Follow-Up after feToscopic sURgical intErventions: the FUTURE study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Retina, choroid and vitreous haemorrhages and vascular disorders
Study type	Observational non invasive

Summary

ID

NL-OMON39565

Source
ToetsingOnline

Brief title
FUTURE study

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders
- Foetal complications
- Obstetric and gynaecological therapeutic procedures

Synonym
complicated Monochorionic Monoamniotic twin pregnancies, Fetal/Neonatal Alloimmune Thrombocytopenia, Lower Urinary Tract Obstruction, primary hydrothorax- congenital lung disease, Retinopathy of Prematurity, selective intrauterine growth restriction, the death of a co-twin following Selective Feticide, twin anemia polycythemia sequence, twin-twin-transfusion syndrom

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Willem Alexander Kinder en Jeugdfonds

Intervention

Keyword: Children, Fetal Therapy, Long-term Follow-up, Neurodevelopment

Outcome measures

Primary outcome

1. The incidence of developmental problems: cognitive functioning at least one standard deviation below the mean (test score < 85), mild to moderate motor problems including hearing and vision problems, learning problems, symptoms of pervasive developmental disorder, attention deficit or behavioral problems.

2. The incidence of neurodevelopmental impairment: cognitive functioning test score at least two standard deviations below the mean (test score < 70), abnormal neurological outcome including severe motor problems and Cerebral Palsy, bilateral blindness or bilateral deafness requiring amplification.

3. Risk factors for developmental problems and neurodevelopmental impairment.

4. Health Related Quality of Life of the children.

5. Parenting stress levels after fetoscopic surgical intervention.

6. ROP-status.

Secondary outcome

Not applicable

Study description

Background summary

An increasing number of fetal diseases are being detected prior to birth and some of them are amenable to fetal therapy1. Fetoscopic laser coagulation of placental vascular anastomoses is nowadays widely accepted as the first-line treatment for Twin to Twin Transfusion Syndrome (TTTS)2-6, while intrauterine blood transfusion (IUT) is considered the mainstay of antenatal treatment for Rhesus Hemolytic Disease (RHD)7;8. In addition, in-utero pulmonary drainage is increasingly being advocated as the preferred treatment in hydropic fetuses with primary hydrothoraces or congenital lung disease, such as congenital cystic adenomatoid malformations (CCAM) 9;10.

Recent advances in fetal therapy, in particular endoscopic surgical interventions, have led to a striking increase in fetal survival rate1;2;11. In TTTS, overall perinatal survival rate with fetoscopic laser surgery is now almost 80%, compared to 0-27% without intervention2. In RHD, a similar increase in perinatal survival is reported after IUT treatment. Survival is almost 95% in specialized centers, even in hydropic fetuses7. In fetuses with isolated hydrothorax or congenital lung disease, treatment with thoraco-amniotic shunts and thoracocentesis has led to an increase in perinatal survival from less than 10% to almost 65%9;10.

Most fetal interventions have become implemented without accurate and systematic methodological evaluation. As with any therapeutic intervention, the golden standard should be based on randomized controlled trials (RCT). To date, only a handful of RCTs have been performed in vention3;12-14. We recently initiated a multicenter RCT in TTTS, the Solomon study, to determine if a new laser technique (the Solomon technique) is associated with a lower rate of perinatal mortality and morbidity compared to the classic selective laser technique.

The advancing techniques and corresponding survival rates necessitate a greater knowledge on the impact of these interventions on long-term child development. However, long-term follow-up after fetal therapy is scarce and based on a few small studies15-20. Alongside perinatal survival rates, clinicians and, in particular, parents are interested in the future quality of life of the child. Is the child at risk for increased cognitive or behavioral problems? Will the child be able to go to a regular school or will it need special assistance? How will the child develop in terms of health related quality of life compared to a *normal* peer or to children with a chronic condition like diabetes? Does raising a child, following the stressful events during pregnancy and in light of the yet unknown long-term outcome, entail additional parenting stress?

An increasing number of fetal diseases are being detected prior to birth of which some are amenable to fetal surgical intervention1. Although the advances in fetal surgery, in particular endoscopic surgical interventions, have led to a striking increase in fetal survival rate, knowledge on long-term outcome is scarce. To establish optimal fetal management and improve the quality of antenatal parental counseling, a greater understanding of the impact of these early interventions on child development is indispensable.

Recently, several reports of severe Retinopathy of Prematurity (ROP) in monozygotic twins with TTTS have emerged, suggesting TTTS might contribute to the development of ROP. ROP is defined as abnormal vessel growth in the

developing retina and is a potentially blinding disease in premature infants. Major risk factors associated with the development of ROP are low gestational age at birth, in particular less than 32 weeks, and birth weight of less than 1500 g. Many other risk factors have been reported such as excessive oxygen use, long duration of artificial ventilation, postnatal cardiovascular and inflammatory disease and multiple blood transfusions.

Study objective

Both RCTs and long-term follow-up studies are required to establish optimal fetal management and provide clinicians a better understanding of the impact of these early interventions on child development in order to improve the quality of antenatal parental counseling. The aim of the current project is: to determine the incidence of developmental problems and neurodevelopmental impairment (NDI), to examine risk factors for impairment and to assess Health Related Quality of Life (HRQoL) as well as parenting stress levels after fetal therapy.
Furthermore, the effect of TTTS and its treatment consisting of fetoscopic laser surgery on the development of ROP in premature born infants < 32 weeks will be evaluated retrospectively.

Study design

The design of the FUTURE study is divided into three parts, according to methodology and subgroups.

Part 1: Solomon Randomized Controlled Trial Follow-up of all long-term survivors from monochorionic (MC) twin pregnancies with TTTS included in the Solomon RCT comparing two laser surgery techniques for the treatment of TTTS.

Part 2: Observational cohort study in 4 small study groups Follow-up of all long-term survivors in the following 4 subgroups: Twin Anemia Polycythemia Sequence (TAPS), Monochorionic Monoamniotic twin pregnancies (MCMA twins), Primary Hydrothoraces/ Congenital Lung Disease and Lower Urinary Tract Obstruction (LUTO).

Part 3: Observational cohort study with case-control design Follow-up of all long-term survivors in the following 3 subgroups: Selective Feticide in MC twins, selective Intra Uterine Growth Retardation (sIUGR) and Fetal/Neonatal Alloimmune Thrombocytopenia (FNAIT). To validate outcomes against controls, parents of children delivered consecutively in the LUMC between 2000 and 2011 will be contacted, at random, and asked for their participation.

Study burden and risks

Participants will be invited to the LUMC for: formal psychological testing of

cognitive development, a physical and neurological examination, an assessment of developmental problems and a brief behavioral screening and questionnaires on Health Related Quality of Life, parenting stress and ROP-status.
Participation does not result in any direct benefit.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

All long-term survivors following fetal therapy for TTTS, Twin Anemia Polycythemia Sequence (TAPS), the death of a co-twin following Selective Feticide, selective Intra Uterine Growth Retardation (sIUGR), Monochorionic Monoamniotic twin pregnancies (MoMo twins), primary hydrothoraces, congenital lung disease, Lower Urinary Tract Obstruction (LUTO) and Fetal/Neonatal Alloimmune Thrombocytopenia (FNAIT).
Children must be at least 2 years of age (corrected for prematurity) to be eligible for the study.

Exclusion criteria

Parents with no live-born children will be excluded from asking consent for participation.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-01-2012
Enrollment:	737
Type:	Actual

Ethics review

Approved WMO

Date:	26-01-2012
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	29-10-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL37798.058.11