birth-weight and other perinatal complications in babies conceived by ART. Further, it was recently reported that IVF and intracytoplasmic sperm injection (ICSI) are associated with imprinting disorders in the offspring such as Beckwith-Wiedemann syndrome and Angelman syndrome.

Congenital disorders very often condition physical development defects and intellectual disability. Therefore, the chromosomes of all newborns, who have certain congenital anomalies (external and internal organs) or who are intellectually disabled, should be analysed. Congenital disorders can be diagnosed at any period of organism development (prenatally and postnatally). If there are members of the familywith such diseases, it is recommended to apply prenatal diagnostics, which allows to diagnose child‘s disease prior to birth. (Sheets et al., 2010).

This work presents the analysis of congenital disorders, that are diagnosed in the Laboratory of the Hospital of Lithuanian University of Health Sciences Kaunas Clinics, in the Laboratory of Clinical Chemistry and Genetics: 1. Downsyndrome (trisomy of the 21 chromosome); 2. Edwards syndrome (trisomy of the 18 chromosome); 3. Patau syndrome (trisomy of the 13 chromosome).

The diagnosis is based on noninvasive methods: the investigation of biochemical serum indicators during the first and the second trimestre of pregnancy and medical ultrasonography. Biochemical serum analysis is important noninvasive method - PRISCA, which helps to defect the patients, who face higher risk of congenital anomalies. The modern serum analysis helps to identify pregnant women, who face higher risk of neutral tube defect and trisomies of the 21 and the 18 chromosomes (Down syndrome and Edwards syndrome) (Langlois et al., 2013).

The majority of Lithuanians have a misleading opinion that congenital disorders and all hereditary diseases is a very rare phenomenon. Unfortunatelly, a child with such a disease can be born in any family. Therefore, the society should know what are

the reasons of this phenomenon and what help can be offered to such family. For instance, entirely several tens of children with Down syndrome are born in Lithuania every year. The frequency of this disease among newborns is 1:700. Approximately 30.000 newborns per year are born in Lithuania, thus, every year approximately 40 newborns, who have the aforementioned disease, should be born in our country.

Based on the studies, the only obvious feature is the connection between forementoned aneuploidies and mother‘s age: a risk to give birth to a child with Down syndrome.

2 Materials and Methods

Stage 1. Noninvasive PRISCA tests are conducted. During the first and the second trimesters of the pregnancy the analysis of biochemical serum indicators and medical ultrasonography are performed. These indicators help to identify pregnant women, who have a higher risk to give birth to a newborn with different chromosomes anomalies (Alexioy, 2009).

Stage 2. Patients, who have a higher risk of PRISCA test results, are consulted by a geneticist.

Stage 3. Patients are offered with the further opportunities of examination, by specifying the diagnosis with the prenatal diagnostics method – amniocentesis.

Stage 4. FISH tests are carried out. (Harada, Korf, 2006). When positive results are received, karyotype is proved by using method of karyotype test. This stage of analysis is analysed in the present study.

After performing analysis mention ed in I – III stages, during 2007 – 2011 years 1156 patients, who had a higher risk to give birth to a newborn with different chromosomes anomalies, were identified. The opportunities of further investigation were offered to the patients, specifying the diagnosis by using the method of invasive prenatal diagnostics – amniocentesis.

3 Results and discussion

In order to diagnose the anomalies of chromosomes number prenatally, during the study by using molecular cytogenetic FISH method and cytogenetic method of karyotype test (analysis system Cyto Vision, Leica Biosystems, Germany), amniocytes material of 1156 patients was tested. The analysis of researches, that were carried out during 2007 – 2011 years in Laboratory Medicine Clinic of Kaunas Clinics and in the Laboratory of Clinical Chemistry and Genetics, was performed. 49 patients were diagnosed with the pathology of trisomies of chromosomes (13, 18 and 21). This number comprises 4.2 % of investigatives, who fell into the risk group, that is, a foetus of every 24th woman was diagnosed with the anomaly of chromosome that is related to Down (47, XX, +21; 47, XY, +21) Edwards (47, XX, +18; 47, XY, +18) and Patau (47, XX, +13; 47, XY, +13) syndromes. 30 patients of investigative group (1156 patients) were diagnosed with Down syndrome (2.6%), 14 were diagnosed with Edwards syndrome (1.3%) and 5 with (Patau syndrome (0.4%). (Table 1).

