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Fluids exclusively enteral from day one in premature infants

Submission date 10/09/2019	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 23/09/2019	**Overall study status** Ongoing	
Last Edited 11/09/2024	**Condition category** Neonatal Diseases	

Plain English summary of protocol

Background and study aims

Around 8% of UK babies are born premature at birth and 12% of these are born between 30 and 33 weeks. Currently, most preterm babies are fed through a drip into their veins (intravenous) and given small amounts of milk by a small tube into their stomach, slowly increasing until they are fully milk fed. Doctors are wary of feeding premature babies with full milk straight after birth due to a potentially life-threatening gut condition called necrotising enterocolitis (NEC).

Evidence suggests that in premature babies who aren't too poorly, larger milk feeds can be successfully given within 48 hours of birth without increasing the risk of NEC and death, and could reduce the risk of severe infection.

We want to know if feeding babies on with milk only from the first day of life, avoiding giving them fluids through a drip (IV), can reduce infections, reduce the number of days in hospital and therefore reduce the overall costs to parents and to the NHS.

Who can participate?

Infants born at 30 - 33 weeks gestation

What does the study involve?

We will compare two different groups: the 'full milk' group will be given milk to provide all their fluid needs from the first day of life and increased over a few days unless they are struggling with this (e.g. if it makes them very sick). In the 'gradual milk' group, babies will be initially fed through their veins, increasing milk feeds slowly and reducing IV fluids until they are fully milk fed, which is current practice.

What are the possible benefits and risks of participating?

We do not know if taking part in the study will benefit parents or babies directly, but by doing this study we are hoping to find the best way of feeding preterm babies which may help to guide the care of premature babies in the future.

If a baby is in the full milk group, they will be given milk from the first day. This amount of milk may be difficult for babies to tolerate and they may vomit and/or develop bloating. If this

happens the doctors and nurses caring for the babies will decide what is best for them and may give smaller amounts of milk more frequently or reduce the amount of milk. There may be benefits from full milk from day 1, such as reducing infections and the need for drips associated with IV feeding in the gradual milk group.

Where is the study run from?
Nottingham Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?
October 2019 to September 2027

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
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Study website
https://www.feed1.ac.uk/home.aspx

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
DHRD/2018/116

Study information

Scientific Title
A randomised controlled trial of full milk feeds versus intravenous nutrition with gradual feeding for preterm infants (30-33 weeks gestational age)

Acronym
FEED1

Study objectives
To investigate whether, in infants born at 30+0 to 32+6 weeks+days (inclusive) gestation, full milk feeds initiated in the first 24 hours of life reduce the length of hospital stay in comparison to IV fluids with gradual milk feeding

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/09/2019, East Midlands Derby REC (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS; +44 (0) 2071048036; NRESCommittee.eastmidlands-derby@nhs.net), ref: 19/EM/0258.

Study design
Multi-centre open parallel randomised controlled superiority trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Neonatal nutrition

Interventions
Mothers will be randomised in a 1:1 ratio, for their infants to receive either:
1. Intervention – infant(s) started on full milk feeds (a minimum of 60ml per kg of the baby's weight each day) from day 1.

2. Control – infant(s) started on a small amount of milk (maximum of 30ml per kg of the baby's weight each day) along with intravenous fluids/nutrition as per usual care.

Milk will then be gradually increased in each arm, as per the local hospitals usual practice, until they reach full milk feeds (defined as 140ml per kg of the baby's weight each day). Routine data will be collected until the infant is discharged from hospital. A further follow-up will be conducted via a questionnaire to be completed by the mother once the infant reaches 6 weeks corrected age.

Intervention: full milk feeding from day one

Comparator: parenteral nutrition/intravenous fluids with gradual milk feeding as per usual local practice

Mothers will be identified at the antenatal clinic or within 3 hours of early arrival. The groups will be decided at random by a computer giving each baby an equal chance of being in either group.

The selection of the outcome measures has been guided by the Core Outcomes in Neonatology (COIN) core outcome set, developed by a steering committee comprised of parents and former patients, healthcare professionals and researchers.

A subsequent funding application will be submitted to extend the scope of this trial to follow-up infants at 2 years of corrected gestational age. We intend to compare data on survival to 2 years of age and neurodevelopmental impairment including the remaining COIN outcomes (general gross motor ability, general cognitive ability, visual impairment or blindness, hearing impairment or deafness).

