ISRCTN15469594 https://doi.org/10.1186/ISRCTN15469594

Feeding late and moderately preterm infants

Submission date
30/04/2018

Recruitment status
No longer recruiting

Registration date
14/05/2018

Overall study status
Completed

Last Edited
10/06/2024

Condition category
Neonatal Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The rates of premature birth are increasing, with most occurring between 32 and 36 weeks gestation, called Late and Moderately PreTerm (LMPT) infants. These babies weigh 1.25-2.5kg at birth and have different nutritional requirements to those born full term. However, most nutrition studies have tended to focus on extremely premature infants (gestation < 32 weeks) and there are few data on growth in LMPT infants. There are strong data to show that breastfeeding results in better outcomes, but establishing breastfeeding in LMPT infants is challenging as many initially require support with nasogastric tubes. The duration of breastfeeding in the UK is shorter than other countries, and most LMPT infants grow more slowly. In later life LMPT infants are more likely to require additional educational support, and more likely to be obese as adults. These later life complications are associated with nutrition in early life.

Who can participate?
Healthy LMPT infants

What does the study involve?
Nutrition data is collected until 2 years of age, including breastfeeding, use of vitamin supplements, growth (weight, length etc), body composition (fat mass etc) and age at introduction of solid foods. If parents choose not to continue breastfeeding, infants are randomly allocated to either a standard milk formula or an intervention formula that only differs in the structure of the fat globule (the amount of fat is the same). The larger fat globule in the intervention formula is more similar to human milk. Differences in weight gain and fat mass are measured.

What are the possible benefits and risks of participating?
The study will provide parents with expert advice on optimal feeding practices based on up to date international consensus guidelines and will strongly support breastfeeding. The specific study design is chosen to be fully supportive of breastfeeding as preferred nutrition in early life, and will adhere to all aspects of the WHO code on the use of breastmilk substitutes as well as supporting the Baby Friendly Initiative (BFI, UNCIEF). It offers all participants regardless of maternal feeding choice the opportunity for close follow-up and advice from a paediatrician.

There are no significant risks for those taking part as all formula used meet current international recommendations. However, there may be minimal disruption to family life as parents will need to return to the hospital for regular clinic visits until 2 years of age.

Where is the study run from?
Royal Victoria Infirmary (UK)

When is the study starting and how long is it expected to run for?
April 2018 to May 2023

Who is funding the study?
Danone Nutricia Research (Netherlands)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CPMS 37485

Study information

Scientific Title
Feeding Late and Moderately Preterm Infants Nutrition and Growth Outcomes (FLAMINGO)

Acronym
FLAMINGO

Study objectives
The rates of premature birth are increasing, with most occurring between 32 and 36 weeks gestation, so-called Late and Moderately PreTerm (LMPT) infants. These babies weigh 1.25-2.5kg at birth and have different nutritional requirements to those born full term. However, most nutrition studies have tended to focus on extremely premature infants (gestation < 32 weeks) and there are few data on growth in LMPT infants.

There are strong data to show that breast-feeding results in better outcomes, but establishing breast-feeding in LMPT infants is challenging as many initially require support with nasogastric tubes. The duration of breast-feeding in the UK is shorter than other countries, and most LMPT infants grow more slowly. In later life LMPT infants are more likely to require additional educational support, and more likely to be obese as adults. These later life complications are associated with nutrition in early life, but there are few longitudinal studies.

The FLAMINGO study (Feeding Late And Moderately preterm Infants Nutrition and Growth Outcomes) will collect nutrition data in LMPT infants until 2 years age, including breastfeeding, use of vitamin supplements, growth (weight, length etc.), body composition (fat mass etc.) and age at introduction of solid foods. The study will provide parents with expert advice on optimal feeding practices based on up to date international consensus guidelines and will strongly support breastfeeding. If parents choose not to continue breast-feeding, infants will be eligible to join a randomised trial. In this, a standard milk formula will be compared to an intervention formula that only differs in the structure of the fat globule (the amount of fat is the same). The larger fat globule in the intervention formula is more similar to human milk. Differences in weight gain and fat mass will be determined.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North East - York Research Ethics Committee, 11/04/2018, ref: 18/NE/0040

Study design
Randomized; Both; Design type: Treatment, Prevention, Dietary, Cohort study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Late and moderately preterm infants

Interventions
Please note that infants are first recruited to an observational cohort. From within this cohort infants who are eligible will be enrolled to an RCT. Outcomes are the same for both groups.

Infants will be enrolled and randomised using an online randomisation programme https://www.sealedenvelope.com. Infants are assigned to a product code (A, B, C or D) using a minimisation process (with a 30% chance of simple random allocation) and will use two stratification factors. All members of the research team are blinded to treatment allocation.

Stratification is applied for:
1. Multiple births (single vs multiple birth)
2. Gestational age (32-33 vs 34-36 weeks)

In case of multiple births, the first eligible sibling is randomised according to the stratification factors above and if applicable, the other sibling(s) will be automatically provided the same treatment code.

Infants will be allocated of two study formula milks (control and intervention) which will be fed on demand until 6 months corrected age (total duration 6 – 7 months). Infants will be reviewed by telephone and at pre-planned clinic visits. After 6 months corrected age the study intervention will stop and infants will be advised on feeding methods according to standard guidelines. Infants will be followed in clinic until 2 years corrected age. The two milk formula meet international recommendations for nutrient intakes in infancy and contain similar amounts of macro- and micro-nutrients. They differ only in the structure of the lipid droplet which is larger in the intervention formula.

