Diaphragm-protective mechanical ventilation in critically ill patients: A proof of concept study.

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

Summary

ID

NL-OMON44635

Source
ToetsingOnline

Brief title
DiaPro

Condition

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

Synonym
respiratory muscle weakness, ventilator-induced diaphragm dysfunction

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Diaphragm dysfunction, Intensive care unit, Mechanical ventilation, Monitoring

Outcome measures

Primary outcome

Primary endpoint of the study is the time that diaphragm activity was within physiological range during the study period. Diaphragm activity will be continuously measured as the trandiaphragmatic pressure (Pdi), using the formula below:

(1) Transdiaphragmatic pressure (Pdi) = Gastic pressure (Pga) - Esophageal pressure (Pes)

Pdi will be analysed on a breath-by-breath basis after conclusion of the study period. Every breath within the range of 3-12 cmH2O will be considered as physiological. The percentage of physiological breaths will be calculated as:

(2) Percentage of diaphragm-protective breaths = (number of physiological breaths) / (total number of breaths) *100%.

Secondary outcome

Secundary outcome parameters include:

-Percentage of time that the pressure-time product of the diaphragm (PTPdi) was within physiological range during the study period

-Effect of the intervention on various clinical parameters including results of blood gas analysis, inflammatory parameters and patient comfort

- Various feasibility parameters, such as the percentage of patients admitted during the study period which were eligeble for inclusion, the number of patients that were prematurely withdrawn from the study, reason of early withdrawal and number of adjustments made to the ventilator settings during the study period.

Study description

Background summary

Despite being life-saving, mechanical ventilation can have detrimental effects on respiratory muscle function of critically ill patients. Like any straited skeletal muscle, disuse of the diaphragm caused by overassistance of the ventilator leads to atrophy and contractile dysfunction. On the other hand, excessive work of breathing caused by ineffective unloading by the ventilator can also contribute to development of Weakness. Together, these processed are refered to asventilator-induced diaphragm dysfunction (VIDD). Dysfunction of the respiratory muscles is associated with adverse outcome, including prolonged weaning from the ventilator and increased mortality. Finding strategies to prevent respiratory muscle dysfunction is therefore of utmost importance.
We hypothesize that both inactivity and excessive activity of the diaphragm can be prevented by monitoring diaphragm activity at the bedside and adjusting the ventilator settings accordingly. This study aims to assess the effect of such a 'diaphragm-protective' ventilation strategy in a diverse ICU population. Outcomes of this study will be used to conduct a large multi-center trial to assess if diaphragm-protective ventilation leads to improved outcomes of critically ill patients. If this strategy is effective and feasible, it can quickly improve outcomes of critically ill patients worldwide, and reduce healthcare costs.

Study objective

Primary objective of this study is to assess the feasibility of using a monitoring and a titration algorithm to prevent inactivity and excessive activity of the diaphragm. This will be determined by comparing the fraction of breaths where diaphragm activity was within physiological range in the intervention group and control group.

Secundary objectives include:
- To assess if diaphragm protective ventilation can be combined with

lung-protective ventilation
- To assess the effect of diaphragm protective mechanical ventilation on patient-ventilator interaction.
- To assess the effects of diaphragm-protective ventilation on various clinically relevant parameters such as blood gas analysis, parameters of inflammation and patient comfort.
- In a subgroup of patients where electrical activity of the diaphragm (EAdi) is readily available: to evaluate te relationship between EAdi and Pdi.

Study design

The study is a single center, single blinded, randomized-controlled pilot trial.

Intervention

In both control and intervention group diaphragm activity will be monitored continuously using esophageal and gastric pressure catheters. In the intervention group, ventilator settings will be adjusted according to the observed diaphragm activity in an attempt to prevent inactivity and excessive activity of the diaphragm. Adjustments will be made using a specially designed titration algorithm (see page 18 of the protocol). Adjustments will be made within the current range used in current clinical practise. There is no further intrusion on regular clinical care.

Study burden and risks

Risks and burden of the intervention are small and manageable. Adjustment of ventilator settings is a standard procedure in the ICU. Other studies that adjusted ventilator settings for various reason found that this is well tolerated by patients. Furthermore, we wil abide to the general safety guidelines of management of ventilator settings currently used in general practise. As such, pressures and volumes administered to the subjects in the intervention group will be within range of those used in general clinical practise today. Furthermore, the attending physician can override the ventilator settings suggested by the study algorithm at any point during the study, if he/she thinks that this is in the patients best interest. These events will be registered and analysed as a feasibility parameter. Risks of the intervention are thus minimal.
The risk and burden of the additional measurements and monitoring instruments are small. The esophageal and gastric pressure catheters are already used in specific patient groups in clinical care today Research staff and nurses have experience with placing these instruments and conducting the measurements. Some subjects will thus have the required instruments available at the start of the study and will no be subjected to additional risks or burden. In case subjects need to be instrumented with esophageal and/or gastric pressure catheters for

this study, consent will be asked for this procedure. Placement is uncomfortable, comparable to the burden and risks of placing a nasogastric feeding tube, but generally well tolerated. From clinical experience and recent literature it is regarded as a safe procedure. Furthermore, high risks groups are excluded from participation in the study. The additional blood samples required for this study are all drawn from indwelling arterial catheters and thus pose no extra risk or burden on the subjects. The amount required is very small (15ml in total), much less than is taken daily for regular clinical practise.
A sound risk - benefit analysis is of utmost importance when conducting studies in critically ill and mechanically ventilated patients. As outlined above, risks posed on the subjects are small and manageable. Weakness of the respiratory muscle is common in mechanically ventilated patients and is associated with adverse outcome. It is therefore highly relevant to find strategies that can effectively prevent the development of respiratory muscle weakness. Such strategies can only be studied in mechanically ventilated patients, making these studies group related. If the titration algorithm in this study is indeed effective in preventing inactivity and excessive activity of the diaphragm, then it will be of benefit to both subjects in this study and to future patients requiring mechanical ventilation.

Contacts

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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 years
-Supportive ventilation mode
-Expected duration of mechanical ventilation at least 24 hours at moment of inclusion

Exclusion criteria

-Current neuromuscular disease
-Contraindication for nasogastric intubation, including recent upper airway surgery and severe bleeding disorders
-Expected difficulties in acquiring reliable pressure measurements

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-04-2018
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	14-11-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL62486.029.17