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**To the trial guardian**

**Information about a health science research project with patients with fluid overload admitted to the intensive care unit.**

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

**Introduction**

The patient in question is admitted to the intensive care unit and disabled as a result of their acute medical condition. We want to ask you, if you, as a trial guardian, will give consent to his/her participation in the study on behalf of the patient. Because the patient in question can’t give consent themself, you are able to do it on their behalf. Participation in the study is voluntary, and you can decline the offer at any point, without it will affect the current or future treatment of the patient.

Before you decide whether you would like to give consent as a trial guardian, it is important that you understand what the study is about, and why we are doing it. We therefor encourage you to read this information thoroughly.

The participant information will be explained to you in person, with the opportunity to ask any question you might have. If you decide that the patient can participate in the study, we would like you to sign the attached consent form. Remember that you have the right to think about it before you decide. The patient and their relatives will be asked for consent as soon as possible.

**Background**

A central part of the treatment of critically ill patients is intravenous administration of crystalloids. This creates a risk of fluid accumulation and overhydration, especially in cases like acute kidney injury and septic shock, where the ability to excrete salt and water is often reduced. Several observational studies have shown a correlation between fluid overload and death in multiple clinical contexts. It is still unknown if this correlation is causal, or if overhydration is simply an expression of severity of the illness and a higher underlying risk of death.

**Aim**

We want to investigate the effect of early, goal directed fluid removal with furosemide versus placebo in adult intensive care patients with fluid overload.

**Description of the trial**

This is a randomised, controlled, double-blinded trial designed to find a difference in mortality between the two intervention groups. We will include 1000 patients with fluid overload of 5% or more, calculated from the cumulated fluid balance and ideal bodyweight. The patients will be randomised to either infusion with furosemide or placebo (saline). The treatment is blinded for both patient, investigators and the treating clinicians. The goal is fluid removal resulting in a negative fluid balance of minimum 1 ml/kg/hour until a neutral fluid balance is achieved. Next, the neutral fluid balance must be maintained for the rest of the intensive care admission, or for maximum 90 days. Our primary outcome is days alive and out of hospital at 90 days.

**The gain of the study**

We expect that early and goal directed treatment of fluid overload will lead to a faster normalisation of the body’s fluid balance and thus increase the chance of survival. Since it is a randomised trial it is not certain that the patient will have any personal gain from participating.

The results of this trial will contribute with important knowledge about fluid therapy in the intensive care population. Hopefully it might improve our future fluid therapy and diuretic treatment, at the benefit of future patients and society.

**Side effects, risks, complications and downsides**

The trial intervention only differs from the usual treatment of fluid accumulation in the way that there is a fixed starting point and a target for how fast the patient is drained. Furosemide is well-known and frequently used to treat fluid overload. It has been used in intensive care units globally for many years. Participation in the study does not cause a higher risk of side effects or complications compared to other patients in the intensive care unit with severe fluid overload, that are treated with diuretics. The most important known side effects of furosemide are:

The most frequent and not serious side effects from furosemide are disturbances in salt balance, hypovolemia, large diuresis, temporarily increase of triglycerides, creatinine and urate. More severe and rare side effects are allergic reactions, a drop in platelets, red and white blood cells, severe drop in blood pressure, pancreatitis, rash and worsening of kidney function. Very rarely hearing loss may occur.

The treatment with saline has no side effects in the volumes which it is given in this trial.

Other risks from participating the trial we have no knowledge about might occur. If we discover side effects that you have not yet been informed about, you will be informed immediately.

**Withdrawal from the trial for the individual patient**

Giving consent to participation in the trial is voluntary, and you can at any time choose to withdraw the patient from the trial, by informing one of the doctors in the intensive care or one of the investigators without it will have any consequence for the further treatment. The doctors in the intensive care can also interrupt the trial, and in that case, you will be informed directly about the reason for this.

**Patient compensation**

In the unexpected case that the trial medicine causes any harm, the patient is covered by public patient insurance. If the patient wants to complain about the participation in this trial, he/she can seek guidance from the investigators or from patient counsellors in the hospital.

**Confidentiality**

All information is treated confidentially and, in the reporting, and publication of the trial results, the patient will remain anonymous. During the trial we will gather the following data from patients record: previous illnesses and hospitalisations, blood test results up to six months before hospitalisation, all blood test results during the current admission, all measurements of heart rate, blood pressure, blood oxygen saturation, temperature, fluid balance, type and amount of medication given, and use of life support (ventilator, dialysis).

The Danish Medicines Agency, the GCP-unit and the doctors responsible for the trial (sponsor and investigator) will have access to the patient’s entire record to ensure that the study is being conducted as agreed upon. Every person with access to the record has a duty of confidentiality. The trial has been reported to the Danish Data Protection Agency and consent to participation in the trial includes access to disclosure and processing of necessary information about the patient’s health, from the entire patient record, and other private and confidential information as a part of the sponsor’s and monitor’s quality control and monitoring, as well as to the National Board of Health’s division of control.

**Information** **on financial matters**

The trial was initiated by senior staff specialist, Morten Bestle and the physicians, Rasmus Berthelsen and Theis Itenov, all from Nordsjælland’s Hospital. The trial is funded by the Novo Nordisk Foundation (5.082.1280 DKK) and Jakob Madsen and his wife Olga Madsen’s Foundation (100.000 DKK). All study sites will receive 400 € for every patient included, to cover the costs of patient inclusion and data gathering.

None of the people responsible for the trial have any economic ties to companies or foundations, that could have potential interest in the outcome of this trial. The patient will not receive any financial compensation for participating in the trial.

## Insurance

During the trial the patient will be covered by the participating hospital’s insurance.

**Access to the results**

The trial is expected to be finished three months after the final patient has participated (summer 2023). Once the results have been processed, they will be published in medical journals and presented at international medical congresses. If you wish to receive information about the results of the trial, you can contact the investigators.

We hope that with this information you have gained enough insight into what it means for the patient to participate in the trial, and that it creates a basis for the decision on the patient’s participation. More information on the trial is available by contacting the investigators and we encourage you to read the attached document “Subjects’ Rights Health Science Research Project” from the Central Committees on Health Research Ethics.

If you wish to receive more information, please contact the investigators.

Kind regards,

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