Evolution of mitochondrial dysfunction and hypermetabolic inflammatory status in septic Intensive Care Unit patients

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Ethical review	Approved WMO
Status	Completed
Health condition type	Infections - pathogen unspecified
Study type	Observational invasive

Summary

ID

NL-OMON48792

Source
ToetsingOnline

Brief title
Mitochondria Intensive Care (MIC)

Condition

- Infections - pathogen unspecified

Synonym
blood poisoning, Sepsis

Research involving
Human

Sponsors and support

Primary sponsor: Wageningen Universiteit
Source(s) of monetary or material Support: Ministerie van OC&W,Ziekenhuisvoorzieningen Gelderse Vallei

Intervention

Keyword: hypermetabole inflammatoire status, Mitochondrial dynamics, Mitochondrial dysfunction, Sepsis

Outcome measures

Primary outcome

The main study parameter is mitochondrial function in PBMCs.

Secondary outcome

The secondary study parameters are (a) parameters of hypermetabolic

inflammatory status (concentrations of catabolic hormones, nutrients in

serum/plasma, catabolic/pro-inflammatory cytokines and anabolic hormones), (b)

mitochondrial dynamics and autophagy and (c) data from medical records.

Study description

Background summary

Sepsis is a major cause of admission to the intensive care unit (ICU) and may result in hospital death rates up to 40-60% of septic shock cases. Mitochondrial dysfunction has been demonstrated in a variety of cells in septic ICU patients, including peripheral blood mononuclear cells (PBMCs). To avoid more invasive sample methods we selected the PBMCs to be used in our present research project. Multiple studies have found a relation between the amount of nutrients (e.g. glucose) in the blood and severity of mitochondrial dysfunction in PBMCs and clinical outcomes. Based on these findings, in sepsis there seems to be interplay between the hypermetabolic inflammatory state (e.g. hyperglycaemia), mitochondrial function/dynamics and clinical outcome. However, this interplay remains vague due to lack of research which includes all of these factors simultaneously. More knowledge on this interplay will undisputedly contribute to better treatment strategies, which is to some extent still subject of controversy, such as insulin therapy or the timing of parenteral nutrition. With respect to the latter, the observed negative effects of early versus late parenteral nutrition on clinical outcome suggest a time-dependent progression of the processes involved in the pathogenesis of sepsis. However, the course of the above mentioned factors over time has never been measured. Mapping the progression of the hypermetabolic inflammatory

state, mitochondrial function/dynamics and clinical outcome in septic ICU patients would create a better understanding on how mitochondrial dysfunction emerges, and how this is related to the hypermetabolic inflammatory state and clinical outcome. Creating more knowledge on the this interplay is a promising way to establish better (nutritional) therapy in septic ICU patients.

Study objective

The main objective is to investigate how mitochondrial function progresses over time in septic ICU patients. The secondary objective of the study is (a) to investigate how mitochondrial dynamics progress over time and how this is associated with mitochondrial function in septic ICU patients, (b) to investigate if and how parameters of the hypermetabolic inflammatory state are related to the progression of mitochondrial function in septic ICU patients and (c) to investigate if and how the progression of mitochondrial function is related to physical performance and clinical outcomes in septic ICU patients.

Study design

Prospective cohort study with matched controls.

Study burden and risks

Among the septic ICU patients three blood samples will be drawn and physical tests will be performed. As the septic ICU patients have vascular access, no extra punctures are necessary. The donation of blood samples can lead to a decrease in hemoglobin concentration in the blood, a decreased circulating volume or a decreased fluid level. These risks are closely monitored within the ICU. If any disturbance is measured, this will be restored by means of administration of physiological saline fluid or a blood transfusion. The control patients will give one blood sample, which has a small risk of complications (such as bruising), and will preferably be combined with blood sampling of other clinical reasons.

Moreover, two physical tests will be performed: The MRC sum score and the Chelsea Critical Care Physical Assessment Tool. The septic ICU patients will perform these tests twice, namely at discharge from the ICU and at discharge from the hospital.

Mitochondrial dysfunction in PBMCs of septic ICU patients has been linked to severity of sepsis and clinical outcomes. New knowledge on mitochondrial dysfunction may contribute to a better understanding of the pathophysiology of this important biological process among septic ICU patients and may potentially lead to information to prevent mitochondrial dysfunction with specific nutrients or medications.

Contacts

Public
Wageningen Universiteit

De Elst 1
Wageningen 6708WD
NL
Scientific
Wageningen Universiteit

De Elst 1
Wageningen 6708WD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Septic ICU patients:
- 18+ years of age
- Diagnosed with sepsis, not origniated from the urinary system

Control patients:
- Short-stay hospitalised patients (e.g. admission for one day), or patients admitted to the outpatient clinic of Gelderse Vallei Hospital
- Free of sepsis
- Metabolically healthy
- Age (+/- 2 years) and gender-matched

Exclusion criteria

*Only applicable for septic ICU patients
**Comprehensively described in appendix of the protocol
(All pre-ICU admission notes are not applicable to control patients), •
Patients referred from another ICU
• Patients with a haemoglobin level lower than 5,5 mmol/lL*
• Patients with a history of solid organ or bone marrow transplant
• Patients with 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
• Patients whom experienced a significant medical or surgical event leading to hospitalization within the previous 6 months
• Patients with a disease process (e.g., end-stage cancer) with a projected survival of less than 6 months (pre-ICU admission)
• Patients whom received treatment with chemotherapy, immunotherapy or radiotherapy within the past 12 months
• Patients with a family history of mitochondrial disease(s) **
• Patients with COPD Gold-Stadium III or IV or other severe respiratory disorders (FEV1 <30% and FEV1/FVC < 0.7)
• Patients with any stage of chronic or acute renal failure (pre-ICU admission, pre-existent SOFA 0 for this SOFA element)
• Patients with any stage of chronic or acute liver failure (pre-ICU admission, pre-existent SOFA 0 for this SOFA element)
• Patients supported with hemodialysis or continuous hemofiltration
• Patients diagnosed with diabetes Mellitus type I and II (pre ICU-admission)
• Patients not able to understand the Dutch language
• Patients currently participating in intervention research.
• Patients treated with any investigational agent within 12 months prior to study treatment administration.
• Pregnant patients
• Patients who are <= 6 months postpartum pregnancy testing to the discretion of the attending physician
• Patients whom consume more than 25 grams of ethanol daily (>2.5 alcoholic beverages/day)
• Patients with a history of drug abuse
• Patients whom received treatment with corticosteroids or other immunosuppressive medications for active autoimmune disease involving the lung, heart, liver, small or large intestine, or neuromuscular system within 3 months prior to ICU-stay
NOTE: Topical, ocular, intra-articular, intranasal, and inhalational corticosteroids (with
minimal systemic absorption) are permitted

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	23-02-2018
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	22-12-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-01-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-02-2020
Application type:	Amendment

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 20834
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL63412.081.17
OMON	NL-OMON20834