GODIF

Goal directed fluid removal with furosemide in intensive care patients with fluid overload

– a randomised, blinded, placebo-controlled trial

Background

Fluid overload is a known risk factor for organ dysfunction and mortality. No guidelines exist for treatment of fluid overload in the ICU. The evidence for when and how fluid overload should be treated is sparce and insufficient.

GODIF is a blinded, randomised, clinical trial including 1000 participants in Europe investigating fast fluid removal from stable ICU patients with moderate to severe fluid overload.

The participants get randomised to furosemide infusion (10 mg/ml) or placebo infusion (NaCl). The intervention continues until neutral fluid balance is met.

Outcomes

Primary outcome:

- Days alive and out of hospital at day 90 after randomisation

Secondary outcomes:

- Days alive at day 90 without life support (vasopressor/inotropic support, mechanical ventilation, or renal replacement therapy)
- All-cause mortality after 90 days and 12 months
- Number of participants with one or more serious adverse reactions/events

Explorative outcomes:

- Health related quality of life and cognitive function 12 months after randomisation

Inclusion criteria

- 18 years or above
- Acute admission to the ICU
- Clinical stable assessed by clinician (minimum criteria: MAP > 50 mmHg, maximum noradrenaline infusion of 0.2 microg/kg/min. and lactate < 4.0 mmol/L)
- Minimum fluid accumulation estimated by treating clinician according to chart

Minimum fluid accumulation on inclusion

Height in cm	Male	Female
≤ 159 cm	+ 3000 mL	+ 2500 mL
160 – 169 cm	+ 3500 mL	+ 3000 mL
170 – 179 cm	+ 4000 mL	+ 3500 mL
180 – 189 cm	+ 4500 mL	+ 4000 mL
≥ 190 cm	+ 5000 mL	+ 4500 mL

Goal for daily minimum negative fluid balance until neutral fluid balance is met

Height in cm	Male	Female
≤ 159 cm	-1300 mL/24 h	-1200 mL/24 h
160 – 169 cm	-1500 mL/24 h	-1400 mL/24 h
170 – 179 cm	-1700 mL/24 h	-1600 mL/24 h
180 – 189 cm	-1900 mL/24 h	-1800 mL/24 h
≥ 190 cm	-2000 mL/24 h	-1900 mL/24 h

Assessment of fluid status

No gold standard measuring method for fluid status exists. Fluid balances and body weight are imprecise measures of fluid status. Loss of muscle mass is expected during an ICU stay and a baseline weight for the healthy normohydrated patient are often not available.

To get the best assessment of the patient's fluid status we ask the clinicians to assess the fluid status according to the available fluid balances, changes in body weight and clinical examinations (oedema, chest X-ray, ultrasound, ect.).

This assessment will be used on inclusion and for stopping the intervention when the patient is in neutral fluid balance.

Trial drug

Starting dose is a bolus of 0.5-4.0 mL according to the treating physician's discretion, followed by infusion with 2 mL/h. The infusion must be adjusted according to effect and goal for the daily negative fluid balance. Infusion rate is 0-4 mL/h. Fluid removal must continue until neutral fluid balance is achieved. The neutral fluid balance must be maintained for the rest of the admittance or maximum 90 days. In case of new fluid accumulation, the trial drug must be restarted.

In case of circulatory instability, the resuscitations-algorithm must be used, and trial drug paused.

Habitual diuretics are allowed. In case of development of hypernatremia thiazides can be prescribed. No other diuretics are allowed during the trial.

Escape procedures

Open label furosemid may only be used in case of:

- Hyperkalaemia (plasma potassium > 6.0 mmol/L)
- Respiratory failure (P/F-ratio < 26 kPa (200 mm)) due to fluid overload assessed by treating physician

Renal replacement therapy may only be started in case of:

- Hyperkalaemia (plasma potassium > 6.0 mmol/L)
- Respiratory failure (P/F-ratio < 26 kPa (200 mm)) due to fluid overload assessed by treating physician
- Severe metabolic acidosis attributable to acute kidney injury (pH < 7.20 and SBE < -10 mmol/L)
- Persistent acute kidney injury > 72 hours (defined as: oliguria/anuria or S-creatinine has not declined to 50% from peak value)

Contact and further information

Nordsjællands Hospital, University of Copenhagen, Department of Anaesthesiology and Intensive Care Medicine, Denmark • More information on www.cric.nu/godif • Hotline phone number: +45 48 29 67 73