GENERAL

Abstracts 1 – 8

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1 A multicenter, prospective, masked comparison of chromosomal microarray with standard karyotyping for routine and high risk prenatal diagnosis

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OBJECTIVE: To evaluate the performance of chromosomal microarray (CMA) as an independent method for prenatal cytogenetic diagnosis

STUDY DESIGN: Villus or amniotic fluid samples from women undergoing prenatal diagnosis at 31 centers were sent to a central karyotyping lab. The samples were split; standard karyotyping was performed on one portion and the other was de-identified and sent to one of four independent microarray labs for CMA. Microarrays consisted of 84 regions of known disease association, 43 centromeric and 41 telomeric regions and a backbone of oligoneucleotides spaced 75 -125 kb with regions >1Mb reported. After a preliminary study, uncultured samples were analyzed primarily, using culture only as a back-up. Karyotype and microarray results were reported to an independent data center. Microdeletions and duplications identified exclusively by CMA were classified as "of known clinical significance" or "benign" using predefined listings. All other copy number variants (CNVs) were designated as "of uncertain clinical significance".

RESULTS: 4401 women were enrolled with indications of AMA (46%), abnormal 1st or 2nd trimester screening (18%), abnormal ultrasound (26%), and other indications (9%). Successful results were obtained by CMA in 98.7% of cases; 88% were obtained using only uncultured material. Of the 4340 samples for which results were available for comparison, 316 (7.3%) autosomal and 57 (1.3%) sex chromosome non-mosaic aneuploidies were identified by karyotype. All of these were identified by CMA however, seven (all from CVS) were reported as mosaic. Notably, 5.8% of cases with a normal karyotype and structural fetal anomalies had either a microdeletion or duplication of potential or known clinical significance, as did 1.7% of those sampled for maternal age or positive screening.

CONCLUSION: For prenatal testing, karyotyping and CMA are equally effective in identifying aneuploidy. Microarray detects additional clinically relevant information both in cases with structural anomalies and in those sampled for routine indications.

Frequency of Micro-deletions/Duplications in Pregnancies with Normal Karyotypes

Presenting Indication for Prenatal Diagnosis	Known Benign CNV (%)	CNV of Uncertain Clinical Significance**		Known Pathogenic CNV (%)	Total CNVs with Clinical Relevance (%)
		Likely Benign CNV (%)	Potential Clinical Significance (%)		
Maternal Age	31.8	2.8	1.3	0.5	1.7
Screen Positive	33.9	2.1	1.1	0.4	1.6
US Anomaly	32.2	2.5	3.2	2.6	5.8
Other*	30.0	1.6	0.8	0.5	1.4
All	32.1	2.5	1.6	0.9	2.5

*Includes: family history, previous pregnancy with abnormalities, elective

** Clinical potential determined by independent advisory committee based on size, gene content, inheritance, the literature and ultrasound findings

2 Induction of labor or expectant management for large-for-dates fetuses: a randomized controlled trial

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OBJECTIVE: To compare induction of labor with expectant management for large for dates fetuses to prevent macrosomia at birth, shoulder dystocia and the associated neonatal morbidity.

STUDY DESIGN: We conducted a randomized controlled trial in collaboration with 20 teaching hospitals, members of the GROG group, in France, Switzerland and Belgium. We included 817 women with a fetus with an estimated weight above the 95th percentile at 37 to 38 weeks of gestation. Women with diabetes treated with insulin and past history of cesarean section or shoulder dystocia were not included. The screening was first performed clinically (estimated weight above the 90th percentile), then a sonography was performed. Women were eligible if the sonographic estimated weight was above the 95th percentile. Women were randomized to induction of labor within 3 days (n=407) or expectant management (n=410). The primary outcome measure was neonatal trauma, including significant shoulder dystocia (defined as resolved by maneuvers other than McRoberts), fracture of the clavicle and brachial plexus injury, or perinatal death.

RESULTS: Baseline characteristics were similar between groups. A difference in mean birthweight of nearly 300 gr between groups was obtained (3831 gr versus 4112 gr). The risk of neonatal trauma was reduced with induction of labor (n=9, 2.2%), compared to expectant management (n=27, 6.6%) (RR: 0.34; 95%CI: 0.16 to 0.71). The likelihood of a spontaneous vaginal delivery was higher (RR 1.14; 95%CI: 1.00 to 1.29) in the induction of labor group. The risk of cesarean section was not increased after induction of labor (28.0% vs 31.7% in the induction and expectant groups, respectively). Other neonatal morbidities were similar between groups, with no recorded cases of wet lung, brachial plexus palsy and perinatal death.

CONCLUSION: Induction of labor in case of suspected large for dates fetus is associated with a lower risk of trauma at birth. This intervention does not result in an increased risk of cesarean section and improve the likelihood of a spontaneous vaginal delivery.

3 Prevention of preterm delivery after successful tocolysis in preterm labour by 17 alpha-hydroxyprogesterone caproate: a randomised controlled trial

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OBJECTIVE: Several small trials have suggested that progesterone might reduce the risk of preterm delivery among women with pre-