Positioning, Performance and Relevance of Cell-based Noninvasive Prenatal Testing

Ripudaman Singh, Lotte Hatt, Line Dahl Jeppesen, Katarina Ravn, Maria Bach Laursen, Maibritt Nørgaard Lauridsen, Mathias Kølvraa, Mads Tang Dalsgaard, Ida Vogel

Background: Non-invasive alternatives to prenatal diagnostic methods used during first and second trimester have been proposed by either studying the cell-free fetal DNA or DNA isolated from intact fetal cells, both circulating in maternal blood. The former referred to as cell-free noninvasive prenatal testing (cfNIPT), and the as latter cell-based noninvasive prenatal testing (cbNIPT).

Objectives: Here the positioning, performance, and relevance of a cbNIPTis presented by giving examples from the development of EVITA TEST COMPLETE, the world's first commercially available cell-based noninvasive prenatal test.

Methods: Performance of cbNIPT was compared with chorionic villi sampling on 92 high-risk pregnancies after combined first trimester screening (cFTS), showing concordant results between cbNIPT and CVS indetecting aneuploidies and non-mosaic copy number variations. In another study, results from both cbNIPT and cfNIPT were compared in 252 high-risk pregnancies. Additionally, cbNIPT's performance was studied on samples collected from 333 pregnant women without combined first trimester risk stratification. 95.5% of these samples rendered fetal cells for analysis, and upon second sampling the call-rate went up to 98.8%.

Results: In all the studies fetal cells were isolated by a patented technology using MACS for enrichment and FACS for single cell sorting. After the whole genome amplification (WGA) andverification of fetal cells by short tandem repeat analysis, DNA was analyzed by chromosomal microarray (CMA).

Moreover, in a study to compare the resolution of genetic analysis on fetal cells between CMA and next generation sequencing (NGS), blood samples were taken from high-risk pregnant women who chose chorionic villus sampling (CVS). Samples showing different deletions and duplications in the fetal genome were analyzed by both CMA and NGS, and these results compared with the results from CMA on CVS biopsy. The results showed that NGS performed on single fetal cells had a better resolution in detecting smaller deletions and duplications as compared to CMA.

Conclusion: A cell-based NIPT is clinically viable and may have the potential to provide a more comprehensive genetic analysis of the fetus as compared to other currently available NIPTs, including prenatal diagnosis of monogenic diseases.