Systemic bioavailability of enteral protein-bound versus free amino acid nutrition during intestinal protein malabsorption in critical illness

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To quantitate the difference in digestion and absorption kinetics of dietary whole protein versus free amino acids in vivo in patients admitted to the ICU suffering from malabsorption.

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

Summary

ID

NL-OMON47682

Source
ToetsingOnline

Brief title
PANINI-trial

Condition

- Other condition
- Malabsorption conditions

Synonym
Protein malabsorption, Protein uptake

Health condition

critical illness (aandoening die IC opname nodig maakt)

Research involving

Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Prijs/beurs van de European Society of Intensive Care Medicine (ESICM/NESTLÉ Award for practice improvement in ICU Nutrition)

Intervention

Keyword: Amino Acid, Malabsorption, Nutrition, Protein

Outcome measures

Primary outcome

Main study endpoint will be the splanchnic extraction of phenylalanine,

calculated from systemic [1-13C]- and L-[ring2H5]-phenylalanine enrichment.

Secondary outcome

Secondary endpoints include the impact of enteral nutrition on whole body

protein balance, glucose and insulin concentrations and faecal energy and

protein loss as a measure of malabsorption.

Study description

Background summary

The importance of the provision of sufficient protein in critical illness is increasingly recognized. Protein malabsorption seems to be an underestimated but substantial problem in critically ill patients, limiting the amount of this important nutrient that actually becomes available within the systemic circulation. Among several contributors to malabsorption in critical illness, exocrine pancreatic insufficiency has recently emerged as a regularly occurring phenomenon during critical illness. Pancreatic insufficiency could lead to reduced digestion and subsequent uptake of enteral provided proteins. A proposed solution to this problem could be the use of elementary feeds containing free amino acids instead of whole protein. Due to the lack of easy applicable and reproducible tests for protein malabsorption the true efficacy of these feeds is still unknown. We hypothesize that enteral nutrition

containing free amino acids leads to higher systemic levels of amino acids and will therefore increase the amount of dietary amino acids available for protein synthesis.

Study objective

To quantitate the difference in digestion and absorption kinetics of dietary whole protein versus free amino acids in vivo in patients admitted to the ICU suffering from malabsorption.

Study design

Randomized, single-blind controlled, single-centre, intervention study.

Intervention

Normal enteral nutrition will be ceased 8 hours before the start of study participation. All patients will receive a primed continuous intravenous infusion of L-[ring2H5]-phenylalanine and L-[3,5-2H2]-Tyrosine for the duration of the study period. After reaching an isotopic steady state (1.5 hours), patients will receive either [1-13C]- phenylalanine labelled milk protein or free amino acids with an identical constitution and [1-13C]-phenylalanine.

Study burden and risks

Total study participation will take 16 hours, including 8 hours of fasting. Arterial blood samples will be collected regularly, with 50 ml of blood being sampled in total, amounting to a maximum of 1.0% of total circulating volume. All infusions, as well as blood sample collection, will be performed through indwelling catheters necessary for normal ICU treatment, meaning no lines or nasogastric tubes will have to be placed for the purposes of the study. Both isotopically labelled protein and free amino acids have been proven safe for use in humans and carry no harmful risks for the study participant. Changes in protein digestion, absorption and metabolism are specific to critical illness and their impact on the clinical condition and recovery of patients is severe. Investigating new strategies to modulate these effects are therefore essential, but require experimental studies in a vulnerable population. The risks in the present study are minimal whereas the results could help improve nutritional management in the intensive care.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1) Age > 18 and < 75 years
2) Faecal weight > 350g/day
3) Critical illness of any origin (e.g. medical, surgical, trauma) requiring admittance on ICU ward.
4) Expected ICU stay for the duration of the study protocol
5) Mechanically ventilated (PaO2/FiO2 ratio of >100 and <300)
6) Nasogastric tube in situ
7) Receiving full enteral nutrition without gastric residual volumes
8) Arterial (any location) line in situ
9) Flexi-seal system in situ

Exclusion criteria

1) Proven (pre-existing) intestinal disease that potentially limits normal gut function and absorption of nutrients (e.g. IBD, short-bowel, entero-cutaneous fistulas including a surgical enterostomy)
2) Proven (pre-existing) primary pancreatic disease or obstruction of the pancreatic duct of

any origin (e.g. pancreatitis, carcinoma).
3) Patients who are moribund (not expected to be in ICU for more than 48 hours due to imminent death)
4) A lack of commitment to full aggressive care during the first week due to severity of illness, comorbidities and potential harm from maximal treatment (anticipated withholding or withdrawing treatments)
5) Absolute contraindication to enteral nutrients (e.g., gastrointestinal [GI] perforation, obstruction or no GI tract access for any reason)
6) Receiving parenteral nutrition.
7) Nasoduodenal or nasojejunal feeding tube
8) Renal dysfunction defined as a serum creatinine >171 *mol/L or a urine output of less than 500 ml/last 24 hours
9) Patients requiring chronic veno-venous hemofiltration
10) Patients on ECMO/ELS
11) Cirrhosis * Child Pugh class C/D liver disease
12) Patients with primary admission diagnosis of burns (>30% body surface area)
13) Weight less than 50 kg or greater than 100 kg
14) Pregnant patients or lactating with the intent to breastfeed
15) Previous randomization in this study
16) Enrolment in any other interventional study
17) Milk/lactose allergy
18) Previous participation in a 13C amino acid tracer study within the last year

Study design

Design

Study type: Interventional

Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-03-2018
Enrollment:	16
Type:	Actual

Ethics review

Approved WMO Date:	21-06-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
CCMO	NL60452.068.17