# Oral furosemide and hydrochlorothiazide /amiloride versus intravenous furosemide for the treatment of nephrotic edema

<b>Submission date</b> 19/12/2020	<b>Recruitment status</b> No longer recruiting	[X] Prospectively registered
		Protocol
Registration date 29/12/2020	Overall study status Completed	Statistical analysis plan
		[X] Results
<b>Last Edited</b> 07/12/2023	Condition category Urological and Genital Diseases	Individual participant data

#### Plain English summary of protocol

Background and study aims

Nephrotic syndrome is a kidney condition characterised by very high levels of protein in the urine (proteinuria), low levels of protein in the blood, and swelling, especially around the eyes, feet, and hands.

Furosemide is a type of medicine called a diuretic. It's used to treat high blood pressure, heart failure and edema (a build up of fluid in the body). It's also sometimes used to help you pee when your kidneys aren't working properly. Diuretics are sometimes called "water pills/tablets" because they make you pee more.

Our aim was to evaluate how nephrotic edema responds to a combined oral dose of furosemide, hydrochlorothizide and amiloride compared to intravenous furosemide.

#### Who can participate?

Adult patients with diagnosis of nephrotic syndrome and diuretic resistant edema.

#### What does the study involve?

Patients will be assigned to one of the two treatment groups.

Group 1 in which intravenous Furosemide is administered

Group 2 in which patients receive oral Furosemide and Hydrochlorothiazide/Amiloride Clinical and laboratory measurements will be performed for 5 days.

What are the possible benefits and risks of participating?

All participants will have the opportunity to receive a detailed general evaluation and possible benefits regarding weight loss. There are the normal possible side effects of both treatments.

Where is the study run from? Fundeni Clinical Institute (Romania)

When is the study starting and how long is it expected to run for? January 2020 to December 2022

Who is funding the study? Fundeni Clinical Institute (Romania)

Who is the main contact? Dr Georgiana Fratila georgianafratila27@gmail.com

# Contact information

#### Type(s)

Scientific

#### Contact name

Dr Georgiana Fratila

#### Contact details

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# Additional identifiers

# EudraCT/CTIS number

Nil known

**IRAS** number

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

46275

# Study information

#### Scientific Title

A prospective, randomized, unicentric study investigating the non-inferiority of combined oral diuretics furosemide and hydrochlorothiazide/amiloride to intravenous furosemide in patients with nephrotic edema and diuretic resistance

#### Acronym

**FANS** 

#### **Study objectives**

Furosemide is traditionally the drug of choice when considering using a class of diuretics and new data show that ENaC blockade improves diuresis in patients with nephrotic edema, with effectively reduced swelling and body weight.

#### Ethics approval required

Old ethics approval format

#### Ethics approval(s)

Approved 08/09/2020, local ethical board of Fundeni Clinical Institute (Fundeni Street no. 258, 022328, Bucharest, Romania; +40 (0)724545131; secretariat@icfundeni.ro), ref: 46275

#### Study design

Prospective randomized unicentric study

#### Primary study design

Interventional

#### Secondary study design

Randomised controlled trial

#### Study setting(s)

Hospital

#### Study type(s)

Treatment

#### Participant information sheet

Not available in web format, please use the contact details to request a participant information sheet

## Health condition(s) or problem(s) studied

Diuretic treatment in nephrotic syndrome and diuretic-resistant edema

#### **Interventions**

The study will include an estimated number of 20 patients, 10 patients in each treatment group. Patients will have a 24 h washout period with no diuretics administered and then, based on their FENa <0.2%, patients will be assigned to of the two treatment groups.

Computer-generated randomization will be performed using online software to generate block randomization.

Group 1 in which intravenous furosemide is administered, starting with a 40 mg bolus and then continuous administration of 5 mg/h, with dose adjustment according to urinary output (>5 l/24 h - dose decreased to 2.5 mg/h; <5 l/24 h - the same dose of 5 mg/h).

Group 2 in which patients receive furosemide 40 mg/day and hydrochlorothiazide/amiloride 50 and 5 mg/day, respectively.

