Information for participation in a 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,

We would like to ask for your permission on behalf of the person you are currently legally representing for 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 is about and for what you might give permission.

Before you decide whether you give permission for this study, we will explain what this study entails and what it means for the person you represent. Please read this information carefully and ask the investigator for an explanation if you have any questions. You can also ask the independent expert, who is mentioned at the end of this document, for additional information. Additional information about participating in a study can be found in the general brochure on medical research.

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. 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 the 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 happens during the study?

Who is eligible for this study?

When the expected duration of ventilation is longer than 24 hours, the representative will be asked for permission to participate in this study. Due to the acute circumstances, the consent of the person you are legally representing cannot be obtained. Therefore, we ask for your consent on his or her behalf to participate in this study. The Medical Ethics Review Committee AMC has granted permission for the use of deferred consent.

The treatment

After permission, the person you represent will be randomized between two strategies to remove mucus from the airways. For this study we made 2 groups:

Group 1: the people that receive treatment with mechanical in- and exsufflation (MI-E) 2 times a day for 7 days.

Group 2: the people that receive 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 are recorded from the medical record (personal data and medical history). Furthermore, we collect daily ventilation data, live status and status of admission until day 28 after ICU admission. All data will be processed coded (see chapter 10. "Use and storage of the data"). All the collected data will be used confidentially.

What is different compared to regular care?

Normally mucus is removed by suctioning and by using a manual cough technique. In this study we will use a cough assist device (mechanical in- and exsufflation) twice a day during 7 days in group 1. After 7 days these patients will receive regular airway care as in group 2.

5. What agreement do we make with you?

We ask your consent for participation of the person you represent in this study and for collection of data. If you give consent, then the mucus will be removed according to the strategy for which is randomized. If you do not consent, then the patient will receive regular airway care (manual hyperinflation) to remove mucus. If you give consent for the study, we kindly ask you to sign the consent form.

When the person you represent is awake and adequate, we will inform him/her about the study and we will ask again for consent to use the already collected data. If the person you represent does not agree with your decision for participation in this study, all collected data will be discarded.

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 occur 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 are allowed to do so. The person you represent will not be ventilated any longer than necessary and there are no other changes in the care. The MI-E can also have side effects that we do not know. MI-E is 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 the person you represent will be allocated to, there will be close monitoring closely by healthcare professionals during ICU admission. When needed the intervention will be stopped.

7. What are possible advantages and disadvantages?

It is important to compare the advantages and disadvantages of participation in this study before making your decision on behalf of the person you represent. If you give consent, 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 give consent for this study on behalf of the person you represent, there are no consequences for the treatment he/she is receiving. You may also decide to withdraw your consent at any time during the study. The collected medical data will not be used. You do not have to clarify why you don't want the patient to participate in this study.

8. When will the study stop?

The participation in the study of the person you represent 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 organisation 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 the person you represent receive the results of the study?
Approximately 2 years after participation the researcher will inform the person you represent about the results of this study. The researcher will also be able to tell in which group he/she was allocated.

10. What do we do with the data of the person you represent?

Do you consent with participation of the person you represent in this study? Then you will give consent to collect, to use and store of the person you represent.

What data do we store?
We will store the following data:

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

Why do we collect, use and store data of the person you represent?
The collection, use and storage of the data of the person you represent 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 the privacy of the person you represent?
To protect the privacy of the person you represent, the data will receive a code. The name and other information that could directly identify this person are omitted. This information can only identify the person you represent 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 a name or other data that will identify the person you represent. In reports or publications about the study, the data will also not be identifiable.

Who has access to the data for review?
Some individuals may have full access to the data of the person you represent 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 the data of the person you represent 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.

The data of the person that you represent may still be of interest after the end of this study for other clinical research regarding invasive ventilation. For this, the 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 the personal data of the person you represent. 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 fine more information about the study?
Information about this research is also included in a summary of medical research i.e. www.clinicaltrials.gov. This does not include any data that can be traced back to the person you represent. After the study, the website may contain a summary of the results of this study. You can find this study under 'ACACIA'.

11. Is there compensation for participation?

Participation in this study is voluntary. You or the person you represent will not receive a reimbursement for participating in this study. Obviously, there are no additional costs for participating in this study.

