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Effects of phrenic nerve electrical stimulation on diaphragm function and weaning outcomes

Submission date
20/06/2021

Recruitment status
No longer recruiting

Registration date
02/07/2021

Overall study status
Completed

Last Edited
25/06/2021

Condition category
Respiratory

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
The diaphragm is the main respiratory (breathing) muscle and plays an important role in ventilation, airway clearance and speech. Mechanical ventilation is a form of life support where a machine takes over the work of breathing when a person is not able to breathe enough on their own. As ICU patients on mechanical ventilation can rapidly develop diaphragmatic weakness, strategies to improve diaphragmatic function are urgently needed. Currently, no drugs have been proven to improve diaphragm function. External diaphragm pacing (EDP) may be a non-invasive treatment, especially for critically patients who are susceptible to diaphragmatic weakness. EDP is inexpensive and easy to operate, and has been used in patients with other diseases. The aim of this study is to find out whether early intervention with EDP in mechanically ventilated patients with mechanical ventilation improves diaphragm function.

Who can participate?
Patients over 18 years old with acute respiratory failure requiring invasive mechanical ventilation

What does the study involve?
Participants will be randomly allocated to receive sham treatment or EDP treatment. Treatment will begin at the time of enrolment of patients until they are weaned from mechanical ventilation. The maximum follow-up is 28 days.

What are the possible benefits and risks of participating?
The patient's condition may improve and this study may help develop a new treatment for other mechanically ventilated patients. Sputum discharge may increase during treatment. If it is not discharged in time, it may increase the risk of aspiration. The researchers will pay close attention to and timely aspirate sputum for patients during treatment. In addition, when the EDP intensity is too high the patient may experience discomfort, and the researchers will continuously help to adjust the intensity to help the patient feel comfortable.

Where is the study run from?
Sir Run Run Shaw Hospital affiliated to the Medical College of Zhejiang University (China)

When is the study starting and how long is it expected to run for?
January 2020 to December 2021

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Ding Yuejia
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Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
20200200106-11

Study information

Scientific Title
External phrenic nerve pacing to preserve diaphragm function and improve weaning outcomes: a feasibility study

Study objectives
Early intervention with EDP in severe mechanical ventilated patients can improve their diaphragm function and weaning outcomes, and EDP is feasible for patients with severe mechanical ventilation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 01/06/2020, Medical Ethics Committee of Run Run Shaw Hospital Affiliated to Zhejiang University School of Medicine (3 Qingchun East Road, Jianggan District, Hangzhou; +86 (0)57186006811; xumingsrrsh@foxmail.com), ref: 20200106-11

Study design
Randomized controlled 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 to request a participant information sheet

Health condition(s) or problem(s) studied
Patients with acute respiratory failure requiring invasive mechanical ventilation

Interventions
After the candidates or their family members sign the informed consent, the research staff contacts the liaison of the lead center for central randomization by specially assigned staff.

Sham treatment group:
ICU standard care is prescribed by the attending physician according to the relevant program /guideline. For EDP treatment, the stimulation intensity will be set to 1 unit (no obvious contraction of the diaphragm).

Treatment group:
EDP treatment will be performed on the basis of ICU standard care (30 minutes, twice a day, 7 days a week).

The small electrode pieces are placed in the outer edge of the sternocleidomastoid muscle, at the lower 1/3 junction (flat cartilage level), and the large electrode piece is placed at the inner edge of the midclavicular line and the second intercostal space. Set parameters (pulse frequency: 40 Hz, pacing times: 9 times/minute, if the EDP and the patient's breathing are not synchronized, adjust the pacing times). The intensity of the stimulus gradually increases from 0 to the maximum intensity that the patient can tolerate. Awakened patients can respond to intensity while sedated patients need to assess whether the intensity is appropriate based on

facial expressions, physical movements, blood pressure, and heart rate. Painful facial expressions include frowning, brow reduction, tight eyelids, contraction of the diaphragm and closure of the eyelids; painful movements of the body may be slow, cautious movement, touching the pain, and seeking attention through movement.
For patients with internal jugular vein catheterization, if the electrode piece is too close to the puncture point, the electrode piece is cut to ensure a distance of 1 cm away from the puncture point. Another option is unilateral stimulation.

Treatment will begin at the time of enrolment of patients until they are weaned. The maximum follow-up is 28 days.

Intervention Type
Device

Phase
Not Applicable

Primary outcome measure
1. Enrollment rate: number of enrolled patients divided by total number of patients meeting the criteria of this study at 48 hours after the establishment of an artificial airway
2.Retention rate (incorporating acceptability of the therapy): number of patients who completed the study divided by number of patients admitted at the end of the entire experiment
3. Response rate: diaphragmatic mobility measured by ultrasound at the first EDP treatment
4. Incidence rate of adverse events measured using number of patients with adverse events divided by patients enrolled in the group during the entire test

Secondary outcome measures
1. Diaphragm thickness: at the end of exhalation and inspiration the thickness of the right diaphragm will be measured using diaphragm ultrasound during tidal breathing to calculate the muscle thickening score. Measured at baseline, every other day, for the first SBT (under EDP) and on day 28
2. Diaphragm mobility: right diaphragmatic mobility, inspiratory time, inspiratory slope and acceleration measured using diaphragm ultrasound at the first SBT (under EDP treatment)
3. Duration of mechanical ventilation, reintubation, weaning success rate and survival rate measured using patient records within 28 days
4. Blood gas analysis using blood gas analysis instrument before and after EDP session every morning

Overall study start date
01/01/2020

Completion date
31/12/2022

Eligibility

Key inclusion criteria
1. Patients with acute respiratory failure requiring invasive mechanical ventilation
*Incorporated within 48 hours after the establishment of the artificial airway
2. Estimated mechanical ventilation time >72 hours
3. Aged over 18 years old

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
60

Key exclusion criteria
1. Pneumothorax or mediastinal emphysema
2. Acute myocarditis, severe arrhythmia
3. Neuromuscular diseases that may affect weaning, including myasthenia gravis, motor neuron disease, and congenital myopathy
4. Hemodynamic instability (mean arterial pressure <60 mmHg and norepinephrine >0.2 ug/kg /min)
5. Paroxysmal sympathetic hyperactivity syndrome
6. Even chest
7. Pregnancy
8. Fitted with a pacemaker/implantable defibrillator
9. Applying neuromuscular blockers (NMBAs) within the past 6 hours
10. History of neck radiation therapy or neck surgery
11. Cancer of the neck and lung
12. Unable to obtain accurate diaphragm ultrasound results

Date of first enrolment
01/07/2020

Date of final enrolment
01/12/2022

Locations

Countries of recruitment
China

Study participating centre
Sir Run Run Shaw Hospital affiliated to medical college of ZheJiang University
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Sponsor information

Organisation
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Sponsor type
Hospital/treatment centre

Website
http://www.srrsh.com/html/main/gb2312/

ROR
https://ror.org/00ka6rp58

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Sir Run Run Shaw Hospital

Alternative Name(s)
, SRRSH

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
China

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
31/12/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from ding_yuejia@zju.edu.cn after article publication. The data will be available beginning 9 months and ending 36 months following article publication. Anyone with any purpose who wishes to access the data is OK. Consent from participants was obtained and the data is anonymous.

IPD sharing plan summary
Available on request