9th Yazd International Congress and Student Award on Reproductive Medicine with 4th Congress of Reproductive Genetics

Key Lectures

K-75
NIPT application and detection of genetic diseases in PND

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Different genetic conditions associated with congenital anomalies/intellectual disability can contribute to long-term disablement, with significant impacts on individuals, families, health-care systems, and societies. Although congenital anomalies may be the result of one or more genetic, infectious, nutritional or environmental insults, it is often difficult to identify the exact causes. Conventional karyotype, quantitative fluorescence-polymerase chain reaction (QF-PCR) and chromosomal microarray are able to detect about 40-50% of the causes of fetal anomalies, with therefore about 50-60% of cases in which it is not possible to define the etiology. In fact, 10-20% of isolated or syndromic congenital anomalies can be associated with monogenic diseases, whose diagnosis is often established based on a family anamnesis, clinical examination, and pedigree pattern and confirmed through genetic examination. Next-generation sequencing enables to sequence of the fetal exomes, furnishing a broader diagnostic capability compared to traditional and molecular cytogenetics prenatal tests. This approach adds at least an extra 10% of clinically relevant information in cases of fetuses with structural anomalies. Moreover, the same noninvasive prenatal test can now be performed for definitive diagnosis of some monogenic recessive and X-linked conditions, or also in paternally inherited dominant and de novo conditions.

We recently demonstrated that trio-whole exome sequencing (trio-WES) using fetal cell free-DNA (cff-DNA) can be analyzed with sufficient sensitivity and that an adequate strategy can identify the cause of pregnancies at risk for malformative disorders. Our work suggested that for fetuses with proven congenital malformation an extended US examination together with trio-WES on cff-DNA may be helpful in detecting an underlying congenital disease.

Furthermore, subsequent analyzes also in couples with low risk or negative anamnesis for genetic pathologies, allowed us to further demonstrate that genome-wide sequencing is an effective method that will likely be more used in the coming years as a clinical tool for diagnosis. Moreover, we are able to demonstrate that the WES analysis on cell-free DNA has a better diagnostic yield than the same test performed on DNA extracted from the amniotic fluid, proving that WES on cff-DNA is especially suitable, with an appropriate genetic counseling, in fetuses with genetic diseases.