Breath synchronized electrical stimulation of the abdominal wall muscles to prevent respiratory muscle atrophy during the acute stages of mechanical ventilation therapy

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Muscle disorders
Study type	Interventional

Summary

ID

NL-OMON46155

Source
ToetsingOnline

Brief title
NMES to prevent respiratory muscle atrophy

Condition

- Muscle disorders
- Thoracic disorders (excl lung and pleura)

Synonym
respiratory muscle weakness due to mechanical ventilation, weaning failure

Research involving
Human

Sponsors and support

Primary sponsor: Intensive care
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Intensive Care Unit, Mechanical ventilation, Neuromuscular electrical stimulation, Respiratory muscle atrophy

Outcome measures

Primary outcome

The main study endpoint is the thickness of the abdominal wall muscles during

end-inspiration (ITabd) and end-expiration (ETabd), for both groups, as

measured by ultrasound.

Secondary outcome

The secondary endpoints are:

- the thickening fraction (TF) of the abdominal wall muscles: TFadb = (ITabd -

ETabd) / ETabd x 100%

- the thickness of the diaphragm during end-inspiration (ITdi) and

end-expiration (ETdi)

- the thickening fraction of the diaphragm: TFdi = (ITdi - ETdi) / ETdi x 100%

- echogenicity of the abdominal wall muscles

- the thickness of the rectus abdominis muscle

- functional respiratory measurements: vital capacity (VC), maximal expiratory

pressure (MEP), maximal inspiratory pressure

(MIP), cough pressure

- blood inflammatory markers (IL-6, IL-1, IL-8)

- weaning outcome

During follow-up:

- readmission to the ICU due to respiratory problems

- pneumonia acquired after ICU discharge.

These outcomes will be compared between both groups.

At last, feasibility parameters will be investigated:

- Estimated sample size for a larger randomized control trial, based on the

primary outcome parameter.

- Time needed to recruit patients

- Number of eligible patients: as number of the total ICU population

- Replacement rate after first stimulation test with ultrasound verification of

contraction during stimulation

Study description

Background summary

Approximately 30-40% of intubated patients at the intensive care unit (ICU) take more than one attempt to wean from mechanical ventilation (MV) and approximately 6-14% of intubated patients take longer than 7 days to wean from MV.[1]-[5]
While MV can be lifesaving, patients requiring prolonged time on the ventilator are susceptible to a wide range of clinical complications and excess mortality.[1], [3], [4], [6] It is therefore imperative for them to wean at the earliest possible time.

Although the pathophysiology of weaning failure is complex and multifaceted, respiratory muscle dysfunction is a major underlying factor for many patients and already occurs during the first five days of MV [7]-[11] Weakness of the diaphragm, abdominal, and intercostal muscles may result in to decreased cough function, poor breathing force, and results in low blood oxygen/elevated carbon dioxide levels. Consequently, patients are susceptible

to ICU acquired pneumonia and have difficulties
weaning.

Recent evidence suggests that neuromuscular electrical stimulation (NMES) can be used as a safe therapy to maintain skeletal
muscle function in critically ill patients, e.g. by stimulating quadriceps muscles in patients receiving MV.[12]-[20] This is a noninvasive
method, which incorporates the use of electrical current to activate skeletal muscles and produce contractions without
active participation of the patient.[13], [14], [21]-[23] It thus follows that a similar approach could be applied to the respiratory
muscles, in particular to the expiratory muscles, during MV therapy.

To test this hypothesis, a bedside transcutaneous electrical muscle stimulator that applies NMES to the abdominal wall muscles
in synchrony with exhalation will be used. It has been demonstrated that this technique acutely improves minute ventilation,
while not affecting the inspiratory load in healthy subjects, COPD patients and patients receiving prolonged MV.[24]-[26]
This study will build upon this previous work and test the hypothesis that exhalation synchronized NMES of the abdominal-wall
muscles can prevent expiratory muscle atrophy during the acute stages of MV.
The long-term goal of this study is to determine
whether this approach can improve lung function and thereby reduce the amount of time it takes to wean patients from MV,
which could have a promising impact in critical care.

Study objective

The primary objective of this study is to investigate whether electrical stimulation applied to the abdominal wall muscles in synchrony with exhalation can be feasible to prevent the development of atrophy of the abdominal wall muscles during the acute stages of MV therapy. The secondary objectives of this study are to analyse whether this intervention also affects: (1) the thickness of the diaphragm, (2) functional respiratory measurements, (3) markers for systemic inflammation, and (4) weaning outcome.
Other objectives are to study recruitment rate and time to collect data.

This data will be used to assess the feasibility, and estimate the sample size, of a follow up fully powered study, which assesses clinically relevant endpoints.

Study design

This study is a multicentre, randomized, sham-controlled intervention pilot trial with patients, caregivers and outcome

assessors blinded to the treatment allocation.
The rationale of performing sham stimulation, and blinding of caregivers and outcome assessors is to ensure that there will be
no difference in care provided between the intervention group and other patients.

Intervention

The intervention will be NMES (versus a sham [control] intervention) applied to the abdominal wall muscles for 30 minutes per
session, twice a day, 5 days per week, for 6 weeks or until the patient is weaned from MV, whichever occurs sooner.
The sham-controlled group will receive the stimlulation as well, however the stimulus intensity will be too low to induce muscle
contraction.

Study burden and risks

The study setting will be a mixed ICU. In addition to standard care, the patients participating in this study will additionally receive two 30-minute sessions of transcutaneous NMES therapy per day. The risks associated with participation are negligible, since other studies have demonstrated the safety of this intervention in ICU and non-ICU patients.[7-15],[22] Furthermore, NMES is already used in the Radboudumc for physiotherapeutic purposes, which means that we are familiar with the equipment.

Ultrasound measurements will be performed every other day to study the effect of NMES. There are no risks associated with this assessment. After the patient is weaned from MV, data from lung function measurements will be obtained. Since these measurements are performed within routine care, this will not induce any risks for participation in this study.

Two venous blood samples will be collected during enrolment and after the third NMES session. This will be taken out of the intravenous catheter the patient already has. Therefore this will not cause any further harm. Next to the fact that all participants receive standard intensive care, each participant will be monitored intensively to avoid any burden or risks.

Finally, all other measurements will be collected from chart review, in which the patient is not directly involved.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- informed consent
- age > 18 year
- invasive mechanical ventilation less than 72 hours
- expected duration of MV after inclusion > 72 hours

Exclusion criteria

- no visible abdominal wall muscles, assessed with ultrasound during routine care
- cardiac pacemaker
- congenital myopathies and/or existing central or peripheral neuropathies
- recent abdominal surgery within four weeks prior to study inclusion
- refractory / uncontrolled epilepsy
- BMI > 35
- pregnancy

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-03-2017
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	Electrotherapy device
Registration:	No

Ethics review

Approved WMO Date:	24-05-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-08-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	27-09-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	31-08-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-07-2018
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

No registrations found.

In other registers

Register	ID
CCMO	NL57078.091.16