12. Is there additional insurance needed 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 who should be contacted to report damage.

13. Will the treating specialist of the patient be informed?

We will inform the treating specialist from the ICU of the person you represent about the participation in this study.

14. Any questions?

If you have any questions, you can contact contact Frederique Paulus (primary investigator). You may contact the independent physician (Daan Velseboer) for advice about participation in this study. He knows a lot about the study, but has nothing to do with this study.
If you have complaints about the study, you can discuss it with the investigator or with the treating doctor of the person you represent. 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.

15. How do I give consent for the study?

When you have had sufficient time for deliberation, you will be asked to decide on participation of the person you represent in this study. If you give permission, we ask you to confirm this by signing the permission statement. Your signature confirms that you have understood the information and agree to participation of the person you represent in the study. The signature sheet is kept by the treating physician. You will receive a copy of this consent form.

Thank you for your attention.

16. 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 the legal representative

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 a person has suffered because he/she has participated in the study. This concerns damage suffered during the study or within 4 years after participation in the study. The person who has participated in the study must report damage to the insurer within 4 years.

Is there 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 eprson and € 5,000,000 for the entire study and € 7,500,000 per year for all studies by the same sponsor.

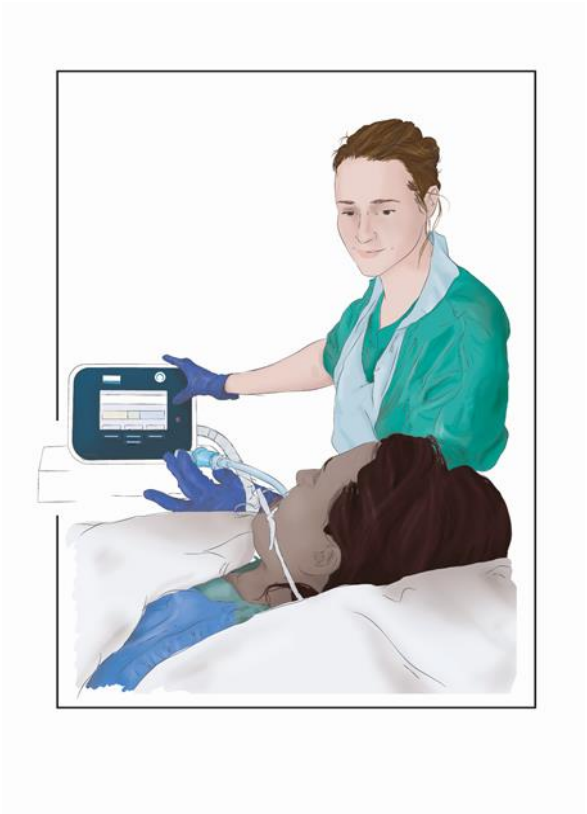
Please note that the insurance does not cover the following damage:
- Damage due to a risk about which we have given you information in this sheet. But this does not apply if the risk turned out to be greater than we previously thought. Or if the risk was very unlikely.
- Damage to your health that would 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 D: Consent form for legal representative

ACACIA – A comparison between two strategies to mobilize mucus

I have been asked for consent on behalf of the person mentioned below to participate in this study.

Surname and initials of the patient: Date of birth: __ / __ / __

- I have read and understand the information letter for the representative. I have had the opportunity to ask questions, which have been answered to my satisfaction. I have had enough time to decide if the person I represent participates in this study.
- I understand that participation is voluntary. I have the right to withdraw my consent at any time without the need to provide an explanation and without effect on the medical treatment of the person I represent.
- I give permission to inform the treating specialist of the person I represent about his/her participation in this study.
- I consent to the data being stored at the research location for 15 years after this study.
- I know that for study monitoring purposes some individuals could have access to all of the data. Those people are listed in this information letter. I consent to that access by these persons.
- □ **I give**

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

  □ **I don’t want**
  to be informed about which group the person I represent has been assigned to.
- I give permission to participation in the trial of the person mentioned above.

Surname and initials legal representative: ----------

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

Relation to the patient: ----------

Signature: Date: __ / __ / __

Signatory declares that the person mentioned above is fully informed about this study.

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 legal representative will receive a full information letter, together with a signed version of the consent form.