Noninvasive prenatal testing for fetal trisomies in a routine first-trimester screening setting

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Objective

Non-invasive prenatal testing (NIPT) by analysis of cell-free DNA (cfDNA) in the maternal blood has shown promise for highly accurate detection of common fetal trisomies. We assessed the performance of NIPT for trisomies screening in a routine screened first-trimester pregnant population.

Methods

This was a cohort study of 505 pregnant women undergoing routine screening for aneuploidies at 11-13 weeks' gestation from 01.01.2014 to 31.12.2016 in our hospital in Zagreb and found to be at high risk for chromosomal anomalies (305 after the combined screening test with NT, free beta-HCG and PAPP-A at a risk cut-off of 1:150 recommended by Croatia National Screening Committee and 200 by advanced maternal age). Plasma cfDNA analysis using chromosome-selective sequencing was used. Plasma samples from the study population were analysed after sending to a laboratory in Hong-Kong by using Nifty Prenatal Test.

Results

Results from chromosome selective sequencing were available from 500 cases. In 5 cases fetal fraction was below the minimal requirement of 4%. In the 500 cases, 478 euploid pregnancies and 22 aneuploid pregnancies (15 trisomies 21, 3 trisomies 18, 2 triosomies 13, 2 monosomies X) were confirmed by fetal karyotyping. A suspected 5p deletion by NIPT was not confirmed by the microarray method. Three cases (one trisomy 13, one trisomy 18 and one monosomy X) were found as false positive. Three cases (one trisomy 21, one trisomy 13, one trisomy 18) were false negative. With screening by the combined test and advanced maternal age and additional ultrasound markers (nasal bone, tricuspid flow, ductus venosus flow) at a risk cut-off of 1:150, all cases of trisomy 21, 18 and 13 were detected.

Conclusion

The performance of screening for trisomy 21, 18, 13 and monosomy X by NIPT using chromosome-selective sequencing is effective with detection rate of 99% and low false-positive and false negative rates. Our results confirmed that prenatal cfDNA testing represent highly accurate approach for advanced screening of most common aneuploidies.