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

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

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?
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Contact information

Type(s)
Scientific

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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 m²

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 m²
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
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Sponsor information

Organisation
Institutul Clinic Fundeni

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