A randomized multicenter open-label controlled trial to show that mucous fistula refeeding reduces the time from enterostomy closure to full enteral feeds (MUCous FIstula REfeeding (*MUC-FIRE*) trial)

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The aim of this study is to assess the effects of mucous fistula refeeding in a prospective randomized trial. We hypothesize that MFR between enterostomy creation and enterostomy closure reduces the time to full enteral feeds after enterostomy…

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56093

Source
ToetsingOnline

Brief title
MUC-FIRE

Condition

- Other condition

Synonym
mucous fistula refeeding

Health condition

Enterostomy

Research involving
Human

Sponsors and support

Primary sponsor: University of Leipzig, Department of Pediatric Surgery
Source(s) of monetary or material Support: German Research Foundation

Intervention

Keyword: enterostomy, mucous fistula, refeeding

Outcome measures

Primary outcome

Time to full feeds (hours), defined as time from enterostomy closure to actual enteral intake of the age-dependent caloric requirements per day for at least 24h and a concomitant reduction of parenteral fluids to < 20ml/kg/24h.

For determining the time to full enteral feeds, the feeding advancement will be carried out according to the predefined nutritional protocol after 6-8 tolerated feedings in 3-4 hour intervals (24 hours). *Full feeds* is therefore defined age-dependent as 90 or 120kcal/kg/24h (full feed kcal goal) actual enteral intake [8, 9, 32, 33]. The nurses will document any increase and decrease of nutrition precisely and daily controls will be carried out by the responsible neonatologist and pediatric surgeon.

The decision about the full feed kcal goal is made before randomization by the treating physician, depending on the birth weight of the infants and mother*s gestation week at birth:

- The nutrition aim is 120 kcal/kg/24h for premature infants with a birth weight < 1000g or premature infants with a birth weight >= 1000g and mother*s gestation week at birth before 37+0.
- The nutrition aim is 90 kcal/kg/24h for born mature infants, e.g. mother*s gestation week at birth at least 37+0.

In the case unforeseen circumstances lead to an unexpected maturation of the infant, at the time of enterostomy closure an infant formerly classified as *premature* can be re-classified as *mature*, following justified reasoning concerning laboratory parameters and consultation with the principal investigators. To rule out a biased decision by the investigators, an independent reviewer will review these decisions at the end of the study.

As the full feed kcal goal is implemented firstly in the study protocol version 3.0 the independent reviewer will also be provided with the data of patients that were randomized before study protocol version 3.0 and that did not achieve time to full feeds with the initial kcal goal of 120 kcal/kg/24h. On the basis of the individual patient information the independent reviewer will assess the primary endpoint with respect to the specific kcal goal defined above.

Secondary outcome

1) Reoperation.

2) Time to first bowel movement after enterostomy closure (mucous stool is

considered a bowel movement) Cleaning and changing of infants diapers will be performed according to a fixed schedule in order to uniformly document the time to first bowel movement following enterostomy
closure.
3) Postoperative weight gain (g/d) (daily documentations recommended, minimum 2x per week), regular Z-Score (standard deviation score) documentation [WHO - weight-for-age] (daily documentations recommended, minimum 2x per week), This will be carried out
according to a fixed schedule during morning rounds prior to feeding in an unclothed status.
4) Days of postoperative total parenteral nutrition (> 20 ml/kg/24h) before and after the 2nd operation (=ostomy takedown) (TPN) Days of postoperative total parenteral nutrition (TPN) are counted, starting on the day of enterostomy closure and ending on the day of full enteral nutrition. The parenteral nutrition is manufactured by the hospital pharmacy on a daily basis, while considering the
simultaneous enteral caloric intake.
5) Laboratory parameters indicating cholestasis (conjugated bilirubin, GGT, ALT, AST, hemoglobin) and sodium resorption (sodium in urine).
Time points for harvesting of blood samples during clinical routine blood withdrawal: Baseline at the time of randomization, then every 2 weeks until enterostomy takedown, at the 3-months follow up and in cases of pathologic clinical signs (jaundice, acholic stools).
6) Weight gain during the subsequent 5 days after reaching the primary endpoint.

7) Central venous line (CVL) duration (days) and number of CVL infections (definition of infection: Neo-Kiss Guidelines).

8) Length of hospital stay (days).

9) Estimated ratio of the diameter of the two bowel loops which are anastomosed.

10) Time to full oral volume intake (based on age-dependent daily fluid requirements), for at least 24h. The feeding advancement will be carried out according to the predefined nutritional protocol. *Full oral volume intake* is therefore defined as 150ml/kg/24h (premature infants) and 120ml/kg/24h (born mature as well as corrected mature infants) actual enteral volume intake.

