The NeoLifes MICKEY MOUSE trial: MICrobiota, KEY between Mother and Off-spring USsing SEquencing techniques.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON28522

Source
NTR

Brief title
NeoLifes Mickey Mouse

Health condition

necrotizing enterocolitis

Sponsors and support

Primary sponsor: n.a.
Source(s) of monetary or material Support: n.a. From the funding of the ministry to universities.

Intervention

Outcome measures

Primary outcome

Development of necrotizing enterocolitis

Secondary outcome

Neonatal: faecal microbiota, faecal human DNA methylation pattern (shedded enterocytes and lymphocytes), faecal bile salts acids, faecal SCFA and iAP, iAP expression in the margins of the resection specimens, urine metabolome, cerebral and intestinal tissue oxygen saturation (as measured with NIRS), peak systolic flow velocity and the mean end-diastolic flow velocity of the superior mesenteric artery and a branch of the medial cerebral artery assessment using Echo Doppler, serum IMA, serum (i)AP, T1/T2 cytokine ratio in umbilical cord blood, iAP in surgical resection material.

Mother: microbiota in mother's milk, placenta and rectal microbiota; amniotic fluid in case of caesarean, validated diet questionnaire ('Wat een Nederland' questionnaire as used by RIVM)

Study description

Background summary

Necrotising enterocolitis (NEC) is the most prevalent acute gastro-enterological disease in the Neonatal Intensive Care Unit (NICU). Its incidence varies from 1-5 per 1000 live born children and is associated with prematurity and low birthweight. NEC occurs in 6% of premature children born with a gestational age of 28-32 weeks but increases to 15% in children born < 28 weeks. Diagnosis is often difficult, just as predicting which child will develop the disease. Signs and symptoms are often non-specific, such as abdominal distension, gastric retention or feeding intolerance. Laboratory and radiological tests also have limited diagnostic accuracy. The disease often progresses rapidly, with potentially life-threatening complications such as bowel perforation necessitating urgent laparotomy in around 50% of cases. Morbidity and mortality are therefore high, in some series up to 40%.

NEC is a multifactorial disease. Several predisposing factors have been identified from which aberrant bacterial colonization of the gut, formula feeding, mode of delivery, an immature immune system, aberrant bile salts and changes in intestinal perfusion and oxygenation are major predisposing factors. Despite all research, this complex interplay of both maternal and neonatal factors has not been unravelled yet. Furthermore, no study has ever combined analyses of all these predisposing factors in the development of NEC in one cohort. Doing so will give us the chance to investigate the relation and interaction between the different aspects of the development of NEC and to predict or diagnose NEC at an earlier stage.

In the present study we aim to address several relevant clinical and pathophysiological questions. Data from the present study will be used to identify a bundle of interventions we can subsequently test to decrease the incidence of NEC.

Study objective

• Identify the origin of the gut microbiota in neonates at a high risk for NEC by investigating

the maternal microbiota in amniotic fluid, placenta, vagina, rectum and in mother's milk as well as in formula feeding and correlate this with the developing gut microbiota of the infant.
• Investigate the neonatal innate immune response in umbilical cord blood and correlate this immune response with microbiota colonization and markers for gut wall integrity and gut wall inflammation and oxygenation.
• Identify quantitative differences in DNA methylation of marker genes in enterocyte DNA isolated from stool samples.
• Investigate the role of specific faecal bile salts in NEC development and investigate whether bile salts are related to certain microbiota, gut wall integrity, breastfeeding and/or antibiotics.
• Generate the faecal SCFA profile in neonates with imminent NEC.
• Generate the metabolic profiles in neonates with imminent NEC using metabolomics technology.
• Relate intestinal perfusion and oxygenation levels and variability to neonatal gut microbiome, and metabolic profiles.
• Relate tissue perfusion and oxygenation levels and variability to levels of ischemia modified albumin (IMA).
• Investigate whether any of the parameters mentioned above can be used to predict NEC early, properly diagnose NEC, either alone or in combination.

Study design

Infants are enrolled for 8 weeks or until transfer to a different hospital. During their participation in this study, stool and urine samples are collected two times per week. In addition, blood samples and mother (or formula) milk are collected every week. Blood is only collected when a blood drawing for clinical purposes is planned, then 5 extra drops are collected. During admission, near infrared spectroscopy (NIRS) will be used to determine intestinal perfusion and oxygenation levels and variability. This will be done continuously in the first 7 days, daily from day 8 to day 14, and two times per week afterwards. In addition, echo dopplers will be performed as standard part of clinical care. In case of definitive NEC (confirmed by pneumatosis or portal gas on abdominal X-ray) stool, urine and blood samples are collected every day (if possible). In case of surgical treatment for NEC, surgical resection material of the intestine will be saved.

From the mother, placenta and cord blood are collected at birth, as well as amniotic fluid in case of a cesarian section. Furthermore, the mother will collect a feces sample after birth and she will fill out a questionnaire on het diet after birth, at 4 weeks and at 8 weeks.

Intervention

n.a.

Contacts

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Eligibility criteria

Inclusion criteria

All children admitted to the neonatology department, which are
- born at a gestational age of ≤ 30 weeks
- and/or born with a birth weight of ≤ 1000 gram,
and parent consent in participating in the study.

Exclusion criteria

Abdominal disease such as abdominal wall defects, congenital intestinal atresia, as well as major congenital heart defects (e.g. Tetrology of Fallot).

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	03-05-2021
Enrollment:	150
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	19-04-2021
Application type:	First submission

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
NTR-new	NL9434
Other	METC UMCG : METc 2019/235

Study results