ProMICstudy

Gepubliceerd: 30-06-2021 Laatst bijgewerkt: 18-08-2022

Analyses of the in vitro regulation of the intramuscular autophagy flux with plasma from patients with regular and high enteral protein feeding might elucidate the possible role of this hypothesis. This study aims to assess the effect of high vs...

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON28381

Bron
NTR

Verkorte titel
TBA

Aandoening

Conditions required ventilator support in the Intensive Care Unit

Ondersteuning

Primaire sponsor: Ziekenhuis Gelderse Vallei, Wageningen University, Karolinska Institute
Overige ondersteuning: Hospital Gelderse Vallei, Ede

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

• To investigate the effect of high vs standard enteral protein provision on the regulation of intramuscular autophagy flux in ICU patients

• To investigate the effect of high vs standard enteral protein provision on the evolution of

mitochondrial dysfunction and hypermetabolic inflammatory status in ICU patients

• To uncover a possible association between PGE2, protein intake and the course of disease in ICU patients

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: The close connections of the Gelderse Vallei hospital to Wageningen University and the Karolinska Institute provides the opportunity to investigate the proposed association between protein provision and functional disease outcome at a basal level by measuring autophagy flux, mitochondrial function and prostaglandin levels. This sub-study will explore explanations behind the associations.

Objective: To investigate the effect of increased protein provision (compared to standard protein provision) during intensive care unit (ICU) admission on ex vivo muscular cell autophagy flux, leucocyte mitochondrial function and oxylipins, specifically prostaglandin E2 (PGE2) in critically ill patients.

Study design: This study consists of a combination of 3 single-centre prospective cohort sub-studies within the PRECISe-trial.
Study population: ICU patients who consented to the PRECISe-trial who meet the additional in- and exclusion criteria for this set of combined sub-studies will be included. A maximum of 60 patients will be included in consecutive order.

Methodology: Within 48 hours after ICU admission, first blood collection will take place. After that, blood will be collected on day 3 and day 6. During each blood collection, a maximum of 75 mL of blood will be obtained.
Primary study parameters/endpoints: Autophagy flux measured in primary human myotubes incubated for 24h with serum from ICU patients, mitochondrial function in peripheral blood mononuclear cells (PBMCs) measured via functional respirometry (oroboros) and prostaglandin E2 (PGE2) levels as measured by LCMSMS.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Included patients will usually already have an arterial catheter in situ; therefore, blood sampling, in this case, contains minimal risk and is entirely painless. No direct benefits are present for the included patients. However, with this study, important information can be obtained, which will be of added value to the results of the PRECISe-trial. In this way, mechanisms that have not been studied before in such a randomized controlled trial (RCT) can be revealed and may contribute to a better understanding of the PRECISe-trial results.

Doel van het onderzoek

Analyses of the in vitro regulation of the intramuscular autophagy flux with plasma from

patients with regular and high enteral protein feeding might elucidate the possible role of this hypothesis.

This study aims to assess the effect of high vs standard protein provision on peripheral blood mononuclear cell (PBMC) mitochondrial function of ICU patients because of these controversies.

Protein plays a vital role in gut-integrity, and therefore, in this clinical observational study, patients' oxylipin profiles and the gut permeability marker lipopolysaccharide (LPS) will be measured and related to clinical outcome measures by principal component analysis.

Onderzoeksopzet

Within 24 hours after inclusion (which is within 48 hours after ICU admission) first blood collection will take place. Thereafter, blood will be collected on day 3 and day 6. During each blood collection, a maximum of 62 mL blood will be obtained.

Immediately after blood sampling, PBMCs will be isolated. Mitochondrial function will be analysed in PBMCs by means of a validated functional profiling test (Oroboros; Human and Animal physiology, WUR, Wageningen). Moreover, validated genomic and proteomic analysis of factors involved in mitochondrial dynamics and autophagy will be performed (e.g.Western blot & quantitative polymerase chain reaction).

Metabolic and inflammatory factors, such as cytokines (e.g., TNF), hormones (e.g. cortisol), proteins associated with catabolism (e.g. uric acid), nutrients and cytokines (e.g. TNF) will be analysed by means of validated blood analysis (e.g. Bio-Plex® Multiplex Immunoassays).

For Oxylipin measurements 8ml EDTA-containing tubes will be put on ice until centrifugation (10′, 10,000 rpm at 4 °C). After centrifugation, plasma will be aliquoted. For analysis, 200 µL plasma will be stored in 1 mL methanol containing paraoxon, BHT, AUDA, indomethacin, and PMSF to prevent oxidation and breakdown.

Onderzoeksproduct en/of interventie

Blood sampling

Contactpersonen

Publiek

Ziekenhuis Gelderse Vallei
Jonathan Huising

0318434343

Wetenschappelijk

Ziekenhuis Gelderse Vallei
Jonathan Huising

0318434343

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

In order to be eligible to participate in the PRECISe study, a potential subject must meet all of the following criteria:

1. Adult ≥ 18 years-old admitted to the ICU
2. Unplanned ICU admission
3. Invasive mechanical ventilation initiated <24 hours of ICU admission
4. Expected ICU stay on ventilator support of ≥ 3 days

There are no additional inclusion criteria for this substudy.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

A potential subject who meets any of the following criteria will be excluded from participation in the PRECISe study:

1. Contraindication for enteral nutrition
2. Moribund or expected withholding of treatment
3. Kidney failure with “no dialysis”-code on admission
4. Hepatic encephalopathy
5. Body-mass index <18 kg/m^2

Additional exclusion criteria for this set of sub-studies:

1. Current NSAID use
2. Use of chronic corticosteroid or other immunosuppressive medication prior to current hospital admission.
3. Current use of fish oil supplements
4. Haemoglobin level lower than 5,5 mmol/lL
5. Patients referred from another ICU
6. Active autoimmune disease involving the lung, heart, liver, small or large intestine, or

neuromuscular system (e.g., myasthenia gravis, multiple sclerosis) AND currently requiring systemic immunosuppressive therapy
7. Patients who experienced a significant medical or surgical event prior to current hospital admission leading to hospitalization within the previous 6 months
8. A disease process (e.g., end-stage cancer) with a projected survival of less than 6 months (pre-ICU admission)
9. Received treatment with chemotherapy, immunotherapy or radiotherapy within the past 12 months
10. Family history of mitochondrial disease(s) or genetic autophagy diseases.
11. COPD Gold-Stadium III or IV or other severe respiratory disorders (FEV1 <30% and FEV1/FVC < 0.7) (pre-ICU admission) (15)
12. Any stage of chronic or acute renal failure (pre-ICU admission, pre-existent SOFA 0 for this SOFA element)
13. Any stage of chronic or acute liver failure (pre-ICU admission, pre-existent SOFA 0 for this SOFA element)
14. Patients supported with haemodialysis or continuous hemofiltration
15. Diabetes Mellitus type I and II (pre ICU-admission)
16. Patients not able to understand the Dutch language
17. Treated with any investigational agent within 12 months prior to study treatment administration.
18. Patients who are ≤ 6 months postpartum pregnancy testing to the discretion of the attending physician
19. (History of) drug abuse

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-08-2021
Aantal proefpersonen:	60
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

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	NL9576
Ander register	METC azM/UM : To be issued

Resultaten