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Sodium citrate versus sodium bicarbonate for increased acidity (metabolic acidosis) in patients with chronic kidney disease

Submission date
21/09/2021

Recruitment status
No longer recruiting

Registration date
22/09/2021

Overall study status
Completed

Last Edited
05/10/2021

Condition category
Urological and Genital Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The buildup of acid in the body due to kidney disease or kidney failure is called metabolic acidosis. When your body fluids contain too much acid, it means that your body is either not getting rid of enough acid, is making too much acid, or cannot balance the acid in your body. Metabolic acidosis is a common complication of chronic kidney disease (CKD). It means a build up of hydrogen ions with a low level of bicarbonate. This retention of hydrogen ions happens from early stages of CKD, when bicarbonate level is normal and later on it translates into metabolic acidosis. This and can cause cardiovascular and bone mineral disorders, but also CKD progression through interstitial inflammation and fibrosis.
Alkali therapy with sodium bicarbonate or citrate on top of alkali-rich diet (low animal protein or enriched in fruits and vegetable diets) it can help to raise serum bicarbonate level and thus slowing CKD progression. It was also demonstrated that alkali therapy is well tolerated, with few to no adverse events.
Current clinical practical guidelines recommend correcting the serum bicarbonate to >22 mEq/l by oral bicarbonate supplementation to maintain serum bicarbonate within the normal range (22-26 mEq/l) and although data support the hypothesis that alkali therapy preserves kidney function in patients with CKD, evidence from large-scale clinical trials is still necessary before definitive conclusions can be drawn. Moreover, to our knowledge there is no clinical trial comparing sodium citrate with sodium bicarbonate for metabolic acidosis in chronic kidney disease.

Who can participate?
Adult patients with diagnosis of metabolic acidosis and chronic kidney disease

What does the study involve?
Patients will be assigned to one of the two treatment groups.
Group 1 will receive sodium bicarbonate capsules
Group 2 will receive sodium citrate solution
Clinical and laboratory measurements will be performed monthly for a year; certain laboratory measurements will be done at 1 mo and at 12th mo.

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?
Septemeber 2021 to January 2024

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

Who is the main contact?
Dr. Gener Ismail
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
59531

Study information

Scientific Title
A parallel-design randomized controlled trial investigating the treatment of metabolic acidosis in patients with chronic kidney disease with either sodium citrate versus sodium bicarbonate

Acronym
SoCiB

Study objectives
Data support the hypothesis that alkali therapy preserves kidney function in patients with CKD, but there is no clinical trial comparing sodium citrate with sodium bicarbonate for metabolic acidosis in chronic kidney disease.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/09/2021, Fundeni Clinical Institute (Fundeni Street no. 258, 022328, Bucharest, Romania; +40 (0)724545131; secretariat@icfundeni.ro), ref: 59531

Study design
Parallel-design randomized controlled 1:1 trial single center

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Alkali therapy of metabolic acidosis in patients with chronic kidney disease

Interventions
Based on their level of serum bicarbonate, subjects will receive either high doses or low doses of sodium bicarbonate or sodium citrate.
Computer-generated randomization will be performed using online software to generate block randomization.

Group 1: treatment will be started with sodium bicarbonate 600 mg/d if serum bicarbonate is 19-22 mEq/l or 600 mg twice daily if serum bicarbonate is under 18 mEq/l and if serum bicarbonate is still under the target value at next visits, increase sodium bicarbonate by one tablet to a maximum dose of 3600 mg.
Group 2: treatment will be started with sodium citrate 1691 mg/306 mg/d if serum bicarbonate is 19-22 mEq/l or sodium citrate 1691 mg/306 mg twice daily if serum bicarbonate is under 18 mEq/l and if serum bicarbonate is still under the target value at next visits, increase sodium citrate taking the oral solution twice, thrice or four times per day to a maximum dose of 7988 mg.

Clinical and laboratory measurements will be performed as follows:
- at baseline and at the end of the study period: urinary albumin/creatinine ratio (RAC), serum soluble plasminogen activator urokinase receptor (suPAR) and arterial stiffness
- at one month: 24 hour Ambulatory Blood Pressure Monitoring (ABPM)
- monthy:
Paraclinical parameters: eGFR ml/min/1.73 m^2, serum creatinine, urea, sodium, potassium, chloride, bicarbonate, albumin, urinary pH and 24-hour urinary potassium
Clinical parameters: systolic and diastolic pressure, body weight, digestive symptoms

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
sodium bicarbonate, sodium citrate

Primary outcome(s)
Decline in renal function assessed by changes in eGFR (CKD-EPI equation) and change in serum bicarbonate assessed by a venous blood sample from baseline (Bs) and monthly to the end of the study (EOS) (12 months)

Key secondary outcome(s))
1. All-cause mortality measured using patient records at the end of the study
2. ESRD measured using a blood sample for CKD-EPI Equation for Glomerular Filtration Rate (GFR) at baseline (Bs) and monthly to the end of the study (EOS).
3. Urinary albumin/creatinine ratio (RAC) measured from a spot urine sample at baseline (Bs) and monthly to the end of the study (EOS).
4. Serum albumin measured using blood sample at baseline (Bs) and monthly to the end of the study (EOS).
5. Serum soluble plasminogen activator urokinase receptor (suPAR) measured from a venous blood sample at baseline (Bs) and monthly to the end of the study (EOS).
6. Arterial stiffness measured by sphygmoCor technology (pulse wave analysis) at baseline (Bs) and monthly to the end of the study (EOS).

Safety endpoints
Percentage of patients who develop during the study:
1. Blood pressure >140/90 mmHg measured using a manual sphygmomanometer
2. Hypervolemia - peripheral edema or dyspnea with crackles (appreciated clinically and on auscultation with a stethoscope) or high blood pressure needing initiation or escalation of antihypertensive medication or diuretics measured using a manual sphygmomanometer
3. Hypokalemia < 3 mEq/l measured using a blood sample
4. Serum bicarbonate >28 mEq/L measured using a blood sample
5. Calciphylaxis diagnosed by clinical presentation
6. Digestive symptoms (nausea, vomiting) by self report

Completion date
01/01/2024

Eligibility

Key inclusion criteria
1. Age >18 years
2. eGFR 15-45 ml/min/1.73 m² CKD EPI
3. Serum bicarbonate 10-22 mmol/l on to two different ocassions
4. Ability to travel to study visits
5. Ability to follow the study treatment regimen
6. A wash-out period of one month if previous alkali therapy (such as sodium bicarbonate, sodium citrate, potassium citrate, baking soda, etc)

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Hipokalemia <3 meq/l
2. Uncontrolled blood pressure (>150/90 mmhg under treatment with more than 3 different classes of antihypertensive drugs, including diuretics)
3. Heart failure with active class III or IV New York Heart Association, known left ventricular ejection fraction ≤30%, or hospital admission for heart failure within the past 3 months
4. Hypervolemia of any cause (nephrotic syndrome, liver, or heart failure) considered unsafe for the patient by the PI for the patient
5. Active hepatic disease
6. Chronic gastrointestinal disorder (treatment adherence unreliable)
7. Active malignancy
8. Pregnancy
9. Patients taking amilorid or sevelamer
10. Patients refusing to sign the informed consent

Date of first enrolment
01/01/2022

Date of final enrolment
01/01/2023

Locations

Countries of recruitment
Romania

Study participating centre
Fundeni Clinical institute
Department of Nephrology
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?
Participant information sheet	in Romanian		22/09/2021	No	Yes
Protocol file			22/09/2021	No	No