Continuous versus Intermittent Nutrition in Paediatric Intensive Care: proof-of-concept

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The aim of the Continuous versus Intermittent Nutrition in Pediatric Intensive Care randomized controlled trial (RCT) is to investigate a strategy of intermittent nutrition with a focus on an overnight feeding interruption period versus 24-hour…

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

Summary

ID

NL-OMON22860

Source
Nationaal Trial Register

Brief title
ContInNuPIC

Condition

- Fatal outcomes

Synonym
critical care

Health condition

All health conditions requiring admittance to the intensive care unit

Research involving
Human

Sponsors and support

Primary sponsor:	European Society for Clinical Nutrition and Metabolism
Secondary sponsors:	Sophia Research Foundation
Source(s) of monetary or material Support:	Nova Biomedical

Intervention

- Food (substances)

Explanation

Outcome measures

Primary outcome

The primary outcome of the proof-of-concept study will be the feasibility (ketogeneic response, nutritional intake, enteral tolerance) and safety (glycaemic control, gastro-intestinal complications) of a daily feeding and fasting cycle in critically ill children of different age-groups while providing equal amounts of daily nutrients as with standard continuous feeding.

Secondary outcome

Secondary parameters of the proof-of-concept study will be validating a fasting response in “Intermittent’ as compared to “Continuous” feeding by means of endocrine and metabolic (glycaemic control, ketone production, lactate, autophagy) measurements, and the evaluation of the circadian rhythm (cortisol/ACTH, sleep quality, chrono-pharmacokinetics and vital sign variability).

Study description

Background summary

Intermittent fasting is a time-restricted feeding strategy with proven health benefits, which is based on multiple metabolic and endocrine changes, in several patient populations and healthy participants. In the pediatric intensive care unit (PICU), artificial feeding is usually administered 24 hours a day, although solid evidence supporting this practice is lacking. This discards the potential benefits of fasting in this population. We hypothesize that intermittent nutrition with a focus on an overnight feeding interruption (intermittent fasting), as compared with 24-hour continuous nutrition, is a feasible and safe strategy, with potential benefits, for critically ill children.

Study objective

The aim of the Continuous versus Intermittent Nutrition in Pediatric Intensive Care randomized controlled trial (RCT) is to investigate a strategy of intermittent nutrition with a focus on an overnight feeding interruption period versus 24-hour nutrition during the first 14 days in the PICU.

Study design

The Continuous versus Intermittent Nutrition in Pediatric Intensive Care study is an investigator-initiated RCT in a tertiary referral PICU. Critically ill children (term newborn to 18 years), expected to stay in the PICU for ≥48 hours, and dependent on artificial nutrition, are eligible for inclusion. This study will randomize critically ill children (n=140) to a continuous versus

intermittent nutrition strategy. In both groups, similar daily caloric targets will be prescribed. In the continuous group (control), nutrition will be administered 24 hours a day, with a maximum interruption period of 2 hours. In the intermittent group (intervention), nutrition will be interrupted during an age-dependent overnight fasting period. The study intervention will last until admission day 14, initiation of oral intake, or discharge from the PICU, whichever comes first. The primary outcome is the difference in ketosis between the groups under the condition of noninferiority regarding caloric intake. Secondary outcomes are feeding intolerance; the proportion of severe and resistant hypoglycemic events and severe gastrointestinal complications; and additional observed effects on nutritional intake, circadian rhythm, and clinically relevant outcome measures of the intermittent feeding strategy compared with continuous nutrition.

Intervention

Intermittent feeding with an overnight fast

Contacts

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Eligibility criteria

Age
Newborns
Newborns
Babies and toddlers (28 days-23 months)
Babies and toddlers (28 days-23 months)
Children (2-11 years)
Children (2-11 years)
Adolescents (12-15 years)
Adolescents (12-15 years)
Adolescents (16-17 years)
Adolescents (16-17 years)

Inclusion criteria

Critically ill children (term newborn – 18 yrs), with expected stay >2 days, and dependent of artificial nutrition in PICU within 2 days.

Exclusion criteria

- Possibility to “oral” feeds, - “Do not resuscitate” code at the time of PICU admission, - Expected death within 24 hours, - Re-admission to the PICU after previous randomization to the ContInNuPIC trial, - Transfer from another ICU after a stay of more than three days, - Ketoacidotic/ hyperosmolar coma on admission, - Metabolic diseases requiring specific diet or with a contraindication to (intermittent) feeding, - Premature newborns (<37 weeks gestational age), - Short bowel syndrome or other conditions which required home-PN.

Study design

Design

Study phase:	N/A
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-05-2020
Enrollment:	140
Type:	Actual

IPD sharing statement

Plan to share IPD: No

Plan description
N/A

Ethics review

Approved WMO

Date:	11-02-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

ID: 48138
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL7877
CCMO	NL70184.000.19
OMON	NL-OMON48138

Study results

Results posted: 17-07-2023

Actual enrolment: 140

Summary results

Between May 19, 2020, and July 13, 2022, 140 critically ill children, median (first quartile; third quartile) age 0.3 (0.1; 2.7) years, were randomised to intermittent (n=67) or continuous feeding (n=73). In the intermittent feeding group, BHB levels were significantly higher (median 0.4 (0.2; 1.0) vs. 0.3 (0.1; 0.7) mmol/L, p<0.001). The ratio of total caloric intake in the intermittent feeding group to the intake in the continuous feeding group was not consistently significantly more than 0.67, thus not proving non-inferiority. No severe, resistant hypoglycaemic events, nor severe gastrointestinal complications related to the intervention occurred, and feeding intolerance did not occur more often in the intermittent than in the continuous feeding group.

Baseline characteristics

Median (first quartile (Q1); third quartile (Q3)) age was 0.4 years (0.1; 3.1 years) vs. 0.3 years (0.1; 2.3 years), and median Paediatric Index of Mortality 3 (PIM3)(28) score -3.4 (-4.5; -2.5) vs. -3.9 (-4.5; -2.5) in the intermittent vs. the continuous

Participant flow

Between May 19, 2020, and July 13, 2022, 140 critically ill children were included in the study; 67 were randomised to the intermittent and 73 to the continuous feeding group.

Adverse events

Serious adverse events (SAEs) included the caecum perforation mentioned above (intermittent feeding group), a rupture of the vena jugularis during an attempt for extracorporeal membrane oxygenation (intermittent feeding group), one event of severe bradyca

Outcome measures

"In the intermittent feeding group, BHB levels were significantly higher than in the continuous feeding group (median (Q1; Q3) 0.4 (0.2; 1.0) vs 0.3 (0.1; 0.7) mmol/L, p<0.001). Regarding nutritional intake, the lower limit of the 90% CI of the ratio of