Information for participation in medical-scientific study

ACACIA – A comparison between two strategies to remove mucus during invasive ventilation

Mechanical Insufflation-Exsufflation (MI-E) versus manual hyperinflation in invasively ventilated patients in the ICU – a randomized clinical trial

Introduction

Dear Sir/Madam,

Your representative granted permission for your participation in a clinical study that compares two strategies to remove mucus from the airways during invasive ventilation in Intensive Care Unit (ICU) patients. In this letter, you can read what the study means and for what you might give permission.

1. General information

This study is designed by the Intensive Care Unit (ICU) of the Amsterdam Medical Center (AMC), and is subsidized by the Dutch Research Council (NWO), funding number 023.011.016). Hereafter, the Intensive Care of the Amsterdam UMC – location AMC will be named 'conductor'. Researchers, this can be physicians or nurses, will perform the study. This study is being conducted in several hospitals in the Netherlands. A total of 50 patients is needed for reliable results of the study.

The Medical Ethics Review Committee AMC has approved this study. General information about medical research can be also found on the website of the Central Government: https://www.government.nl/topics/medical-research.

2. Purpose of the study

The purpose of this research is to compare two different strategies to remove mucus from the airways. Both methods are used interchangeably in the ICU:

1. Mechanical Insufflation-Exsufflation (MI-E)
2. Manual hyperinflation – regular airway care

3. Background of the study

During mechanical ventilation a patient is less able to cough causing mucus to retain in the airways. Presence of mucus can cause infections or (partial) closing of the airways. There has been little research about the most safe and effective ways to remove this mucus. Currently, mucus is removed by endotracheal suctioning and a manual cough technique, so called manual hyperinflation. Both interventions can bring risks, like lung damage. Additionally, research has shown that the current technique is experienced as painful and stressful by patients. Possibly, a mechanical chough (MI-E) is feasible and may be less harmful and less stressful and therefore better for the patient, but this is not certain. An example of MI-E is provided in appendix C.

4. What happened during the study?

Why were you able to participate in this study?

When the expected period of ventilation was longer than 24 hours, we asked your regal representative permission for participation in this study. Due to the acute circumstances, your

consent could not be obtained. Therefore, deferred consent for your participation was obtained from a representative on your behalf. The Medical Ethics Review Committee AMC granted permission for the use of deferred consent.

The treatment
After permission from your legal representative, there was randomized between two strategies to remove mucus from the airways. For this study we made 2 groups:
Group 1: the people that received treatment with mechanical in- and exsufflation (MI-E) 2 times a day for 7 days.
Group 2: the people that received regular airway care to remove mucus with endotracheal suctioning and a manual cough technique.

Research and measurements
During the IC admission until day 28, medical data that is important for the examination was recorded from your medical record (personal data and medical history). Furthermore, we collected daily ventilation data. All data will be processed coded (see chapter 10. "Use and storage of the data"). All the collected data will be used confidentially.

What was different compared to regular care?
Normally mucus is removed by suctioning and by using a manual cough technique. In this study we use a cough assist device in group 1 during 7 days. After 7 days these patients will receive regular airway care as in group 2.

5. What agreement do we make with you?
We want the study to be performed well. For this reason we make the following agreement with you:
If you give your consent to use the already collected data for this study, we kindly ask you to sign the consent form. All data are and will be handled confidentially (see part 10. Use and storage of your data).
If you do not give your consent, then the collected data will be discarded.
Please contact the researcher when your contact information changes.

6. Possible side effects, adverse effects or discomforts
The use of MI-E can bring possible side effects. Participation in this study means that possible side effects could have taken place like a temporary decrease in peripheral oxygen saturation of blood pressure or pneumothorax. During the study all possible complications are registered securely. In case the treating healthcare professionals found it necessary to adjust the method of mucus removal, they were allowed to do so. You have not been ventilated any longer than necessary and there are no other changes in the care that you have received. The MI-E can also have side effects that we do not know. MI-E is CE registered and certified for use in the intensive care. Use of MI-E is not part of usual care.

Regular airway care
Also regular airway care can have the same side effects as MI-E. The most important are lung damage, a temporary decrease in peripheral oxygen saturation of blood pressure or pneumothorax.
Regardless the group you have been allocated to, you have been monitored closely by healthcare professionals during your admission in the ICU. When needed the intervention is stopped.

7. What are possible advantages and disadvantages if you participate in this study?

Participation can bring advantages and disadvantages. Hereby we provide an overview. Consider these and discuss the with others.
If your give consent for the use of data in this study, you will support the search for better treatment of patients who are mechanically ventilated in the ICU. Possibly MI-E is less painful and stressful than regular airway care, but this has not been proven.
If you decide you would rather not consent to the use of the collected data for scientific research, there are no consequences for the treatment you receive as a patient. The collected medical data will not be used. You do not have to clarify why you don't want the collected data to be used.

