The effect of an isocaloric, protein- and mineral-enriched ('postdischarge') formula on growth, body composition and bone mineralization of late preterm infants.;Follow-up: The effect of an isocaloric, protein- and mineral-enriched (*postdischarge*) formula on growth, body composition and neurocognitive development of late preterm infants at the corrected age of 2 years.

Published: 27-11-2014
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The main objective is to compare growth and body composition of late preterm infants at 6 months corrected age, fed either an isocaloric, protein- and mineral-enriched ('postdischarge') formula (PDF) or standard term formula (TF) between...

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

Summary

ID

NL-OMON55631

Source
ToetsingOnline

Brief title
LEGO ;Follow-up: LEGO 2.0

Condition

- Other condition
- Bone, calcium, magnesium and phosphorus metabolism disorders

Synonym
(catch up) growth, metabolic syndrome

Health condition

(inhaal) groei, hypertensie, cognitieve/motorische/taal-ontwikkeling

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Hero Benelux,Unrestricted research grant.

Intervention

Keyword: Body composition, Growth, Late preterms, Nutrition

Outcome measures

Primary outcome

Primary objective: to compare growth and body composition between late preterm

infants at 6 months corrected age, fed either isocaloric, protein- en

mineral-enriched postdischarge formula or standard term formula between term

age and 6 months corrected age.

- growth; weight, length and headcircumference

- body composition; fat mass and fat free mass

Follow-up:

- growth: Weight, length, head circumference, waist circumference,

- body composition: fat mass and fat free mass

Secondary outcome

Secondary objective(s): to compare cardio-metabolic risk factors, bone mineral content (and associated serum bone markers) and endocrine parameters between late preterm infants at 6 months corrected age, fed either isocaloric, protein-en mineral-enriched ('postdischarge') formula or standard term formula between term age and 6 months corrected age.

Furthermore we will compare all of these parameters between infants fed formula and infants fed (enriched) human milk.

- cardio-metabolic risk factors; insulin, glucose, triglycerides, cholesterol
- bone mineralization; bone mineral density / bone mineral content
- endocrine paramaters; IGF-1, IGF-II, FGF-23

Follow-up:

- Neurodevelopment (Bayley-III)
- cardio-metabolic risk factors; insulin, glucose, triglycerides, cholesterol
- bone mineralization; calcium, phospate, alkaline phosphatase
- endocrine paramaters; IGF-1, IGF-II, FGF-23
- other parameters: Hb, ferritin

Study description

Background summary

Preterm infants are at risk long term for adverse (metabolic) effects, which may be explained by the *fetal origins hypothesis* and the *catch up growth hypothesis*. Prematurity and excessive growth during early childhood are risk factors for the development of obesity, diabetes, hypertension and cardiovascular disease in later life. Research mostly focuses on early preterm born children (<32 weeks gestational age). Limited research has been performed to look into the effects on late preterms (gestational age between 32 and 36 weeks) so far. Lapillonne et al. (JPeds 2013) state that late preterms require special attention since they have unique and often unrecognized medical vulnerabilities and nutritional needs. We think this assumption has yet to be supported by evidence so the specific needs can be further explored and specified.
Research among preterms in general, aims at an optimal balance between sufficient growth on one side and risks associated with excessive (catch-up) growth and fat accumulation on the other side. We hypothesize that an isocaloric, protein- and nutrient-enriched (postdischarge) formula fed to late preterm infants will promote both growth and a favorable body composition and thereby diminish the previously mentioned health risks. For SGA born children we expect this effect to be even more pronounced since both term and preterm SGA infants seem to benefit from nutrient enriched formula. Male infants seem to profit most from PDF feeding. With stratification for both gender and being SGA or not, we hope to give more insight in those differences.

In the Netherlands, 6.4% of new-borns are born with a gestational age between 32 and 36 weeks (so called late preterms). Although this is a large group, little is known about the exact needs of late preterms. As a consequence, there is an enormous variety in Dutch nutrition-guidelines for late preterm infants used in hospitals and after discharge.
The third trimester of pregnancy is considered not only a critical phase for growth, but also for the programming of body functions. Evidence for subsequent problems that preterms experience later in life is mainly derived from studies in preterms born <32 weeks GA and a birth weight <1500g. Cardiovascular disease, obesity, insulin resistance and increased blood pressure are a few of the long term consequences associated with preterm birth. Adipose tissue and in particular the distribution of it, may play an important role in the development of metabolic complications.
Some studies have suggested that these long term consequences are also relevant for late preterm infants. However, research mainly focused on conditions like respiratory distress, hyperbilirubinemia, hypoglycaemia, etc.Several authors underline the importance of expanding the knowledge about late preterm born children. Since late preterms miss part of the vital intra-uterine period, they could also be prone to develop nutritional deficits. Most of today*s nutritional recommendations have been extrapolated from data for very low birth weight (VLBW), very preterm (<32 weeks gestational age) and term infants.

Nutrition and growth is therefore an important field yet to be explored for the late preterm group, especially with regard to long term outcomes.

Follow-up:
We would also like to refer to the above. Follow-up at the longer term is important to be able to get insight in the effects of early nutrition on early growth (pattern), vody composition and metabolic risk factors in late preterm infants. Furthermore, at the age of 24 months it is possible to assess neurocognitive develpoment of these children, and to compare this with term born children (based on available norm values).
Even though late preterms are the majority of the whole group of preterm children in the Netherlands, we know little about the consequences, especially on the longer term. With this follow-up study we can contribute to the current knowledge and understanding of the effects of nutrition on growth, body composition and neurodevelopment in late preterm infants born in the Netherlands.

Study objective

The main objective is to compare growth and body composition of late preterm infants at 6 months corrected age, fed either an isocaloric, protein- and mineral-enriched ('postdischarge') formula (PDF) or standard term formula (TF) between term age and 6 months corrected age.
The secondary objective is to compare cardio-metabolic risk factors, bone mineral content (and associated serum bone markers) and endocrine parameters.

Overall, we will compare the formula fed infants with the infants fed human milk.

Follow-up:
The main objective is to assess long-term effects of feeding an isocaloric protein- and mineral-enriched formula compared to a standard term formula between term age and 6 months corrected age, on growth, body composition, neurodevelopment and cardiometabolic risks parameters of late preterm born infants, at 24 months corrected age.

Study design

Double-blind randomized controlled multicentre trial.
- Intervention group: standard term formula (*Hero baby Standaard 1*)
- Intervention group: isocaloric, protein- en mineral-enriched ('postdischarge') formula (*Hero baby Prematuur 1*)
- *Control* group: human milk

Setting: VU University medical centre, Amsterdam, The Netherlands and affiliated clinics between birth and discharge. Outpatient clinic of VU

University Medical Centre, between discharge and six months corrected age.

Follow-up:
Follow up of a double-blinded randomized controlled multicenter trial (LEGO-study).

Intervention

All infants will be fed human milk and/or protein and mineral enriched formula from birth to term age. At term age, formula fed infants are randomized to PDF or TF and are fed this diet until six months corrected age. Stratification for gender and birth weight (p10) will be performed. Infants are fed 150-175 ml/kg/d according to the current guidelines and after discharge the amount of formula per day is advised by the coordinating investigator.

Follow-up: not applicable

Study burden and risks

In the first week after birth a blood sample (3ml) will be taken, either together with a routine clinical venepuncture or with placement of an IV-cannula for parenteral nutrition. Subjects will visit the outpatient clinic of the VU University medical center twice (around term age and corrected age 6 months). At both visits anthropometry, measurement of body composition in the PEA-POD and a whole body DEXA-scan will be performed and a blood sample of 4.2ml will be taken. During the period from discharge until 6 months, parents will keep a diary of the nutritional intake of their child.

Follow-up:
During the outpatient visit at 24 months corrected age, anthropometry, body composition (using BOD POD, air-displacement plethysmography) and blood pressure will be measured. Furthermore, a blood sample (3.7 ml) will be taken and neurodevelopment will be assessed. Parents will be asked to fill in a diary/questionnaire concerning the nutritional habits of their child.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

Birth at gestational age between 32 0/7 and 35 6/7 weeks., Follow-up: participants of the LEGO-study

Exclusion criteria

- gastro-intestinal surgery and disease known to influence growth (i.e. cystic fibrosis and severe gastro-oesophageal reflux)
- known presence of growth hormone, IGF-1 or other pituitary hormone deficiencies
- concurrent therapies with substances known or suspected to be associated with alteration of growth (i.e. oral steroids)
- cardiac, renal, pulmonary and liver disease
- chromosomal and/or genetic syndromes
- known skeletal disease
- severe illness in general

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-06-2015
Enrollment:	300
Type:	Actual

Ethics review

Approved WMO Date:	27-11-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-08-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-01-2022
Application type:	Amendment
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

ID: 28261
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL47957.029.14
OMON	NL-OMON28261