Intervention Type
Other

Primary outcome measure
Length of hospital stay

Secondary outcome measures
1. Survival to hospital discharge
2. Survival to 6 weeks corrected gestational age (i.e. term gestation + 6 weeks)
3. Incidence of microbiologically-confirmed (positive blood/cerebrospinal fluid [CSF] culture) or clinically suspected (defined by diagnostic criteria) late-onset sepsis until hospital discharge
4. Necrotising enterocolitis (Bell's stage 2 or 3) until hospital discharge
5. Time taken to maintain full milk feeding (defined as at least 140 ml/kg/d for three consecutive days)
6. Time to regain birth weight
7. Growth (z scores for gestational age at hospital discharge (as per UK-NICM growth charts))
7.1 Weight in kg
7.2 Length in cm
7.3 Head circumference in cm
8. Breastfeeding at hospital discharge
9. Breast milk fed at hospital discharge
10. Number of days of peripheral cannula until full milk feeding (defined as at least 140 ml/kg/d for three consecutive days) achieved
11. Number of IV cannulae inserted until full milk feeding (defined as at least 140 ml/kg/d for

three consecutive days) achieved
12. Number of days of parenteral nutrition, until hospital discharge
13. Number of central venous lines inserted (including umbilical and percutaneous or surgically inserted venous lines) until hospital discharge
14. Number of central line days until hospital discharge
15. Time until objective discharge criteria are met
16. Hospital visits (including day care and overnight admissions) up to 6 weeks of corrected age (i.e. term gestation + 6 weeks)
17. Breast feeding at 6 weeks of corrected age (i.e. term gestation + 6 weeks)
18. Breast milk fed at 6 weeks of corrected age (i.e. term gestation + 6 weeks)
19. Parental satisfaction and wellbeing at 6 weeks of corrected age (i.e. term gestation + 6 weeks), using the Preterm Birth Experience and Satisfaction Scale (p-BESS) questionnaire

Overall study start date
01/04/2019

Completion date
30/09/2027

Eligibility

Key inclusion criteria
1. Infant born at 30 weeks + 0 days to 32 weeks + 6 days gestation, inclusive
2. Infant <3 hours (180 minutes) old (since recorded time of birth)

(Infants requiring respiratory support (such as via continuous positive airway pressure) or other supportive treatments will be included in the study if the attending clinician is in equipoise about the infant being randomised to either the “full milk” or the “gradual milk” arm. Similarly, well infants should only be included if the attending clinician is in equipoise about the best feeding regime and the infant being randomised to either “full milk” or “gradual milk” groups.)

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
2088

Total final enrolment
2088

Key exclusion criteria
1. Infant with known congenital abnormalities of the gastrointestinal tract or other congenital conditions that make enteral feeding unsafe
2. Infant who are small for gestational age (birth weight <10th centile) AND evidence of

reversed end-diastolic flow on antenatal umbilical artery Doppler ultrasound*
3. Mother has participated in the trial during a previous pregnancy#

*Small for gestational age infants with antenatal Doppler ultrasound scan showing absent umbilical artery flow or whose mother's did not have antenatal umbilical Doppler ultrasound may be eligible for the trial if they meet the other inclusion criteria.

#The trial will recruit over 36 months. It is possible that the mother of an infant(s) who has already participated in the trial has another pregnancy in this duration. In such circumstances, the infant(s) born in subsequent pregnancies will be excluded to avoid bias due to the experience of previous participation.

Date of first enrolment
01/10/2019

Date of final enrolment
14/07/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Nottingham Clinical Trials Unit
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Room A17
University Park
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United Kingdom
NG7 2RD

Sponsor information

Organisation
University Hospitals of Derby and Burton NHS Foundation Trust

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Research and Development,. Royal Derby Hospital
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Sponsor type
Hospital/treatment centre

Website
https://www.uhdb.nhs.uk/

Funder(s)

Funder type
Not defined

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
30/12/2025

Individual participant data (IPD) sharing plan
The datasets analysed during the current study will be available upon request from the NCTU (ctu@nottingham.ac.uk), a minimum of 6 months after publication of the main results paper. Access to the data will be subject to review of a data sharing and use request by a committee

including the CI and sponsor, and will only be granted upon receipt of a data sharing and use agreement. Any data shared will be pseudoanonymised which may impact on the reproducilbilty of published analyses.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V1.1	16/08/2019	23/09/2019	No	Yes
Protocol article		20/01/2022	24/01/2022	Yes	No
HRA research summary			28/06/2023	No	No