8. When will the study stop?

Your participation in the study stops when:

- the continued observation period, 28th day after start of ventilation, has passed
- you decide that the collected data cannot be used
- one of the following organizations decides the study has to stop:
  - The Intensive Care in Amsterdam UMC, location AMC
  - the government, or
  - Medical Ethics Review Committee AMC.

9. What happens after this study?

Will you receive the results of the study?
Approximately 2 years after your participation the researcher will inform you about the results of this study. The researcher will also be able to tell you in which group you were allocated. When you prefer not to know this, please tell this to the researcher. He/she will not inform you.

10. What do we do with your data?

Do you consent with participation in this study? Then you will give consent to collect, to use and store your personal data.
What data do we store?
We will store the following data:

- your name
- your gender
- your address
- your age
- data with regard to your health
- medical data we collect during the study

Why do we collect, use and store your data?
The collection, use and storage of your data is required in order to answer the questions asked in this study and to be able to publish the results. The data will not be shared with the manufacturer of MI-E.

How do we protect your privacy?
To protect your privacy, your data will receive a code. Your name and other information that could directly identify you are therefore omitted. This information can only identify you with the key. The key to the code will be stored securely in the local research facility. The data that are shared with the sponsor only contains a code, but not your name or other data that can identify you. In reports or publications about the study, the data will also not be identifiable.

Who has access to your data for review?
Some individuals may have full access to your data at the study site. Also to the data without a code. This is needed in order to check whether the study is performed properly and reliably. Individuals who have access to your data for review are:

- the principal investigator and coordinating researchers
- the controller that works for the sponsor of the study
- the Health Care Inspectorate and Youth (IGJ).

They will keep the data confidential. We ask your consent for this access.

How long will your data be stored?
The data must be stored for 15 years at the study site.

Your data may still be of interest after the end of this study for other clinical research regarding invasive ventilation. For this, your data will be stored for 15 years. You can indicate on the consent form if you do or do not agree with this. If you do not consent to this, the data will be used for this study only.

Withdrawal of consent
You can always withdraw your consent for the use of your personal data. This applies to this study and also for the storage and use for future research. Of Note: when you withdraw consent and researchers have collected data already for the study? They are allowed to use the data that have been collected until that moment.

More information about your rights when processing data

- For general information about your rights concerning the processing of your personal data, please consult the website of the Dutch Data Protection Authority (https://www.autoriteitpersoonsgegevens.nl/en).
- If you have any questions about your rights, please contact the organization responsible for the processing of your data. For this study, that is the following:
  The Amsterdam UMC – location AMC. See appendix A for contact information.
- If you have any questions or complaints regarding the processing procedure, we recommend that you contact the study site. You can also contact the Data Protection Officer for the AMC or the Dutch Data Protection Authority.

Where can you find more information about the study?
Information about this research is also included in a summary of medical research i.e. www.clinicaltrials.gov. After the study, the website may contain a summary of the results of this study. You can find this study under 'ACACIA'.

11. Do you receive compensation for participation in this study?
Participation in this study is voluntary. You will not receive a reimbursement for participating in this study. Obviously, there are no additional costs for participating in this study.

12. Are you insured during this study?
Insurance has been taken out for everyone who participates in this study. The insurance covers damage resulting from the study. Not all damage is covered. In Appendix B you can find more information about the insurance and the exceptions. It also states whom you should contact if you want to report damage.

13. Any questions?

If you have any questions, you can contact Frederique Paulus (primary investigator). You may contact the independent physician for advice about participating in this study. Daan Velseboer (ICU physician) knows a lot about the study, but has nothing to do with the study.
If you have complaints about the study, you can discuss it with the researcher or your treating doctor. If you prefer not to do this, you can contact the complaints committee of your hospital. All information can be found in Appendix A: Contact details.

14. How do I give consent for the study?

Firstly, you will have sufficient time for deliberation. Afterwards you will tell the researcher that you have understood the information and if you agree to the use of collected data for research. If you give permission, we ask you to confirm this by signing the permission statement. The signature sheet is kept by your treating physician. You will receive a copy of this consent form.

Thank you for your attention.

15. Appendices to this information

A. Contact information AMC
B. Insurance information during the study
C. Example of MI-E in a mechanically ventilated patient
D. Consent form for patient

Appendix A: Contact information AMC

Principal Investigator

Dr. Frederique Paulus
Intensive Care Afdeling
020-5662739
(direct contact possible via the nurse)

Independent Physician

Dr. Daan C. Velseboer, intensivist
Intensive Care Unit
020-5659237
(direct contact possible via the nurse)

In case of complaints

AMC Complaints Officer
020-566 3355
Available on workdays, 9:00-15:30

Data protection officer in Amsterdam

Contact via email: privacy@amsterdamumc.nl

Appendix B: Insurance information during the study

The Amsterdam UMC – location AMC has taken out insurance for everyone who takes part in the study. The insurance pays for the damage you have suffered because you participated in the study. This concerns damage you suffer during the study or within 4 years after you participated in the study. You must report damage to the insurer within 4 years.

