Influence of first trimester biochemistry methodology on detection rate in screening for trisomy 21


Department of Obstetrics and Perinatology, Medical University of Warsaw, Warsaw, Poland

Objective

Maintenance of a high standard of both ultrasound examinations at 11-13+6 weeks (CRL and NT measurements) and clinical biochemistry tests is crucial for the quality of screening for chromosomal defects. To ensure this, Fetal Medicine Foundation provides training and certification in 11-13+6 weeks ultrasound and certifies laboratory methods for first trimester biochemistry. One of the major problems hindering introduction of biochemical tests for a more common use in Poland, is a limited number of analysers certified by FMF. ELISA tests (e.g. DPC) are more available and have been long used for assaying test substances. The purpose of the study was to compare trisomy 21 detection rates in screening at 11-13+6 weeks, based on biochemical tests certified by the FMF (Delfia Express) and non-certified (DPC - PRISCA).

Methods

In 2267 fetuses from singleton pregnancies crown to rump length (CRL), fetal hart rate (FHR) and nuchal translucency (NT) were measured by the FMF certified doctors and maternal age (MA) was noted. Two 5 mL blood samples were collected from each patient. Serum samples were tested for free β-hCG and the PAPP-A using 2 analysers (Delfia - Perkin Elmer and Immulite 2000 - DPC), the results were expressed in MoM values and used for computer calculation of the risk of trisomy 21 (Astraia for Delfia and Prisca for Immulite). The cut-off value for the high T21 risk was 1/300, in both groups. High-risk patients were offered an invasive test (amniocentesis) for karyotyping. In cases where the patient declined invasive investigations, the karyotype was determined after birth when the neonatologists suspected Down's syndrome.

Results

In the comparison of free β-hCG MoMs, DPC and Delfia results demonstrated statistically significant differences in healthy, and trisomy 21 fetuses respectively. Similarly, statistically significant differences were noted for PAPP-A MoMs. The above differences in MoMs resulted in altered sensitivity in screening for aneuploidy. The application of the certified method ensures a markedly higher detection rate (74%) compared to non-FMF-certified tests (64%), both at 5% FPR. ROC analysis was performed in order to assess the clinical efficacy of both tests (DPC and Delfia along with maternal age and NT measurement) in relation to detection of trisomy 21. In terms of the T21 BC risk scale for both Delfia and the DPC method, no significant (p>0.05) discrimination ability in relation to prediction of T21 was found. The difference between results obtained using Delfia and DPC methods is AUC=0.0129 and is not significant (Z=0.4798, p=0.6314). However, results of T21 BC NT risk scales using the Delfia and DPC methods are highly significant (p<0.0001), which means that their discrimination ability is high - over 90%. The difference between results obtained using the Delfia and DPC methods is AUC=0.0150 and is statistically significant (Z=2.4728, p=0.0134).

Conclusion

The use of FMF certified analysers in first trimester biochemistry testing improves detection rate for trisomy 21. The use of non-certified analysers in the biochemistry test causes reduction of efficacy of the combined test and causes an increased rate of indications for invasive procedures.