Is it time to change from classical karyotyping to rapid testing in prenatal diagnosis?


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INTRODUCTION

The golden standard for prenatal diagnosis:

• culture of foetal cells (chorion villi sampling, amniocentesis, cordocentesis)

• karyotype analysis
ISSUES FOR CONSIDERATION

• High percentage of miscarriages after early pregnancy prenatal diagnosis – CVS, early amniocentesis

• Referral of women on advanced stages of pregnancy for prenatal diagnosis (~50% > 17 week of gestation)

• In case of classical cytogenetic methods the results are issued after a long time (2-3 weeks)

• High anxiety levels in pregnant women
RAPID ANEUPLOIDY TESTING

• Methods: QF-PCR, MLPA, RAPID-FISH

• Decreases the time of waiting for the results of prenatal testing
  – normal result: reduction of maternal anxiety during the waiting period
  – abnormal result: important when considering termination of pregnancy
RAPID-FISH

- Detection of numerical aberrations of 13, 18, 21, X and Y chromosomes (as well as poliploidy)

- High risk of aneuploidy is the indication for prenatal testing in 80-90% of pregnancies
RAPID-FISH versus classical karyotyping
MATERIALS AND METHODS

• 363 amniotic fluid samples (II 2005-IV 2008)
• Written informed consent
• RAPID-FISH followed by classical karyotyping
• Causes for referral:
  – maternal age
  – positive results from non-invasive biochemical screening
  – ultrasound abnormalities (increased NT, hypoplasia of NB)
  – previous child with chromosomal abnormality
RESULTS

2 weeks later

2 weeks later

2 weeks later
AGE

- under 34 years of age: 119 (33%)
- 35 years and over: 244 (67%)
INDICATIONS

- 1 indication: 9 (2.5%)
- 2 indications: 64 (17.6%)
- 3 indications: 290 (79.9%)
INDICATIONS

- Maternal age: 186
- Abnormal USG scan: 25
- Increased NT: 25
- PAPP A: 31
- Triple screen: 12
- Previous child with aberration: 11
COMPLIANCE

46,XX
46,XY
47,XX,+13/47,XY,+13
47,XX,+18/47,XY,+18
47,XX,+21/47,XY,+21
47,XXX
47,XXY
47,XYY
45,X
45,XY,der(13;14)
45,XX,der(13;14)
46,XX,t(8;14)
46,XX,add(18)
46,XX,der(6)t(4;6)
46,XX,dup(9)
COMPLIANCE

- 45,XY,der(13;14)
- 45,XX,der(13;14)
  - previous child with chromosome abnormality, in both cases mother was found to be a carrier of a balanced translocation
- 46,XX,t(8;14)
  - maternal age
- 46,XX,add(18)
- 46,XX,der(6)t(4;6)
  - malformations found on ultrasound
- 46,XX,dup(9)
  - NT=2,9 mm
CONCLUSION

The reliability and rapidity of RAPID-FISH diagnosis of the most common numerical chromosomal aberrations in prenatal testing creates the foundation for introducing it as a routine method of prenatal diagnosis in cases of increased risk of aneuploidy of chromosomes 13, 18, 21, X and Y in the offspring.
INDICATIONS FOR RAPID ANEUPLOIDY TESTING

• maternal age $\geq 35$
• previous child with numerical chromosome aberrations
• abnormal biochemical screening results
• increased NT

Additionally: anomalies found on ultrasound suggestive of a poliploidy in the foetus
INDICATIONS FOR CLASSICAL KARYOTYPING

- foetal anomalies found on the ultrasound scan
- one of the parents is a known translocation carrier
GOOD LABORATORY PRACTICE

• analysis of indications for prenatal testing

• following the producer’s instructions and standards of quality control

• if aneuploidy found – confirmation of the result by classical karyotyping or a second RAPID-FISH test performed by another person with different reagents
Thank you for your attention!