Short term variation analysis versus visual evaluation of cardiotocography in fetal growth restriction

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The purpose of this study is to assess the outcomes of monitoring the fetal condition with STV in cCTG compared to visual interpretation of the CTG in order to time delivery in pregnant women with severe, early-onset FGR.

Ethical review	Approved WMO
Status	Pending
Health condition type	Pregnancy, labour, delivery and postpartum conditions
Study type	Observational invasive

Summary

ID

NL-OMON57066

Source
ToetsingOnline

Brief title
SAVE FGR

Condition

- Pregnancy, labour, delivery and postpartum conditions

Synonym
fetal growth restriction, impaired growth of the unborn baby

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: European Research Council

Intervention

Keyword: Cardiotocography, Fetal growth retardation, Perinatal mortality, Pregnancy

Outcome measures

Primary outcome

The primary endpoint of this study is perinatal death, defined as antenatal death or neonatal/infant death before discharge from NICU. Our hypothesis is that in the pregnant women monitored by STV in cCTG, a decrease in the primary outcome will be observed, compared with pregnant women monitored by visual interpretation of CTG.

Secondary outcome

•Major neonatal morbidity until discharge home. Major neonatal morbidity is a composite outcome defined as intraventricular hemorrhage grade 3 or more, periventricular leukomalacia grade 2 or more, moderate or severe bronchopulmonary dysplasia, necrotizing enterocolitis Bell stage 2 or more, or retinopathy of prematurity requiring therapy.

•Individual neonatal morbidities of the abovementioned composite outcome and additionally persisting ductus arteriosus, persistent pulmonary hypertension of the newborn (PPHN), respiratory distress syndrome (RDS), period of invasive mechanical ventilation in days, medication need, hypoglycaemia, neonatal jaundice, sepsis and cardiovascular function.

•Neurodevelopmental impairment, defined as an abnormal test on Bayley III Dutch version (or version IV if available) (composite cognitive score < 85, composite motor score < 85), cerebral palsy, with a Gross Motor Function Classification System (GMFCS) grade > 1, hearing loss needing hearing aids, or severe visual

loss (legally certifiable as blind or partially sighted) assessed at two years

of corrected age, where available by local protocol.

•ASQ, physical growth and Lexilijst, in addition to neurodevelopmental outcome

measures.

•Delivery characteristics including Apgar scores and umbilical cord pH.

•All remaining outcomes required by the core outcome set for fetal growth

restriction will also be collected.

•Serum biomarkers and fetal electrocardiography, when available.

Study description

Background summary

Severe, early-onset fetal growth restriction (FGR) is a condition in which the fetus does not reach its growth potential due to placental insufficiency[. This condition affects about 0.3% of pregnancies, accounting for an estimated 15,000 babies in Europe being born premature below 32 weeks gestation. The main clinical dilemma of FGR lies in the timing of birth, given the intricate balance of risks of antenatal mortality and severe damage to organs and the aggravated neonatal effects of prematurity: death or survival with severe neurodevelopmental impairment. The mainstay of clinical management in these cases pivots around the anticipation of the risk of fetal demise from placental oxygenation failure. The monitoring variables that are currently available comprise assessment of the severity of metabolic insufficiency (fetal size and growth, Doppler ultrasound, serum biomarkers) and the early detection of progressive fetal hypoxia with cardiotocography (CTG). The common approach is to deliver the fetus when signs of advanced hypoxia appear on CTG. A delicate balance exists between having the fetus born (too) early and facing the risks of extreme prematurity combined with a very low birthweight; and between delivering the fetus (too) late when the fetus has the disadvantage of hypoxia at birth. The decision when to deliver the fetus, is made mainly based on the CTG. The inter- and intra-observer variability could be overcome by software analysis according to the original Dawes&Redman algorithm. The software calculates the short-term variation (STV) of the inter-beat interval expressed in milliseconds, and a range of secondary calculations. In contrast with repeated decelerations, when fetal hypoxia is considered evident, the place of the software analysis of the fetal heart rate variability is less clear.

Although the advantages of mathematized and uniform quantification of the fetal heart rate variability appear self-evident, there are no studies with sufficient power to detect an association of intervention based on STV at any threshold with the most important outcomes: fetal death and long-term infant outcome.

Study objective

The purpose of this study is to assess the outcomes of monitoring the fetal condition with STV in cCTG compared to visual interpretation of the CTG in order to time delivery in pregnant women with severe, early-onset FGR.

Study design

Stepped wedge cluster-randomized trial.

Intervention

-Visual interpretation of cardiotocography.
-Short term variation analysis in computerized cardiotocography.

Study burden and risks

Based on the scarce evidence on cCTG with STV, we expect a decrease of 11% in the primary outcome. Since no RCT*s are available directly comparing STV with visual interpretation of CTG, we cannot make an estimation on whether there will be a significant difference in gestational age at delivery and length of NICU stay. However, based on the hypothesis that the STV reflects early signs of hypoxia, we hypothesize that the gestational age at delivery and birthweight will be slightly lower in the intervention group. We hypothesize that the advantage of the lack of hypoxia outweigh the disadvantage of (probably one to several day(s)) potential lower gestational age at delivery and birthweight, however no literature is available to directly answer this question. A retrospective analysis of liveborn FGR infants born below 30 weeks of gestation, delivered before CTG abnormalities occurred, compared with appropriate grown infants born < 30 weeks, showed similar short- and long-term outcomes. Also, the TRUFFLE study did not show significant differences in short- and long-term outcomes, when comparing STV with early or late ductus venosus changes; however, in this study no significant differences in gestational age at delivery and birthweight appeared. No specific risks related to the study are anticipated for the mother, since only the decision on the moment of delivery will be influenced by the intervention.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Inclusion criteria

- Pregnant women with a singleton pregnancy between 24 weeks and 0 days and 31 weeks and 6 days with severe, early-onset fetal growth restriction, admitted in hospital or frequently evaluated ambulatory by CTG (according to local protocol) for fetal monitoring. - Fetal growth restriction is defined as biometric ultrasound measurement of the abdominal circumference OR a combination of measurements resulting in an estimated fetal weight below the 10th percentile AND umbilical artery Doppler pulsatility index >p95. - Maternal age >= 16 years. - written informed consent

Exclusion criteria

- Known congenital or chromosomal anomalies influencing perinatal outcome. - Imminent labour or expected maternal indication for delivery < 48 hours.

Study design

Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2024
Enrollment:	360
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	14-10-2024
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL84591.000.24