GODIF

To the Legal Representative (physician)

Information about a Health Science Research Project Involving Patients with Fluid Overload in the Intensive Care Unit

Study Title:
Goal-directed fluid removal with furosemide in intensive care patients with fluid overload – A randomised, blinded, placebo-controlled clinical trial (GODIF).

Introduction

The patient in question is admitted to the intensive care unit and is incapacitated due to an acute medical condition. We are asking if you, on behalf of the patient, would be willing to provide legal representative consent for their participation in a health science research project, as they currently cannot consent themselves. Participation in the study is voluntary, and you may decline without affecting the patient's current or future treatment.

Before deciding whether to provide consent, it is important that you fully understand the purpose and nature of the study. Please read this information carefully.

You will receive an oral explanation of this participant information and can ask any questions. If you decide that the patient may participate, we will ask you to sign the attached consent form. You are entitled to a period of consideration before making your decision. The patient and their relatives will be asked for consent as soon as possible.

Background

A central part of treatment for critically ill patients involves intravenous administration of crystalloids. This carries a risk of fluid overload, particularly in conditions such as acute kidney injury and septic shock, where the ability to excrete salt and water is often impaired. Several observational studies have found an association between fluid overload and mortality in different clinical settings. However, it remains unclear whether this relationship is causal or whether fluid overload merely reflects disease severity and an underlying higher risk of death.

Purpose

We aim to investigate the effect of early, goal-directed fluid removal with furosemide or placebo in intensive care patients with fluid overload.

Study Description

This is a randomised, controlled, double-blind study designed to determine whether there is a difference in survival between two intervention groups. A total of 1,000 patients with fluid overload of 5% or more will be included. The degree of fluid overload will be assessed based on an assessment of the cumulative fluid balance, changes in body weight, and other clinical examinations (ultrasound, X-ray, signs of oedema, etc.).

Patients will be randomly assigned to receive either a continuous infusion of furosemide or a placebo (saline solution). The treatment is blinded for the patient, investigator, and treating clinicians. The goal is to remove fluid to achieve a negative fluid balance of at least 1 ml/kg/hour until neutral fluid status is reached. Thereafter, neutral fluid status will be maintained for the remainder of the ICU stay, up to a maximum of 90 days. The primary outcome measure is the number of days alive outside the hospital at 90 days.

A **one-year follow-up** will be conducted via a telephone interview, including a brief cognitive test and questions about health-related quality of life.

Potential Benefits of the Study

We expect that early, targeted treatment of fluid overload will lead to a faster normalisation of the body's fluid balance and thereby improve survival chances. Since allocation to the study groups is randomised, it is not guaranteed that the patient will personally benefit from participation.

The results of this study will provide important information about fluid management in the intensive care unit, which may help improve fluid therapy and diuretic treatment for future patients and benefit society.

Side Effects, Risks, and Disadvantages

The study treatment differs from standard care only in terms of a predetermined initiation time and a target rate of fluid removal. Furosemide is a well-known and frequently used diuretic for fluid overload and has been employed in intensive care units worldwide for many years. Participation in the study does not pose an increased risk of side effects or complications compared to other ICU patients with severe fluid overload treated with diuretics.

The most common and non-serious side effects of furosemide include:

- Electrolyte imbalances
- Hypovolemia
- High urine output
- Temporary increases in triglycerides, creatinine, and uric acid

More serious and rare side effects include:

- Allergic reactions
- Decreased platelet, red, and white blood cell counts
- Severe drops in blood pressure
- Pancreatitis
- Skin rash
- Worsening of kidney function
- Very rarely, hearing impairment

Saline solution, as used in this study, has no side effects at the administered doses.

There may be risks associated with the study that are not yet known. If any previously unknown side effects are discovered, you will be informed immediately.

Withdrawal from the Study

Participation is voluntary, and you may withdraw the patient from the study at any time by informing one of the attending physicians or the investigators. This will not affect the patient's further treatment. The attending physicians may also choose to terminate the patient's participation, in which case you will be informed of the reason.

Patient Compensation

In the unlikely event of harm caused by the study medication, the patient is covered by public patient insurance. If the patient wishes to file a complaint related to the study, guidance can be provided by the investigators or a patient advisor.

Confidentiality and Data Protection

All information will be handled confidentially. The patient will remain anonymous in reports and publications.

During the study, we will collect the following data from the patient's medical records:

- Medical history
- Laboratory results (up to 6 months before admission and throughout the ICU stay)
- Vital signs (heart rate, blood pressure, temperature, fluid balance, medication use, and organ support treatments)

The Danish Medicines Agency, the GCP unit, and the responsible investigators (sponsor and investigator) have access to the full medical record to ensure compliance with study protocols. All individuals with access to the records are bound by confidentiality obligations. The study is registered with the Danish Data Protection Agency. Consent includes permission to collect, process, and share necessary health data for quality control and monitoring purposes.

Financial Information

The study is initiated by **Professor and Consultant Morten Bestle** and is funded by:

- Novo Nordisk Foundation (5,082,180 DKK)
- Jakob Madsen and Wife Olga Madsen's Fund (100,000 DKK)
- Grosserer Jakob Ehrenreich and Wife Grete Ehrenreich's Fund (200,000 DKK)
- Svend Andersen's Fund (840,000 DKK)
- Sygeforsikringen Danmark (5,156,965 DKK)

Each participating site will receive **3,000 DKK per included patient** to cover recruitment and data collection costs.

None of the investigators have financial ties to companies or foundations that could influence the study results. The patient will not receive any financial compensation for participation.

Access to Results

The study is expected to conclude by the end of 2027. Results will be published in medical journals and presented at international conferences. If you wish to receive information about the study results, please contact the investigators. A summary of the results will also be available on the **European Clinical Trials Database**:
https://euclinicaltrials.eu/ (search for registration number **2024-512186-14-00**).

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