Have you suffered damage as a result of the study? Please report this to this insurer:

The insurance company of this study is:	
Name Insurer:	Centramed B.A.
Address Insurer:	Postbus 7374 2701 AJ Zoetermeer
Phone number:	070 301 70 70
E-mail:	info@centramed.nl
Polisnumber:	624.528.303

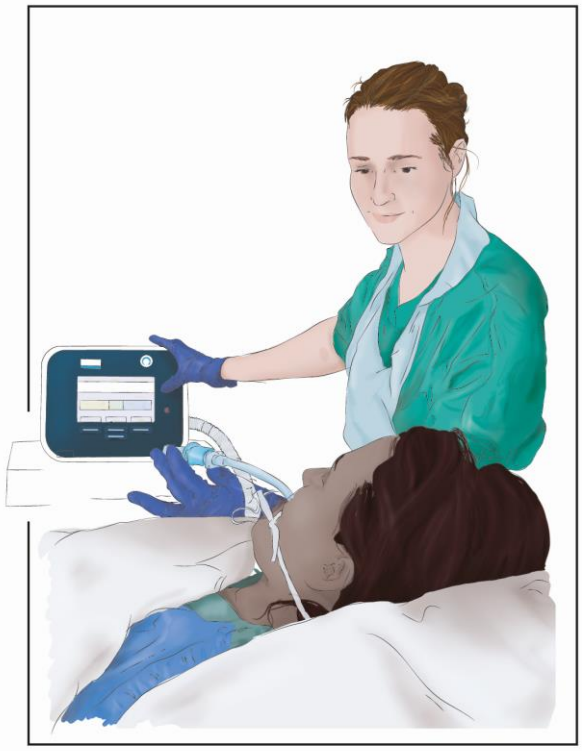
The insurance pays a maximum of € 650,000 per person and € 5,000,000 for the entire study and € 7,500,000 per year for all studies by the same sponsor.
Please note that the insurance does not cover the following damage:

- Damage due to a risk about which we have given you information in this sheet. But this does not apply if the risk turned out to be greater than we previously thought. Or if the risk was very unlikely.
- Damage to your health that would also have happened if you had not taken part in the study.
- Damage that happens because you did not follow directions or instructions or did not follow them properly.
- Damage to the health of your children or grandchildren.
- Damage caused by a treatment method that already exists. Or by research into a treatment method that already exists.

These provisions can be found in the 'Besluit verplichte verzekering bij medisch-wetenschappelijk onderzoek met mensen 2015' ('Medical Research (Human Subjects) Compulsory Insurance Decree 2015'). This decision can be found in the Government Law Gazette (https://wetten.overheid.nl).
Furthermore, the subject is requested to contact Dr. F. Paulus, +31 (0) 20 566 2739.

Appendix C. Example of MI-E in a mechanically ventilated patient

A MI-E mimics a mechanical cough by insufflating air in the lungs followed immediately by exsufflating air out of the lungs. The amount of air and the speed by which this is performed is defined in standard settings. During mechanical ventilation the patient will be prepared for MI-E. The patient will receive some additional oxygen and will be informed about the procedure. Additionally the MI-E will be connected to the endotracheal tube and the nurse will perform a treatment with MI-E. When needed, airway mucus will be removed by suctioning. Afterwards the endotracheal tube will be connected to the mechanical ventilator. The MI-E is CE certified (number G1.015581 0608 Rev. 00).



Appendix B: Consent form for the patient

ACACIA – A comparison between two strategies to mobilize mucus

I have been asked for consent to use my data collected for this research.

- I have read and understand the information form. I have had the opportunity to ask questions, which have been answered to my satisfaction. I have had enough time to decide whether the collected data for this study can be used.
- I have the right to withdraw my consent to use my data for this study or potential future studies at any time without having to provide an explanation.
- I know that for study monitoring purposes some individuals could have access to all my data. Those people are listed in this information letter. I consent to that access by these persons.
- I consent to my data being stored at the research location for 15 years after the end of this study.
- I consent to my data collected for this research being used in the way and for the purpose stated in the information letter.
- □ **I give**

  □ **I don’t give**
  permission to use my personal data for future research in the field of ventilation.
- □ **I want**

  □ **I don’t want**
  to be informed about which group I have been assigned to.
- I want to participate in this study.

Surname and initials of the patient: ----------

Signature: Date: __ / __ / __

I declare that I have fully informed the patient about the aforementioned research.

If information comes to light during the course of the study that could affect the patient’s consent, I will inform him/her in a timely fashion.

Name of investigator/doctor (or his/her representative): ----------

Signature: Date: __ / __ / __

The test subject will receive a full information letter, together with a signed version of the consent form.