



Do angiogenic factors improve detection of late-onset FGR?

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Objective

To evaluate performance of soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PLGF) ratio in the detection of late onset fetal growth restriction (FGR). Setting: Perinatal center with over 5, 000 deliveries per year.

Methods

Prospective cohort study. Patients with singleton pregnancies (n=525) were investigated at four clinical visits: • 12-14 weeks: CRL measurement, first trimester combined screening including personal history, PIGF, PAPP-A, free β hCG, mean arterial pressure (MAP) and Uterine Arteries PI (UtA) • 20-22 weeks: biometry and morphology scan, umbilical artery PI (UA) and UtA • 30-32 weeks: biometry, PI middle cerebral artery (MCA), UA, UtA and cerebroplacental ratio (CPR) were obtained as well as sFlt-1 / PLGF ratio • 36-37 weeks: biometry, MCA, UA, UtA and CPR were obtained as well as sFlt-1 / PLGF ratio Delivery and neonatal data were collected. Exclusion criteria: multiple pregnancy, early-onset FGR (<32 weeks), premature delivery (<32 weeks), fetal abnormalities, no consent given. Fetal biometry and newborn size evaluated using Intergrowth-21st international standards. FGR diagnose based on Consensus definition of fetal growth restriction: a Delphi procedure (Gordijn S. J. et al., Ultrasound Obstet Gynecol. 2016). Timing of delivery based on Stage-based Protocol (Figueras F., Gratacos E., Prenat Diagn 2014). sFlt-1 and PLGF were analyzed on Brahms Kryptor. Attending physicians were blinded to biochemical markers. Statistical analysis was performed using IBM SPSS 25.

Results

Out of 525 newborns: mean gestational age at delivery 39. 0w (min 32, max 42), median 39. 0w (Q1 = 38, Q3 = 40), mean newborn weight 3, 350g (min 1, 390, max 5, 100), median 3, 360g (Q1 = 3, 070, Q3 = 3, 650), mean newborn weight centile 57. 18 (min 0. 8, max 100), median 60. 58 (Q1 = 34. 8, Q3 = 80. 5), only 40 newborns (7. 6%) were below 10th centile according to Intergrowth-21st. We encountered 1 case of stillbirth. There were 19 (3. 6%) cases of late-onset FGR. In 44 (8. 4%) cases operational delivery (caesarean section or forceps) was necessary for fetal distress during labor. At 30-32 weeks mean sFlt-1 / PLGF ratio was 9. 1 (min 0. 1, max 1, 524. 1), median 3. 3 (Q1 = 1. 9, Q3 = 5. 7) and at 36-37 weeks mean 27. 7 (min 0. 7, max 622. 1), median 12. 9 (Q1 = 5. 8, Q3 = 29. 4). Both sFlt-1 / PLGF ratios correlate with birthweight centile (Spearman's Rho 0. 320 and 0. 271 respectively, $p < 0. 001$) as well as with diagnosis of late-onset FGR (Mann-Whitney test, $p < 0. 001$). At 36-37 weeks high sFlt-1 / PLGF ratio is correlates with need for operative delivery for fetal distress during labor (Mann-Whitney test, $p < 0. 001$).

Conclusion

Growth restricted fetuses are at higher risk of fetal distress during labor. Longitudinal ultrasound scans can detect a proportion of fetuses at risk. Using sFlt-1 / PLGF ratio in third trimester could help us identify additional fetuses that will benefit from active approach.