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Critical illness myopathy and timely electrical muscle stimulation

Submission date
10/06/2010

Recruitment status
No longer recruiting

Registration date
17/02/2011

Overall study status
Completed

Last Edited
04/08/2022

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
No. 192/2, WE 4386/1-1

Study information

Scientific Title

Critical illness myopathy and timely electrical muscle stimulation: an observer-blinded randomised controlled clinical trial

Study objectives
AIM 1 - Hypothesis: Electrical muscle stimulation (EMS) of both lower and upper extremities is associated with increased muscle strength upon emergence from sedation and a lower degree of functional impairment at discharge from intensive care unit (ICU).
Test: We will investigate and compare muscle strength (MRC score), functional impairment (functional independence measure) and secondary clinical outcome parameters in both study groups at the end of sedation and at ICU discharge.

AIM 2 - Hypothesis: EMS prevents thick filament loss.
Test: The extent of thick filament loss will be visualised by histopathological staining and electron microscopy and will be compared between both study groups. Regulation of atrophy gene expression (MURF-I and Atrogin) will be investigated.

AIM 3 - Hypothesis: EMS improves systemic insulin sensitivity as well as oxidative metabolism of skeletal muscles in the intervention group.
Test: We will investigate key molecules of insulin signalling, MAP-kinase and AMP-kinase in muscle biopsies by Real Time PCR and Western blotting. We will perform RT-PCR studies on the expression pattern of key mitochondrial genes as well as western blots of voltage-dependent anion channels of the outer mitochondrial membrane (VDAC) indicating mitochondrial muscle mass and will compare these parameters between the intervention and control group.

AIM 4 - Hypothesis: EMS promotes activation of specific metabolic pathways. Thus, the metabolic adaptations may be critical for the development of CIM in critically ill patients and the metabolic profile may thus serve as a reliable biomarker for disease prediction.
Test: Metabolite profiling will be performed on a Pegasus 3 time-of-flight mass spectrometer (Leco) equipped with a Direct Thermal Desorption injector (ATAS GL International) coupled to an HP 5890 gas chromatograph and a dual-arm autosampler with automatic de-vitalisation and liner exchange. Chromatograms will be processed using Leco ChromaTOF software (version 3.25) and peaks with signal to noise ratios >10 and will be exported before using an in-house developed algorithm. Mass spectra will be compared to the in-house mass spectral library according to mass spectral similarity and retention. Principal component analysis (PCA) will be performed on the obtained data to illustrate disparities between intervention and control group on metabolite levels.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Charite - Berlin Medical University (Charite - Universitätsmedizin Berlin) Ethics Committee approved in May 2010 (ref: EA2/041/10)

Study design
Randomised controlled observer blind clinical trial

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Intensive Care Unit-acquired weakness (ICUAW)/Critical illness myopathy (CIM)

Interventions
Current intervention as of 15/10/2021:
Patients allocated to the intervention group will receive EMS treatment of M. quadriceps femoris (M. vastus lateralis and M. rectus femoris), M. tibialis anterior, M. biceps brachii, M. triceps brachii, M. brachioradialis and ventral auxiliary muscles (Th9 - Th11) twice per day.

Patients allocated to the control group will receive sham stimulation of respective muscles twice per day by electrode placement without application of electrical current.

Within the intervention group, the applied electrical current depends on visible or palpable contracation or patient discomfort (maximum current applied: 70mA, maximum duration of intervention: 28 days).

Gender-specific sub-analysis will be performed to investigate potential differences and account for gender bias.

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Previous intervention:
Patients allocated to the intervention group will receive EMS treatment of M. quadriceps femoris (M. vastus lateralis and M. rectus femoris), M. tibialis anterior, M. biceps brachii, M. triceps brachii, M. brachioradialis and ventral auxiliary muscles (Th9 - Th11) twice per day.

Patients allocated to the control group will receive sham stimulation of respective muscles twice per day by electrode placement without application of electrical current.

Within the intervention group, the applied electrical current depends on visible or palpable contracation or patient discomfort (maximum current applied: 70mA, maximum duration of intervention: 28 days).

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure

1. Clinical: muscle strength assessd by MRC score after the end of sedation and functional impairment at ICU discharge as indicated by FIM
2. Molecular: incidence of histologically proven CIM, measured during the study enrolment period

Secondary outcome measures
1. Clinical (assessed during the study enrolment period):
1.1. Ventilator-free days
1.2. ICU stay
1.3. EMG/ENG
1.4. Weaning failure
2. Molecular (analysed once patient enrolment has ended):
2.1. Signalling pathways (insulin/IGF-1, AMP-Kinase, MAP-Kinase)
2.2. Tissue metabolism
2.3. Atrophy gene regulation
2.4. Mitochondrial function
2.5. Caveolae dynamics

Overall study start date
01/10/2010

Completion date
30/09/2013

Eligibility

Key inclusion criteria
1. Adults with a Sequential Organ Failure Assessment (SOFA) score greater than or equal to 9
2. Mechanical ventilation
3. Written informed consent of legal proxy
4. Aged greater than 18 years, either sex

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
80

Total final enrolment
50

Key exclusion criteria
1. Patients with mechanical ventilation and SOFA less than or equal to 9 for more than 72 hours prior study screening
2. Age less than 18 years
3. No written informed consent by legal proxy
4. Pre-existing neuromuscular disorder
5. Coagulation disorder refractory to therapy
6. Pregnancy
7. Poor prognosis with expected death within the next hours or days

Date of first enrolment
01/10/2010

Date of final enrolment
30/09/2013

Locations

Countries of recruitment
Germany

Study participating centre
CC7
Berlin
Germany
13353

Sponsor information

Organisation
Charité - University Medicine Berlin (Charité - Universitätsmedizin Berlin) (Germany)

Sponsor details
c/o Prof Friedrich Luft
European Clinical Research Center
Charite Campus Buch
Max-Delbrück-Centrum für Molekulare Medizin (MDC)
Berlin-Buch
Robert-Rössle-Str. 10
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13092

Sponsor type
Research organisation

Website
http://www.charite.de

ROR
https://ror.org/001w7jn25

Funder(s)

Funder type
Research organisation

Funder Name
Charité - University Medicine Berlin (Charité - Universitätsmedizin Berlin) (Germany)

Funder Name
German Research Council (Deutsche Forschungsgemeinschaft [DFG]) (Germany) (ref: No.192/2, WE 4386/1-1)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2019	12/09/2019	Yes	No
Results article	results	10/09/2019	12/09/2019	Yes	No
Results article	Retrospective analysis	03/08/2022	04/08/2022	Yes	No