ISRCTN05274566 https://doi.org/10.1186/ISRCTN05274566

Necrotizing enterocolitis and exclusively human milk feeding through 33 weeks postmenstrual age

Submission date
14/05/2013

Recruitment status
No longer recruiting

Registration date
23/05/2013

Overall study status
Completed

Last Edited
03/02/2015

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
We are carrying out a study of premature infants born before 33 weeks gestation. Our goal is to determine whether a human milk diet works. Necrotizing enterocolitis (NEC) is a serious problem for the premature infant's small intestine. NEC occurs in 7 to 10% of infants with birth weights less than 1.5 kg. Premature infants typically receive cows milk-based products when the mothers own milk (MOM) is not available. Elimination of cow's milk products from the premature infants diet, including cow's milk-based milk fortifiers, has been suggested as a possible way to reduce NEC.
We want to observe the rate of NEC in very premature infants when they receive a diet of exclusively human milk until they reach a minimum of 33 weeks postmenstrual age. The studys findings should help to determine the rate of NEC associated with an entirely human milk diet.

Who can participate?
The study aims to recruit all premature infants born before 33 weeks gestation admitted to a single neonatal intensive care unit during a 30-month period.

What does the study involve?
Mothers of infants admitted to a neonatal intensive care unit (NICU) was encouraged to provide milk for their infants. Until infants were ready for milk feedings, they received nutrition intravenously. Milk production requires the mother to use electric pumps and hands on the breast to express their milk. Lactation consultants provide mothers with training and supplies. The MOM was refrigerated or frozen until it was used for feeding. In case they were unable to supply enough MOM, mothers were offered pasteurized donor human milk (DHM) from a milk bank as an alternative to cows milk formula. Mothers provided written consent in order to receive DHM. In the event that a fortifier of MOM or DHM was recommended, a DHM-based fortifier was provided. After 33 weeks, routine feeding practices permit artificial milk products when MOM was not available. At the end of the study we will evaluate the group for the appearance of NEC in relation to the diet provided.

What are the possible benefits and risks of participating?
The risk of NEC associated with an EHM diet is unknown; The EHM diet is the diet recommended by the American Academy of Pediatrics (AAP) for premature infants: MOM is the first choice, DHM is the second choice and formula is the last choice. DHM and DHM-based milk fortifier are expensive and they are nutritional products. Participating infants benefit from receipt of DHM products which are expensive and nutritional. The hospital pays for these products. The risk of using MOM includes infections or medications acquired by the infant from its mothers milk. If necessary, DHM can be substituted for MOM, which is a potential benefit to the infant. The potential risk of the EHM diet leading to slower growth (compared to formula) which is balanced by providing DHM-based fortifier. The potential risks of a formula diet include an increased rate of NEC, excessive weight gain leading to obesity, and poorer developmental outcome at later ages. The balance of the multiple risks and benefits are not clear.

Where is the study run?
The study site is at the Deaconess-Womens Hospital, located in Newburgh, IN, USA.

What is the study period?
July 2010 through December 2012.

Who is funding the study?
The Deaconess-Womens Hospital.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Study information

Scientific Title
Necrotizing enterocolitis and exclusively human milk feeding through 33 weeks postmenstrual age: single arm-cohort prospective trial

Study objectives
A portion of the incidence of necrotizing enterocolitis (NEC) is associated with bovine-based artificial milk feeding provided before 33 weeks postmenstrual age (PMA).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Studies evaluating the safety of nutrition products are exempt from institutional review approval. Mothers own milk and DHM are not regulated by the FDA. Investigators are not permitted to determine their own exemption status; The Research Institute of Deaconess Clinic performs the exemption status determination: (http://www.deaconess.com/DeaconessClinic/Clinical-Research.aspx).

Study design
Single arm-cohort prospective trial

Primary study design
Observational

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Risk of necrotizing enterocolitis (NEC) associated with a diet entirely of human milk.

Interventions
Premature infants receive an entirely human milk diet from birth through 33 weeks postmenstrual age

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
The occurrence of necrotizing enterocolitis (NEC) greater or equal to Bell's stage II. This is an event that has a dramatic onset. The onset is recorded in the EMR as a date. Retrospectively, the chronological day of onset (date of onset minus the date of birth) is determined. Similarly, the Postmenstrual Age (PMA) at onset (gestational age plus the chronological age) is also retrospectively determined.

Key secondary outcome(s))
Assessed after completions includes:
1. Duration of parenteral nutrition (TPN): PN orders are written daily, beginning at the time of birth. PN is determined to stop on the day that no new parenteral orders are written. The duration is calculated retrospectively by PMA for the day PN stops: (gestational age plus the chronological age).
2. Duration of NICU hospitalization (postmenstrual age at discharge): The duration of hospital

stay ends on the date the infant leaves the hospital and goes home with its parents. The duration is calculated retrospectively by PMA for the day the infant goes home: (gestational age plus the chronological age).
3. Markers of milk feeding intolerance: Enteral feeding tolerance is measured retrospectively, based on the feeding provided on the day the infant is discharged to the parents. Feeding categories include: breast milk; bovine based artificial milk with intact proteins; bovine based artificial milk with hydrolyzed proteins; amino-acid based artificial milk. (Intolerance of feeding occurs when bovine based artificial milk with hydrolyzed proteins or an amino-acid based artificial milk is prescribed on the day of discharge to the parents).
Enteral feeding is measured retrospectively, determined by the use of a medication (metoclopramide), used at any duration of time for any reason prior to discharge to the parents. (Intolerance of feeding is suspected if metoclopramide is used on any day).

Completion date
31/12/2012

Eligibility

Key inclusion criteria
All infants admitted to a single neonatal intensive care unit (NICU) from July 1, 2010 through December 31, 2012, and born before 33 weeks gestation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Key exclusion criteria
All infants admitted to the neonatal intensive care unit (NICU) in the study period are evaluated. Infants of parents that do not provide mother's own milk and also do not consent for donor human milk are excluded in the analysis of human milk-fed infants.

Date of first enrolment
01/07/2010

Date of final enrolment
31/12/2012

Locations

Countries of recruitment
United States of America

Study participating centre
4199 Gateway Boulevard
Newburgh
United States of America
47630

Sponsor information

Organisation
The Deaconess Women's Hospital (USA)

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Deaconess-Women's Hospital (USA)

Funder Name
Australian Research Council (DP11110103125) (Australia)

Alternative Name(s)
arc_gov_au, The Australian Research Council, Australian Government Australian Research Council (ARC), ARC

Funding Body Type
Government organisation

Funding Body Subtype
Other non-profit organizations

Location
Australia

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/05/2014		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes