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

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Ethical review	Not approved
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON48138

Source
ToetsingOnline

Brief title
ContInNuPIC: Proof-of-concept

Condition

- Other condition
- Food intolerance syndromes

Synonym
Critically ill children

Health condition

Algemene kritieke zieke populatie. Groot scala aan aandoeningen en ziektebeelden mogelijk

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Sophia Stichting voor Wetenschappelijk Onderzoek;European Society of Parenteral and Enteral Nutrition research grant

Intervention

Keyword: Critical illness, Enteral Nutrition, Paediatrics, Parenteral Nutrition

Outcome measures

Primary outcome

The primary outcome of the proof-of-concept study will be the feasibility (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 (IGF-I, T3/rT3) and metabolic (glycaemic control, ketone production, lactate, bilirubin, urea, autophagy) measurements, and the evaluation of the circadian rhythm (cortisol/ACTH, sleep quality, chrono-pharmacokinetics and vital sign variability).

Study description

Background summary

We have recently shown in a large randomised study in paediatric ICU patients that withholding Parenteral Nutrition during the first week of critical

illness, as compared with an early start (<48 hours), reduced length of intensive care dependency and the number of nosocomial infections. The benefit of this counterintuitive nutritional strategy, through which low macronutrient intakes were accepted, is presumed to be caused by activation of autophagy due to a fasting response. Autophagy is an intracellular recycling process crucial for maintaining cellular integrity and function. Its protective role against various forms of critical illness induced organ failure, including ICU acquired muscle weakness, is strongly activated during periods of fasting. Currently, artificial feeding is usually administered through continuous infusion, although solid evidence supporting this practise is lacking. Intermittent, as compared with continuous, (par)enteral nutrition may provide a more physiological feeding/fasting pattern which activates autophagy, while providing sufficient nutrition during critical illness. A physiological feeding/fasting pattern could also sustain circadian rhythm. Thus, such strategy could impact essential mechanisms such as immunology, metabolism, neuropsychology, and pharmacodynamics, to improve recovery from critical illness.

Study objective

The main research objectives for the proof-of-concept study are to show the feasibility and safety of a daily cycle of feeding and fasting in critically ill children of different age-groups, that will trigger an adequate fasting response while providing equal amounts of daily nutrients as with standard continuous feeding. We hypothesise that in critically ill children intermittent versus continuous feeding is feasible and safe, and will lead to a fasting response, which could potentially activate autophagy while providing sufficient nutrition. Ultimately we hypothesize that such strategy will lead to accelerated recovery and reduced ICU dependency, which is to be tested in a large multicentre RCT with clinically relevant outcome parameters in a multicentre setting within the Rotterdam-Leuven consortium.

Study design

A randomized non-blinded proof-of-concept study will be performed to explore the feasibility and safety of intermittent feeding in critically ill neonates (<28d, n=30), infants (<1yr, n=30) and children (*1yr, n=30) while overall providing equal amounts of daily nutrients as with standard continuous feeding. Based upon adult pilot data (unpublished data) and glycaemic control data from the PEPaNIC RCT (n=1440, CCMO projectnr: NL38772.000.12 / MEC-2012-412 / EudraCT 2012-000811-10 / S54127 / NCT01536275), a 12hrs fasting period is expected to be optimal. The study intervention will last a maximum of 14 days or until PICU discharge, or the ability for *oral nutrition*, whichever comes first. Methods for evaluating the fasting response, autophagy and the circadian rhythm in the planned subsequent RCT will be tested during the proof-of-concept study.

Intervention

The *Continuous Nutrition* strategy will be the nutritional management currently recommended and acting as *control*. Both enteral nutrition (EN) and (after day 7) parenteral nutrition (PN) will be provided continuously 24 hrs/day. The *Intermittent Nutrition* strategy, acting as the *intervention*, comprises a physiological *overnight fast during which no artificial nutrition (EN and/or PN) will be provided for a duration of 12 hours.
For both study arms, daily caloric targets are similar in both randomization groups and increase during the first week in the PICU. Isocaloric nutrition between study arms will be achieved with higher intakes during the day and/or with energy-dense formulas in the intermittent group. Enteral and/or parenteral nutrition (timing and requirements) will be initiated and administered according to the most recent nutritional guidelines for all patients; EN will be started as early as possible (< 24 hrs) unless strictly contraindicated, and increased in a step-wise manner. PN (glucose/amino acids/lipids) will be started after day 7 if EN is still insufficient (<80% target intake). To prevent hypoglycaemia during the overnight fasting period, 1) insulin (if administered) will be stopped one hour prior the fasting interval and 2) neonates (±1 mg/kg/min glucose) and infants (±0.5 mg/kg/min glucose) will be provided with a guaranteed glucose intake, unless they develop hyperglycaemia with such regimen (at what time the glucose intake will be tapered down and eventually stopped).

Study burden and risks

The burden is expected to be minimal. Based on studies in the literature, there is equipoise over the feeding patterns. The risk in participating to the study and being randomised to one of the nutritional strategies are minimal (based on PEPaNIC data), and specifically compass an increased risk of developing hypoglycaemia in the fasting periods of the *Intermittent* nutrition. Another potential burden or risk in the intervention group (*Intermittent*) might be gastrointestinal intolerance to the administration of more nutritional intake in a shorter time frame. However, safety measures (standardized and regular checks; hypoglycaemia / lactate / gastro-intestinal tolerance) will be taken to further decrease these risks. Further risks are negligible, and will only entail 1) additional blood draws, which will be taken from clinical lines or in addition to pricks for clinical purpose and 2) neuro-monitoring / sleep measurements, which will be performed non-invasively.
Clinical equipoise between Continuous and Intermittent nutrition is a specific problem for critically ill patients in an ICU environment. A similar study has also been performed in adult ICU patients in Leuven (unpublished data). However, although the results of this study have provided essential information for the design of our study, this pilot study can NOT be translated one-on-one to the paediatric patient, as critically ill children of different age groups have different metabolic and nutritional issues. The patient group of

critically ill children (0 * 18 yrs), represents a significant proportion of the worldwide ICU population. Therefore, the feasibility and safety needs to be determined in our population of critically ill children.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

All critically ill children admitted to the PICU are evaluated for nutritional risk and eligibility for inclusion in this study. All critically ill children, (term born * 18 yrs), with expected stay at least two days, and dependent of artificial nutrition in PICU within 2 days are eligible for inclusion.

Exclusion criteria

Exclusion criteria are possibility to *oral* feeds, a *do not resuscitate* code and/or expected death within 24 hours at the time of PICU admission, re-admission to the PICU after previous randomization to the ContInNuPIC trial, transfer from another ICU after a stay of more than three days, ketoacidosis or hyperosmolar coma on admission or inborn metabolic diseases requiring specific diet, premature new-borns (<37 weeks gestational age), short bowel syndrome or other conditions which required home-PN.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	90
Type:	Anticipated

Ethics review

Not approved

Date:	26-08-2019
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 22860
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL70184.000.19
OMON	NL-OMON22860