A randomised, double-blind, controlled, parallel-group, multi-country study to investigate the effect of a partially hydrolysed infant formula with added synbiotics on gut microbiota composition and clinical effectiveness in infants at high risk of developing allergy.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Allergic conditions
Study type	Interventional

Summary

ID

NL-OMON50109

Source
ToetsingOnline

Brief title
TEMPO study

Condition

- Allergic conditions

Synonym
infants at high risk of developing allergy

Research involving
Human

Sponsors and support

Primary sponsor: Nutricia
Source(s) of monetary or material Support: Nutricia Research BV

Intervention

Keyword: Allergy prevention, Infant Formula/ Follow on Formula, Partially hydrolysed protein, Synbiotics

Outcome measures

Primary outcome

To investigate a bifidogenic effect of a (HP synbiotics) compared to standard

infant formula in infants at high risk of developing allergy.

Secondary outcome

This study investigates the effect of HP synbiotics compared to standard infant

formula on the development of allergic manifestations up to the age of 12

months in infants at high risk of developing allergy.

Study description

Background summary

Over the past decades, the prevalence of allergic disorders has increased exponentially around the world with variation in physical location of the manifestation (skin, lung, GI tract) dependent on geographical spread. Although allergic disorders have a hereditary element, the gene-environmental interaction is clearly important in explaining the rapid increase over the last decades. Knowing that the intestinal microbiome can significantly influence human physiology, the early colonization process is thought to form a crucial process laying the foundation for optimal health later in life. There is increasing evidence that modifications in the pattern of microbial exposure early in life represents a critical factor underlying the development of an allergic phenotype. The role of the unbalanced endogenous microbiota in

developing allergy is supported by the positive correlation of environmental factors that both impact the early microbial colonization process and the risk to develop allergic disorders (i.e. antibiotic use and caesarean section), as well as correlations of allergic disorders with an altered infant microbiome and increasing evidence of successful prevention or reduction of allergy through nutritional concepts that modulate the gut microbiota.
It is generally acknowledged that breastfeeding is one of the main pillars in allergy prevention. Many studies have examined the benefits of breastfeeding on the development of allergic disease. From these studies, it can be concluded that breastfeeding up to 4-6 months decreases the risk of atopic dermatitis in infants at increased risk. When a mother is unable or chooses not to breastfeed her infant, an infant formula based on the composition of human milk is recognized as the best alternative. For infants at increased risk to develop allergy a partially hydrolysed cow*s milk protein formula is developed.
The PATCH study (n=1047) performed by Nutricia Research, demonstrated that the gut microbiota composition and activity of infants at increased risk of allergy receiving the partially hydrolysed cow*s milk protein formula supplemented with oligosaccharides was more similar to breastfed infants than to infants receiving standard cow*s milk formula, which was driven by increased levels of bifidobacteria. These observations may imply that microbial succession of species and metabolite cross-feeding at specific developmental stages in early life are essential in establishing a balanced gut community and environment that supports gut development, but also homeostasis with our immune system thereby having the potency to reduce the risk of allergy development.

Study objective

The aim of the present study is therefore to investigate the bifidogenic effect of a hypoallergenic formula (based on partially hydrolysed whey protein) supplemented with a specific combination of prebiotics and probiotics (synbiotics) compared to standard infant formula in infants at high risk of developing allergic disease. This study will secondary assess the effects of this HA concept on the development of allergic manifestations up to the age of 12 months, which will be verified in a separate clinical study MAESTRO as primary outcome. Furthermore, the effects on growth and safety will be studied.

Study design

This is a randomised, double blind, controlled, parallel-group, multi-country study.

Intervention

Active product: Formula /follow-up formula with partially hydrolysed whey protein supplemented with prebiotics and probiotics (HP synbiotics)

Control product: standard formula/follow-up formula (complete protein)

Study burden and risks

No adverse events are expected in the breastfeeding group. For the active formula group, there is a closely monitored event where if the doctor suspects septicaemia, the intake of formula will be stopped and blood test will be performed to find the origin of the infection. For the active formula and control formula, the overall interaction with food as stated on the label will be expected. The use of probiotics is associated with softer stools (where it looks more like the stools of breastfed infants). The test product contains cow milk proteins. These proteins can cause an allergic reaction in children with a cow milk, soy protein, cow meat, corn or fish protein allergy. The taking of a blood sample can give mild pain, cause a bruise, an inflammation of the vein, hemorrhage or infection of the place where the needle has gone into the skin and rarely can cause nerve damage. Taking a nasal swab may cause temporary discomfort. Filling in the diary will cost extra time for parents. The skin prick test can cause discomfort and mild red skin and itching of the skin punctured specify which usually disappears within hours.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1) Healthy term infants (gestational age * 37 and * 42 weeks) at high risk of developing allergy based on family history of allergy., 2) Infants aged * 16 weeks (max. 16 weeks + 0 days), preferably as soon as possible after birth. , 3) Infants with birth weight within normal range for gestational age and sex (10th to 90th percentile according to local applicable growth charts). , 4) Infants who start formula feeding within 16 weeks of age (infants of mothers who have chosen not to breastfeed or mothers who completely/partially cease breastfeeding before the subject*s age of 16 weeks)
OR
Infants who are exclusively breastfed and whose mothers have the intention to exclusively breastfeed at least until their infant is 16 weeks of age., 5) Written informed consent from one or both parents (according to local laws) and/or legal guardian.

Exclusion criteria

1) Consumption of any amount of infant formula based on intact protein before randomization, except from consumption during the first 72 hours of life., 2) Consumption of any amount of infant formula with added probiotics and/or probiotic supplement before randomisation., 3) Existing allergic manifestations (e.g. allergic skin disorders, food allergy) before randomisation according to investigator*s clinical assessment., 4) Severe congenital abnormalities which could influence the subjects* growth (e.g. cystic fibrosis, bronchopulmonary dysplasia, tracheomalacia, tracheoesophageal fistula, major congenital heart disease, or any other condition according to investigator's clinical judgement)., 5) Severe neonatal illnesses (e.g. respiratory distress syndrome, severe sepsis intraventricular hemorrhage, severe neonatal jaundice, necrotizing enterocolitis, persistent pulmonary hypertension of the newborn, or any other condition which required the use of intravenous and/or intrmuscular antibiotic)., 6) Known underlying disease predisposing to infection (e.g. HIV, viral hepatitis B, and C, auto-immune diabetes, immune deficiency). , 7) Severe renal failure and hepatic failure according to investigator's clinical judgement., 8) Incapability of the parents to comply with study protocol or investigator's uncertainty about the willingness or ability of the subject to comply with the protocol requirements, 9) Participation in other studies involving investigational or marketed products concomitantly or within two

weeks prior to screening visit.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	30-03-2017
Enrollment:	44
Type:	Actual

Ethics review

Approved WMO Date:	24-01-2017
Application type:	First submission
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	08-03-2017
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	07-09-2017

Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	22-12-2017
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	03-05-2018
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	27-09-2018
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)
Approved WMO Date:	29-07-2019
Application type:	Amendment
Review commission:	IRB Nijmegen: Independent Review Board Nijmegen (Wijchen)

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
ClinicalTrials.gov	NCT03067714
CCMO	NL59111.072.16

Study results

Date completed: 21-01-2020

Actual enrolment: 44

Summary results

Trial is onging in other countries