Immune effects of acidic and neutral oligosaccharides in the nutrition of preterm infants.

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Investigate the effect of acidic and neutral oligosaccharides supplemented enteral nutrition on infectious morbidity, feeding tolerance and short-term outcome in VLBW infants. Furthermore, an attempt is made to elucidate the role of acidic and...

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal conditions NEC
Study type	Interventional

Summary

ID

NL-OMON31597

Source
ToetsingOnline

Brief title
CARROT study

Condition

- Gastrointestinal conditions NEC
- Bacterial infectious disorders
- Neonatal and perinatal conditions

Synonym
bacterial intestinal colonization, gutflora

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,Numico,RIVM Bilthoven

Intervention

Keyword: Gastrointestinal tract, Immune effects, Prebiotica, Preterm infants

Outcome measures

Primary outcome

To determine the effect of acidic and neutral oligosaccharides supplemented enteral nutrition on infectious morbidity, intestinal microflora, feeding tolerance, and short-term outcome in VLBW infants.

Secondary outcome

1. To elucidate the role of acidic oligosaccharides in modulation of the immune response and postnatal adaptation of the gut.

2. To determine the long term effects of acidic and neutral oligosaccharides supplemented enteral nutrition in the neonatal period on the development of allergic and infectious disease in the first years of life (by questionnaire) and neurodevelopmental outcome, neuromotor development at the corrected age of 1 and 2 years and mental/motor development (BSIDII) at the corrected age of 2 years (as part of the regular follow-up of NICU infants).

3. To determine the effect of acidic and neutral oligosaccharides supplemented enteral nutrition on the response to immunizations with Diphteria-Tetanus-acellular pertussis-inactivated polio-Haemophilus influenzae type B-Pneumococ (DTaP-IPV-HIB-Pneu) vaccins (initial 3 doses), and booster

immunization (4th dose). In infants with parents from endemic Hepatitis B parts of the world and in infants born to Hepatitis B positive mothers, the response to immunization with Hepatitis B vaccin will also be evaluated.

4. To determine the transplacental transport of IgG against Measles, Diphteria, Tetanus, Pertussis, Polio, Haemophilus Influenzae type B, Pneumococcus, Mumps, Rubella and Hepatitis B in preterm infants.

5. To deteremine physiological variations of blood IL6 (arterial, venous, capillar) in preterm infants.

Study description

Background summary

Prevention of serious infections in very low birth weight (VLBW) infants is a challenge, since prematurity and low birth weight often require many interventions and high utility of devices. Furthermore, administration of enteral nutrition is limited by immaturity of the gastrointestinal tract. The acid and neutral oligosaccharides plays an important role in the development of the intestinal bacterial colonization and functional integrity of the gut. In preterm infants, the intestinal bacterial colonization is delayed compared with term infants with possible negative effects on susceptibility to serious infections. An abnormal intestinal bacterial colonization may also have negative effects on functional integrity of the gut and may lead to immunosuppression.

Study objective

Investigate the effect of acidic and neutral oligosaccharides supplemented enteral nutrition on infectious morbidity, feeding tolerance and short-term outcome in VLBW infants. Furthermore, an attempt is made to elucidate the role of acidic and neutral oligosaccharides supplemented enteral nutrition in postnatal adaptation of the gut and modulation of the immune response.

Study design

Double blind placebo-controlled randomised controlled trial whereby between days 3 and 30 of life, acidic and neutral oligosaccharides supplementation (20/80 mixture) is administered in a maximum dose of 1.5 g/kg/day to breastfeeding or preterm formula in the intervention group.

Interventions:
Enteral acidic and neutral oligosaccharides supplementation
Registration daily amount of feedings
Registration of perinatal data, clinical relevant data as severe infections, respiratory support, admission time.

Additional research:
< 48 uur:
- blood for cytokine profiles and IgG measurement
- faecal samples for FISH, pH, faecal calprotectin/IL-8
- sugarabsorptiontest
- blood for IgG measurement
Day 4:
- sugarabsorptiontest
Day 7:
- blood for cytokine profiles
- faecal samples for FISH, pH, faecal calprotectin/IL-8
- sugarabsorptiontest
Day 14:
- blood for cytokine profiles
- faecal samples for FISH, pH, faecal calprotectin/IL-8
- gastrointestinal transport time
Day 30:
- faecal samples for FISH, pH, faecal calprotectin/IL-8
Month 5:
- blood for immune response and IgE/IgG4
- faecal samples for FISH, pH, faecal calprotectin/IL-8
1 year:
- blood for immune response and IgE/IgG4
- faecal samples for FISH, pH, faecal calprotectin/IL-8

* At one timepoint in the first month in a subgroup of 20 preterm infants blood for physiological variations of blood cytokines (IL6) (0,2ml blood)

* At one timepoint in a subgroup of 20 healthy adults blood for physiological variations of blood cytokines in venous (1ml) and capillary blood 0,5ml

For IgE/IgG4 0,6ml blood is needed, for cytokine profiles ca 0.5ml, for immune

response 2ml.

To measure the response to vaccinations bloodsamples will be taken at patients home or during regular hospital visits. To determine the frequency of side-effects of immunizations, standardized questionnaires will be given to the parents at the time of immunizations.

The development of allergic and infectious disease in the first years of life (by questionnaire) and neurodevelopmental outcome, neuromotor development at the corrected age of 1 and 2 years and mental/motor development (BSIDII) at the corrected age of 2 years (as part of the regular follow-up of NICU infants) will be measured.

Intervention

Between days 3 and 30 of life, acidic and neutral oligosaccharides (20/80 mixture)supplementation is administered in a dose 1,5 g/kg/day to breastfeeding or preterm formula in the intervention group.

Study burden and risks

The pedatrician is responsible in making any descisions about doing the tests. Sampling of faeces will be done during regular care times. Extra bloodsamples will be taken during regular intravenous sampling times and if possible from intravenous lines.

Previous research has shown that enteral supplemented acidic and neutral oligosaccharides to premature infants cause no extra risks.

Previous research has shown that the sugarabsorptiontest causes no extra burdening for the patients.

See also study design

Contacts

Public
Vrije Universiteit Medisch Centrum

Postbus 7057
1007 MB Amsterdam
NL
Scientific
Vrije Universiteit Medisch Centrum

Postbus 7057
1007 MB Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

1. Written an informed consent from both parents or a legal guardians
2. Infants born with a gestational age of less than 32 weeks and/or a birthweight of less than 1500 gram

Exclusion criteria

1. Severe congenital disorders, like cardiac disorders, syndromal disorders, immunodeficiency disorders
2. Congenital disorders of the gastrointestinal tract

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2007
Enrollment:	108
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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
ISRCTN	ISRCTN16211826
CCMO	NL14256.029.07