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

Submission date	Recruitment status	[X] Prospectively registered		
21/09/2021	No longer recruiting	[X] Protocol		
Registration date	Overall study status	Statistical analysis plan		
22/09/2021	Completed	Results		
Last Edited	Condition category	Individual participant data		
05/10/2021	Urological and Genital Diseases	<ul><li>Record updated in last year</li></ul>		

## 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? September 2021 to January 2024

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

Who is the main contact? Dr. Gener Ismail gener.ismail@umfcd.ro

## Contact information

## Type(s)

Scientific

#### Contact name

Dr Gener Ismail

#### Contact details

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## Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

ClinicalTrials.gov (NCT)

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<sup>2</sup>, 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 m<sup>2</sup> 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

## 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