11) Assessment of safety: Assessment of possible (serious) adverse events (AEs/SAEs) after randomization (e.g. death, sepsis, bowel perforation, stoma prolapse, abscess).

Study description

Background summary

Enterostomies in infants may be created for different reasons. During the presence of an enterostomy, the regular stool transfer is interrupted since the distal part of the bowel (the part following the enterostomy) does not participate in the processing of stool. Therefore, it does not contribute to the resorption of enteral nutrients. As a consequence, these infants need additional parenteral nutrition. Due to the negative side-effects of parenteral nutrition all patients should return to enteral nutrition as soon as possible. Consequently, many pediatric surgical centers worldwide routinely perform mucous fistula refeeding (MFR) into the former unused bowel after enterostomy creation because case reports and retrospective analyses show low complication rates and faster postoperative weight gain. Several providers, however, shy away from this approach because to date there is still no high-quality evidence for the benefit of this treatment.

Study objective

The aim of this study is to assess the effects of mucous fistula refeeding in a prospective randomized trial. We hypothesize that MFR between enterostomy creation and enterostomy closure reduces the time to full enteral feeds after enterostomy closure compared to standard care. Moreover, the side effects of parenteral nutrition may be reduced and the postoperative hospital care of infants undergoing ostomy closure shortened.

Study design

This is a randomized, multicenter (approx..=13), open-label, parallel group, controlled research study to demonstrate that mucous fistula refeeding between enterostomy creation and enterostomy closure reduces the time to full enteral feeds after enterostomy closure compared to standard of care.

Intervention

All patients will receive standard care with standardized enterostomy creation and closure and will be treated according to a standardized feeding protocol.

Experimental intervention:
Perioperative mucous fistula refeeding between enterostomy creation and enterostomy closure

Control intervention:
No perioperative mucous fistula refeeding between enterostomy creation and enterostomy closure

Follow-up per patient:
3 months and 6 months postoperatively, following enterostomy closure (12-month follow-up only applicable for patients that are recruited early enough to complete this follow-up within the 48 month of overall study duration). Duration of intervention per patient of the intervention group: minimum 21 days/3 weeks until patient*s weight >2000g (averaged 6 weeks between enterostomy creation and enterostomy closure).

Study burden and risks

In general, blood draws are safe from a medical point of view and no significant problems are expected. The blood is taken from the vein with a cannula. In principle, taking a blood sample is associated with only a very small risk. These include temporary pain, bleeding and bruising (bruising). In addition, there is a small risk of infection at the puncture site. In extremely rare cases, errors in pricking, nerve damage (also chronic), inflammation of the veins with the formation of blood clots (thrombosis), dizziness, anesthesia and/or fainting may occur.

To avoid additional traumatization, an attempt is made to carry out the planned examinations by means of the same blood samples during the course of the examination. Only in rare cases is an additional blood sample necessary.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

1. Only infants younger than 366 days of age with status post ileostomy or jejunostomy creation (double loop enterostomies and split enterostomies (with mucous fistula)) will be included in the study to create a homogenous cohort of patients with similar diseases (e.g. necrotizing enterocolitis [NEC], focal intestinal perforation [FIP]). Also, infants of this age group are unique in several respects such as the response to parenteral nutrition and its hepatic toxicity resulting into neonatal cholestasis. The ostomy localization is

restricted to the jejunum and ileum. Therefore, the cohort of
patients shows a similar bowel length for fluid-, vitamin- and electrolyte resorption.
2. All patients with meconium ileus are included into the study. If later (required) diagnostics verify cystic fibrosis, the diagnostics as well as the diagnosis need to be documented in the eCRF and in further analysis subgroups will be established.
3. Signed written informed consent obtained by parents/legal guardians and willingness
of parents/legal guardians to comply with treatment and follow-up procedures of their
child.

Exclusion criteria

1. The resection of the ileocecal valve is an exclusion criterion because of its association
with extensive bowel resection and therefore prolonged parenteral nutrition [10].
2. Colostomy.
3. Patients with small bowel atresia are excluded because of prenatally underdeveloped
bowel distal to the atresia.
4. Multiple ostomies (more than just an enterostomy and a mucous fistula).
5. Patients with chromosomal abnormalities (if known at the time of randomization) are
excluded because of potential malabsorption and malnutrition due to an underlying
syndrome.
6. Hirschsprung disease secondary exclusion.
7. Participation in another drug-intervention study.
8. Intestinal perforation due to congenital heart defects with impaired hemodynamics.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2023
Enrollment:	16
Type:	Anticipated

Ethics review

Approved WMO Date:	14-02-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-06-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-08-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NCT03469609
CCMO	NL80496.078.22