Intervention Type
Other

Primary outcome measure
Daily weight gain from randomisation until 3 months corrected age. Weight measured using standard weighing scales at baseline, discharge, term equivalent age (TEA), 3,6,12 and 24 months corrected age

Secondary outcome measures
1. Growth (weight, length and head circumference) from term equivalent age (TEA) until 3 months. Length and head circumference are measured using standard linear length boards and head circumference using non-stretchable tape measures at term and 3 months corrected age
2. Body composition measured by Dual X-Ray Absorptiometry (DEXA) before/at term and 3 months corrected age. DEXA will provide lean body mass, total body fat mass, % fat and lean body mass, fat mass index, fat free mass index, bone mineral density, bone mineral content, ulna and lower leg length
3. Anthropometry: weight, length, head, mid-upper arm and mid-thigh circumference (using

tapes) at baseline, discharge, term equivalent age (TEA), 3,6,12 and 24 months
4. Skinfold thicknesses using Harpenden calipers: triceps, biceps, supra-iliac, subscapular at baseline, discharge, term equivalent age (TEA), 3,6,12 and 24 months
5. Arm muscle area, arm fat area and arm fat % calculated from mid-upper arm circumference and triceps skinfolds
6. WHO Z-scores of anthropometric parameters at baseline, discharge, term equivalent age (TEA), 3, 6, 12 and 24 months:
6.1. Weight-for-age z scores
6.2. Weight-for-length z scores
6.3. Length-for-age z scores
6.4. Body Mass Index-for-age (BMI-for-age) z scores. BMI is automatically calculated from weight divided by height squared [kg/m2]
6.5. Head circumference-for-age z scores
6.6. Mid-upper arm circumference-for-age z scores (from 3 months corrected age onwards)
6.7. Skinfold-for-age z-scores (subscapular, triceps; from 3 months corrected age onwards)
7. Gain in above mentioned growth and body composition parameters and (when applicable) their z-scores during the study, including at least the following time intervals: randomization /term to 3 months corrected age, randomization/term to 6 months corrected age, 6 to 12 months of corrected age and 12 to 24 months corrected age
8. Number, type and severity of (serious) adverse events up to 12 months of corrected age
9. Number, type and severity of serious adverse events which could potentially be related to the use of study product, and the corresponding medication used, during the follow-up period (until 24 months of corrected age)
10. Use of medication and nutritional supplements up to 12 months corrected age at baseline, discharge, term equivalent age (TEA), 3, 6, 12 and 24 months
11. Gastrointestinal tolerance parameters at discharge, term equivalent age (TEA), 3, and 6 months corrected age via parental recall, including:
11.1. Occurrence and severity of gastrointestinal symptoms (stooling, reflux, spitting up /vomiting, flatulence, crying and/or fussiness, diarrhea), using a 5-point scale to indicate severity
11.2. Stool characteristics recording by parental recall using questions that are already provided together with educational material in an information booklet
11.3. Stool frequency (number of stools)
11.4. Stool consistency, scored on a 4-point scale using pictures to indicate score: watery (=1), soft (=2), formed (=3) or hard (=4)
12. The Parent Report of Children's Abilities-Revised (PARCA-R) questionnaire scores are recorded to assess cognitive and language development at 24 months corrected age
13. Baby eating behaviour questionnaire outcomes at term and 3 months
14. Infant's eating behaviour (Baby Eating Behaviour Questionnaire: BEBQ)
15. Infant's bottle-emptying behaviour is assessed by asking the main caregiver to answer 2 questions relating to bottle emptying on a 5-point scale [never (= 1) / rarely (= 2) / sometimes (= 3) / most of the time (=4) / always (=5)]: "How often does your baby drink all of his or her bottle of formula?" and "How often does your baby drink all of his or her cup or bottle of pumped milk?"
16. Questions to record age at introduction of complementary feeding, age at introduction of infant formula (breastfed reference) and duration of (any) breastfeeding will be asked at term, 3 and 6 months
17. Food frequency questionnaires to assess dietary intake at 6 and 12 months of corrected age
18. Child eating behaviour questionnaire at 12 and 24 months of age

Overall study start date
01/04/2018

Completion date
21/05/2023

Eligibility

Key inclusion criteria
1. Healthy moderate to late preterm infants (gestational age ≥ 32 and ≤ 36 6/7 weeks)
2. Age at inclusion ≤ term equivalent age
3. Birth weight between 1.25-2.5 kg
4. Infants who are predominantly formula fed (max. 1 breastfeeding per day) using a standard term infant formula
5. Written informed consent from parent(s) and/or legal guardian, aged ≥ 18 years, to be enrolled into a randomised trial

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 250; UK Sample Size: 250

Total final enrolment
182

Key exclusion criteria
1. Any gastrointestinal, congenital or other problem likely to affect growth and nutrition, or requiring use of specialised milk formula or other diet e.g. due to confirmed allergy; or where the attending medical team feel that trial participation is inappropriate for any other medical condition
2. Ongoing child protection procedures or maternal drug misuse requiring social services involvement
3. Family circumstances where follow-up not likely to be possible e.g. family travel abroad for prolonged periods, or where it appears likely that the family will be unable to comply with the necessary research visits
4. Participation in another interventional study that may potentially confound or interact with this study
5. Family unable to understand English

Date of first enrolment
21/05/2018

Date of final enrolment

28/02/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Victoria Infirmary
Ward 35 Neonatal Unit
Newcastle Hospitals NHS Foundation Trust
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Sponsor information

Organisation
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Industry

Funder Name
Danone Nutricia Research

Results and Publications

Publication and dissemination plan
It is anticipated that the study protocol will be published prior to publication of study outcomes. Planned publication of the study results in a high-impact peer reviewed journal is planned for May 2023.

Intention to publish date
01/05/2023

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		08/03/2021	26/03/2021	Yes	No
HRA research summary			28/06/2023	No	No
Results article		01/10/2022	10/06/2024	Yes	No