Clinical and laboratory measurements will be performed as follows:

- 1. Clinical measurements: daily body weight, urinary output, systolic and diastolic blood pressure (2 times a day) and hydration status by bioimpedance
- 2. Laboratory measurements: serum markers (creatinine, urea, albumin, hematocrit, Na, K, Ca, Mg, bicarbonate, pH) at admission, at 24 hours and daily after randomization, urinary markers

(creatinine, Na) for FENa and (Na, K) daily after randomization and 24 hours proteinuria, ACR 24 hours prior to randomization and at 5 days.

#### Intervention Type

Drug

#### Phase

Not Applicable

#### Drug/device/biological/vaccine name(s)

Furosemide, hydrocholorothizide, amiloride

#### Primary outcome measure

- 1. Weight measured at baseline and daily after randomization during the follow up period
- 2. Hydration status measured by bioimpedance at baseline and daily after randomization during the follow up period

#### Secondary outcome measures

- 1. Low blood pressure is established by daily measuring of blood pressure using a manual sphygmomanometer
- 2. Severe hyponatremia is established by daily measurement of serum sodium (blood test)
- 3. Hypokalemia and hyperkalemia is established by daily measurement of serum potassium (blood test)
- 4. Severe hypomagnesemia is established by daily measurement of serum magnesium (blood test)
- 5. Alcalosis is established by daily measurement of acid base balance (pH of venous blood gas sample)
- 6. Acute kidney injury is established by daily measurement of serum creatinine (blood test) and urinary output (over 24 h)
- 7. Aggravated hypervolemia at 3 days is established by fixed or increased body weight with clinical increased peripheral edema and urinary output <1.5 l/24 h

#### Overall study start date

01/06/2020

### Completion date

01/05/2023

# Eligibility

#### Key inclusion criteria

- 1. Age >18 years old
- 2. Nephrotic syndrome in patients without diabetes mellitus
- 3. Diuretic resistance
- 4. eGFR >30 ml/min/1.73 m<sup>2</sup>

#### Participant type(s)

Patient

#### Age group

#### Adult

#### Lower age limit

18 Years

#### Sex

Both

#### Target number of participants

20

#### Total final enrolment

22

#### Key exclusion criteria

- 1. Age <18 years old
- 2. Nephrotic syndrome in patients with type 1 or type 2 diabetes
- 3. eGFR < 30 ml/min/1.73 m<sup>2</sup>
- 4. Hypokalemia and hyperkalemia
- 5. Severe hyponatremia
- 6. Alcalosis
- 7. Severe pulmonary congestion
- 8. Active infection
- 9. NSAIDs use within the last month
- 10. Pregnancy
- 11. Kidney transplant
- 12. Known allergy to furosemide, hydrochlorothiazide or amiloride
- 13. Patients with a defibrillator/pacemaker/metal prosthesis

#### Date of first enrolment

01/02/2021

#### Date of final enrolment

31/12/2022

# Locations

#### Countries of recruitment

Romania

# Study participating centre Fundeni Clinical institute

Department of Nephrology Fundeni Fundeni Street no. 258 District no. 2 Bucharest Romania 022328

# Sponsor information

#### Organisation

Institutul Clinic Fundeni

#### Sponsor details

Fundeni Street no. 258 District no. 2 Bucuresti Romania 022328

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gener732000@yahoo.com

#### Sponsor type

Hospital/treatment centre

#### Website

https://icfundeni.ro/

#### ROR

https://ror.org/05w6fx554

# Funder(s)

#### Funder type

Hospital/treatment centre

#### **Funder Name**

Fundeni Clinical Institute

# **Results and Publications**

#### Publication and dissemination plan

Planned publication in nephrology journals such as American Journal of Kidney Diseases, BCM Nephrology, Kidney International etc.

#### Intention to publish date

31/12/2023

#### Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Gener Ismail (gener732000@yahoo.com).

# IPD sharing plan summary

Available on request

**Study outputs** 

Output typeDetailsDate createdDate addedPeer reviewed?Patient-facing?Results article01/11/202307/12/2023YesNo