Long-term muscle protein synthesis in ICU patients

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

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON24760

Bron
Nationaal Trial Register

Verkorte titel
D2O-ICU

Aandoening

Sepsis, ICU-acquired weakness, muscle wasting,

Ondersteuning

Primaire sponsor: Maastricht UMC+ (azM)
Overige ondersteuning: Deptartments of Intensive Care Medicine, Surgery and Human Biology

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

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.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-09-2018
Aantal proefpersonen:	12
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7168
NTR-old	NTR7391
Ander register	METC / ABR : METC182010 / NL65590.068.18

Resultaten