Table 1. The frequency of diagnosed syndromes in 2007 – 2011.

Year / Syndrome	2007	2008	2009	2010	2011	In total 2007-2011m.
	n / %	n / %	n / %	n / %	n / %	
Down syndrome	4 / 2.9%	3 / 1.3%	9 / 2.6%	5 / 2.3%	9 / 4.1%	30 / 61%
Edwards syndrome	2 / 1.5%	5 / 2.1%	3 / 0.87%	3 / 1.4%	1 / 0.45%	14 / 29%
Patau syndrome	0 / 0%	1 / 0.4%	2 / 0.58%	0 / 0%	2 / 0.9%	5 / 10%
The total number of investigatives	136	237	345	216	220	1154
The total number of pathologies	6 / 4.4%	9 / 3.8%	14 / 4.1%	8 / 3.7%	12 / 5.5%	49 / 4.2%

n – diagnosed trisomy;

% – set proportion of trisomies shows how many new cases of disease are diagnosed during a year, comparing to the number of all investigatives every year.

The results of present study showed, that in chromosomal anomalies group (n = 49) three cases of children with chromosomal anomalies were conceived after ART. In general population group chromosomal anomalies are rare: 1 out of 800 children conceived naturally ($p<0.05$).

4.Conclusions

The number of observed pathological cases is not so big to make exact conclusions, but results of present study supports hypothesis, that ART are associated with greater risk of chromosomal anomalies in conceived children.

5. References

1. Sheets K. B., Blythe G. Crissman, Cori D. Feist, Susan L. Sell, Lisa R. Johnson, Kelly C. Donahue, Diane Masser-Frye, Gail S. Brookshire, Amanda M. Carre, Danielle LaGrave, Campbell K. Brasington. Practice Guidelines for Communicating a Prenatal or Postnatal Diagnosis of Down Syndrome, *National Society of Genetic Counselors*, 2011, p. 42 - 60. ISSN: 1059-7700.

2. Langlois S., Brock J.A., Wilson R.D., Audibert F., Brock J.A., Carroll J., Cartier L., Gagnon A., Johnson J.A., Langlois S., Macdonald W., Murphy-Kaulbeck L., Okun N., Pastuck M., Senikas V. Current status in non-invasive prenatal detection of down syndrome, trisomy 18, and trisomy 13 using cell-free DNA in maternal plasma. *Obstet gynaecol Canada*, 2013, p. 81 - 125. ISSN: 0300-5577.

3. Magli M.C., Gianaroli L., Ferrareti A. Chromosomal abnormalities in embryos. Molecular and Cellular Endocrinology, 2001, p. 69 - 82. ISSN: 1874-8057.

4. Momsen G.,Sundberg K., Friis-Hansen L., Jorgensen F.S. First-trimester risk calculation for trisomy 13, 18, and 21: comparison of the screening efficiency between 2 locally developed programs and commercial software. *Clinical Cemistry*, 2011, p. 57 - 72. ISSN: 1530-8561.

5. Hill P. Down Syndrome Prevalence In The United States. *American Academy of Pediatrics*, 2009,p. 9 - 21. ISSN: 1689-2564.

6. Harada S., Korf B. R. Overview of molecular genetic diagnosis.*Current Protocols in Human Genetics*, University of Alabama at Birmingham, 2006, p. 29 - 41. ISSN: 1934-8258.

7. Harper P. *Practical genetic counseling*. Human Genetics at Cardiff University, 2010. 407p. ISBN: 978-0-340-99069-8.