Prenatal Diagnosis through Chromosomal Microarray Analysis (CMA)

SBU ASSESSMENTS | ASSESSMENT OF METHODS IN HEALTH CARE AND SOCIAL SERVICES

FEBRUARY 2016 | WWW.SBU.SE/246E

Executive summary

Conclusions

- When one or more fetal anomalies are detected by ultrasound, more genetic changes affecting anatomy, development or function can be identified using Chromosomal microarray analysis (CMA) than through karyotyping, QF-PCR, or FISH analysis1[1]. This applies in particular to anomalies detected in the heart or if the anomalies were detected in more than one organ system.

- Few additional genetic changes affecting anatomy, development or function are identified using CMA beyond those detected through karyotyping when the reason for testing is:
  - advanced age of the pregnant woman
  - parental anxiety
  - high probability of chromosomal abnormality based on maternal serum screening.

- CMA reveals more genetic changes with unclear significance to anatomy, development or function compared to karyotyping, QF-PCR or FISH analysis.

- For genetic changes that can be resolved with karyotyping, QF-PCR or FISH analysis, CMA has the same diagnostic accuracy as the reference test.

- CMA can provide extensive information on an individual's genetic makeup. It is therefore of utmost importance that the information obtained is used in an ethically acceptable manner. Due to the extensive and complex nature of the genetic information this test can provide, great care and attention is required when presenting the results to the clients to ensure the results are fully understood. This is particularly true when presenting unclear or unexpected findings, or when the findings relate to genetic deviations that impact the future health of the child to varying degrees.

- Additional well-conducted studies are needed to investigate how expectant parents perceive the value of the information that CMA can provide.

[1] *QF-PCR and FISH analysis are two rapid diagnostic methods.*

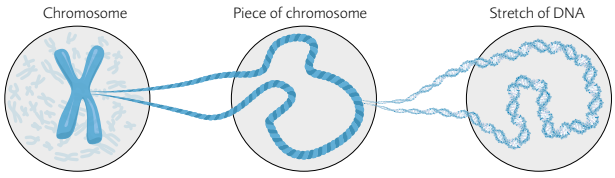

ILLUSTRATION: MATTIAS KARLÉN

Background

CMA can be used to analyse the entire genetic makeup of an individual and thereby detect genetic changes that may affect anatomy, development or function. These genetic changes, often referred to as copy number variants (CNV), can be very large, such as when an extra copy of a whole chromosome is acquired. CNV can also refer to the loss or gain of a much smaller piece of a chromosome.

A method called karyotyping has traditionally been used to identify genetic changes prenatally. Karyotyping entails examining an individual's chromosomes from cultured cells using a light microscope. Karyotyping provides high diagnostic reliability for detecting large CNV, including extra chromosomes and major structural changes. However, CMA can detect genetic changes that are more than 100 times smaller than those detectable with karyotyping.

CMA is primarily used for prenatal diagnostics in response to fetal anomalies detected by ultrasound, such as structural aberrations in one or more organ, abnormal growth of the fetus or placenta, or unusual amniotic fluid volume.

Objective

This report evaluates the reliability of the results obtained from CMA for use in prenatal diagnostics. It also evaluates how often additional genetic changes are detected through CMA as compared to karyotyping, QF-PCR or FISH analysis. The report also highlights ethical aspects of using CMA for prenatal diagnosis, and how expectant parents perceive the value of the analysis. Health economic aspects are not addressed in this report.

Method

This evaluation is performed following SBU's method.

Ethical and social aspects

Prenatal diagnosis raises ethical questions about human dignity, parental autonomy, and the health of both the fetus and the parents. This SBU report presents ethically relevant advantages and challenges associated with CMA compared to karyotyping. General ethical aspects of prenatal diagnosis can be found in a 2011 report from the Swedish National Council on Medical Ethics.

The main advantage of using CMA for prenatal diagnosis is that CMA can identify smaller genetic changes than karyotyping. An important ethical problem is the increased difficulty of fully informing those involved about all of the potential findings in a manner that is both clear and understandable. Secondary findings, and variants of uncertain significance in particular, can cause concern and may be difficult for parents to use in their decision making process.

Because CMA can detect more genetic changes than karyotyping, it may lead to more problems from an autonomy standpoint, i.e. the individual's right to self-determination. The increased use of CMA may contribute to the perception that it is the parents' responsibility to ensure that their offspring do not have any genetically caused health problems. This perception could make it more difficult for parents to feel they can decline the offer of prenatal diagnosis. Increased access to CMA may also allow healthcare professionals to expand their perception of what entails a serious a condition. This could contribute to stigmatisation of individuals with the genetic changes that the method is capable of identifying.

Project group

Experts
Ann-Charlotte Thuresson (Associate Professor, Clinical Molecular Geneticist, Uppsala)
Niklas Juth (Associate Professor, Senior Lecturer, Stockholm)
Maria Soller (Associate Professor, Senior Physician, Region Skåne)

SBU
Christel Hellberg (Project Manager)
Anna Attergren Granath (Project Administrator)
Agneta Brolund (Information Specialist)
Irene Edebert (Assistant Project Manager)
Miriam Entesarian Matsson (Assistant Project Manager)
Rebecca Silverstein (Assistant Project Manager)

Scientific reviewers
Jon Jonasson (Associate Professor, Senior Physician, Region Östergötland)
Erik Iwarsson (Associate Professor, Senior Physician, Stockholm)
Göran Lingman (Professor, Lund)

SBU Assessments no 246 (2016)
www.sbu.se/en • registrator@sbu.se
Graphic Design: Anna Edling, SBU