Long-term muscle protein synthesis in ICU patients

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON24760

Source
Nationaal Trial Register

Brief title
D2O-ICU

Health condition

Sepsis, ICU-acquired weakness, muscle wasting,

Sponsors and support

Primary sponsor: Maastricht UMC+ (azM)
Source(s) of monetary or material Support: Deptartments of Intensive Care Medicine, Surgery and Human Biology

Intervention

Outcome measures

Primary outcome

Fractional synthesis rates (FSR) of muscle protein using muscle protein-bound and plasma 2H-alanine enrichments

Secondary outcome

- changes in leg skeletal muscle mass (ultrasound of rectus femoris CSA)

- urinary 3-methylhistidine concentrations

- transcriptional changes of genes involved in muscle protein synthesis and breakdown

Study description

Background summary

Rationale: Muscle wasting occurs rapidly in septic patients and impacts both short and long term outcomes. Altered protein metabolism drives muscle loss in ICU patients, with muscle protein breakdown exceeding muscle protein synthesis (MPS). Interventions aimed at attenuating muscle loss by stimulating MPS rates are hampered by a lack of knowledge on altered muscle protein turnover rates during critical illness. Only a few studies have specifically assessed muscle protein synthesis by using contemporary intravenous stable isotope infusions, which allows the assessment of MPS over a short (<9 hours) period of time. Results from such acute studies can be difficult to extend or translate into long-term clinical practice and outcomes. Oral deuterated water (2H2O) dosing provides an alternative method that can be utilized to extend the measurement of muscle protein synthesis over a period of several days or weeks. It could therefore provide a valuable tool to study muscle protein synthesis during ICU admission and the impact of different anabolic interventions. Although multiple studies using the deuterated water methodology have been performed in both healthy volunteers and patients, it has not yet been performed in critically ill patients.

Objective: The present study aims to assess the feasibility of deuterated water dosing in critically ill patients to assess long-term in vivo skeletal muscle protein synthesis rates.

Study design: The study design consists of an observational study with (invasive) measurements to determine changes in muscle protein synthesis in critically ill patients during 3 consecutive days of ICU admission.
Study population: The study population will consist of 12 adult critically ill patients (18 – 75 years) with sepsis admitted to the intensive care unit of the Maastricht University Medical Centre. After inclusion of 4 patients, an interim analysis will be done to ensure feasibility of the current dosing protocol to reach sufficient body water and plasma alanine labelling before further continuation of the study.

Methodology: A 5 day deuterated water dosing protocol will be conducted during ICU

admission to measure diurnal rates of muscle protein synthesis. Patients will receive 400ml of 70 mol% enriched deuterated water on day 1, followed by a daily maintenance dose of 50 ml for four consecutive days. Blood samples (60 ml total) will be collected during the study to measure plasma free 2H-alanine enrichments. On day 2 and 5, a skeletal muscle biopsy will be taken from the m. vastus lateralis to measure muscle protein-bound 2H-alanine enrichment levels.
Main study parameters/endpoints: Primary study parameters are the fractional rates of muscle protein synthesis (%/day) using muscle protein-bound 2H-alanine enrichments, plasma 2H-alanine enrichments and intramuscular free 2H-alanine enrichment. Secondary study parameters include: body water 2H2O enrichment, plasma muscle-specific protein synthesis rates (virtual biopsy), changes in leg skeletal muscle mass, urinary 3-methylhistidine concentrations, transcriptional changes in genes involved in muscle protein synthesis and breakdown and plasma amino acid concentrations.

Study objective

Oral deuterated water dosing can be used in septic ICU patients to study long-term diurnal muscle protein synthesis rates

Study design

Primary endpoint (FSR) based on biopsies on day 2 and 5
Muscle ultrasound on day 1, 5, 7 and 12

Intervention

A 5 day enteral deuterated water dosing protocol will be conducted during ICU admission to measure diurnal rates of muscle protein synthesis. Patients will receive 400ml of 70 mol% enriched deuterated water on day 1, followed by a daily maintenance dose of 50 ml for four consecutive days. Blood samples (60 ml total) will be collected during the study to measure plasma free 2H-alanine enrichments. On day 2 and 5, a skeletal muscle biopsy will be taken from the m. vastus lateralis to measure muscle protein-bound 2H-alanine enrichment levels.

Contacts

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Eligibility criteria

Inclusion criteria

1) Age >18 <75 years

2) Sepsis on admission (as defined by the Sepsis-3 criteria*)

3) Arterial line (any location) in situ

4) Nasogastric feeding tube in situ

5) Urinary catheter in situ

6) Expected ICU stay >5 days

Exclusion criteria

1) Coagulation disturbances (not including use of anti-coagulants in prophylactic dosages)

2) Contraindication to enteral infusion (e.g. due to GI-tract perforation)

3) Any trauma resulting in severe injury or fracture of any extremity.

4) Rhabdomyolysis

5) Proven (pre-existing) skeletal muscle weakness (e.g. due to neuromuscular disorders or immobility)

6) Renal dysfunction defined as a serum creatinine >171 □mol/L or a urine output of less than

500 ml/last 24 hours

7) Patients requiring chronic veno-venous hemofiltration

8) Patients on any form of extracorporeal life support (ECMO/ELS)

9) Weight less than 50 kg or greater than 100 kg

10) Pregnant patients or lactating with the intent to breastfeed

11) Previous enrollment in this study

12) Previous participation in a 2H amino acid tracer study within the last year

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2018
Enrollment:	12
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL7168
NTR-old	NTR7391
Other	METC / ABR : METC182010 / NL65590.068.18

Study results