

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

Submission date 19/12/2020	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 29/12/2020	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 07/12/2023	Condition category Urological and Genital Diseases	<input type="checkbox"/> 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, hydrochlorothiazide 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
18 Aleea Sinaia
84A Building
Entrance 1
Apartment 60
10th Floor
Bucuresti
Romania
022765
+40 (0)747853133
valentina-georgiana.fratila@drd.umfcd.ro

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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

Study type(s)

Treatment

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 one 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, hydrochlorothiazide, amiloride

Primary outcome(s)

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

Key secondary outcome(s)

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. Alkalosis 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

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 m²

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

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 m²
4. Hypokalemia and hyperkalemia
5. Severe hyponatremia
6. Alkalosis
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

ROR

<https://ror.org/05w6fx554>

Funder(s)

Funder type

Hospital/treatment centre

Funder Name
Fundeni Clinical Institute

Results and Publications

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 type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/11/2023	07/12/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes