The assessment of long-term in vivo muscle protein synthesis rates in ICU patients using deuterated water methodology

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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.

Ethical review	Approved WMO
Status	Completed
Health condition type	Bacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON55410

Source
ToetsingOnline

Brief title
Long-term muscle protein synthesis in ICU patients

Condition

- Bacterial infectious disorders
- Protein and amino acid metabolism disorders NEC
- Musculoskeletal and connective tissue disorders NEC

Synonym
Muscle wasting, Protein synthesis

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Critical illness, Deuterated water, Muscle, Protein synthesis

Outcome measures

Primary outcome

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 outcome

Secondary study parameters include: body water 2H2O enrichment, plasma muscle-specific protein synthesis rates (virtual biopsy), transcriptional changes in genes involved in muscle protein synthesis and breakdown and plasma amino acid concentrations.

Study description

Background summary

Muscle wasting occurs rapidly in critically ill 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. Interventions aimed at attenuating muscle loss by stimulating muscle protein synthesis 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 muscle protein synthesis 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.

Study 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 5 consecutive days of ICU admission.

Intervention

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. This protocol has been previously approved in young and older volunteers in MEC 15-3-008, 15-3-003, 15-3-035, 15-30-55, and 15-30-38.

Study burden and risks

The burden and risks associated with participation are minimal. Blood sampling is minimal (60 ml divided over 5 days) and will be conducted through indwelling arterial catheters already in place for routine clinical care, thus avoiding the need for puncture and associated hematoma risks. Muscle biopsies will be taken under local anaesthesia by an experienced physician, but carries a small risk of a small local hematoma and may cause some minor discomfort up to 24 h after completion. The discomfort is comparable to muscle soreness or the pain one has after bumping into a table. The majority of subjects are expected to be sedated during muscle biopsy, further limiting any discomfort experienced. Repeated leg ultrasounds will be performed (4 times), which do not pose any harm to the individual subjects. For the duration of the study protocol, 50 ml of 70% deuterated water will be administered daily via a nasogastric feeding tube placed for routine care to enrich the body water pool to approximately

~0.7 APE (Atom Percent Excess). Deuterated water dosing to achieve a body water enrichment of ~0.7 APE is completely safe as it is far below the threshold for biological toxicity in humans (approximately 20 APE) and will be returned to baseline enrichments within 30 days. There is no direct benefit for the participants except for their contribution to the scientific knowledge of skeletal muscle wasting, in particular muscle protein synthesis rates during critical illness, which will be obtained from this study and used in the future.

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 <90 years
2) Arterial line (any location) in situ

3) Enteral feeding tube in situ
4) 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) Rhabdomyolysis
4) Renal dysfunction defined as a serum creatinine >171 *mol/L or a urine output of less than 500 ml/last 24 hours
5) Patients requiring chronic veno-venous hemofiltration
6) Patients on any form of extracorporeal life support (ECMO/ELS)
7) Pregnant patients or lactating with the intent to breastfeed
8) Previous participation in a 2H amino acid tracer study within the last year

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	28-03-2019
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO

Date:	08-08-2018
Application type:	First submission

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-02-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-12-2021
Application type:	Amendment
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	NL65590.068.18

Study results

Date completed: 01-07-2024

Summary results
Trial ended prematurely