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Bicarbonate for Chronic Kidney Disease and Acidosis

Submission date
14/02/2012

Recruitment status
No longer recruiting

Registration date
17/02/2012

Overall study status
Completed

Last Edited
18/03/2021

Condition category
Urological and Genital Diseases

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Many people with chronic kidney disease have higher than usual levels of acid in the blood. Higher levels of acid may worsen kidney function, blood vessel health and bone health, as well as stopping your muscles from working as well as they should. This in turn may make people feel tired and reduce quality of life. Acid levels can be treated with sodium bicarbonate (used in baking powder); this is used as a treatment in some people with kidney disease and high levels of acid. We do not know whether the benefits of this treatment (on muscle, bone, kidneys, blood vessels and quality of life) are greater that the potential side effects (such as raising blood pressure, fluid retention and having to take extra tablets).
We therefore aim to test whether taking daily bicarbonate tablets improves physical function, quality of life, bone and blood vessel health in patients with advanced chronic kidney disease and high levels of acid in the blood.

Who can participate?
People aged 60 and over who have advanced chronic kidney disease, but who are not on dialysis

What does the study involve?
The study takes 2 years in total to complete. The study is of randomised, double-blind design. This means that you will be asked to take medication by mouth three times a day. This will either contain bicarbonate, or a placebo (dummy) medication. The one that you will be given is decided in a random way (a bit like tossing a coin, but done by a computer). Neither you nor the research team will know which you are taking until after the study is finished. This means that the results of the study cannot be influenced by you or the researchers knowing what you are taking. Participants will receive either sodium bicarbonate or placebo (dummy tablets), starting with 1 tablet three times a day, rising to two tablets three times a day after 3 months. We will do the following tests at each study visit, which take place before the start of the study then at 3, 6, 12 and 24 months. We will measure your blood pressure while you are sitting down. We will check your height and weight. We will take a blood test (about two tablespoons of blood)). Blood samples will be stored and tested at the end of the study. We will ask you to bring a urine sample with you. You will be asked to do some mobility tests: - standing tests, balance tests, timed getting up from a chair and a test to measure your hand grip strength. You will be asked to walk up and down a corridor for six minutes at your own pace. We will measure how far you

can walk in that time. We will ask you two questionnaires about your quality of life and how your kidney problems affect your quality of life.

What are the possible benefits and risks of participating?
Taking part in the trial will allow us to see if bicarbonate treatment improves the health and physical function of people with acidosis and chronic kidney disease. This dose of sodium bicarbonate is commonly used in people with kidney disease. Increase in blood pressure, fluid retention and bloating are experienced by some people, and we will be asking you about these side effects at each visit. Having blood taken can cause some bruising. The blood pressure cuff causes mild discomfort to some people.

Where is the study run from?
The study is run from the University of Dundee and centres in Aberdeen, Canterbury, Dundee, Salford, Sheffield, Preston, Portsmouth, Mid Essex, Manchester, Leicester, North Midlands, Pennine, Wolverhampton, Highland, Wirral, Sussex, Exeter, Plymouth, Southend, Fife, Gloucestershire and Birmingham (UK).

When is the study starting and how long is it expected to run for?
The study will start recruitment in July 2012. Results are anticipated to be available in June 2018; participants will be recruited for the first 18 months of the trial.

Who is funding the study?
The Health Technology Assessment board (HTA) of the National Institute for Health Research, UK

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2011-005271-16

Protocol serial number
2010NE02; HTA 10/71/01

Study information

Scientific Title
Does oral sodium bicarbonate therapy improve function and quality of life in older patients with chronic kidney disease and low-grade acidosis?

Acronym
BiCARB

Study objectives
To determine whether oral bicarbonate therapy improves physical function and quality of life compared to placebo in older people with Chronic Kidney disease and mild acidosis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of Scotland Research Ethics Service REC 2, 16/03/2012

Study design
Randomised double-blind parallel-group placebo-controlled trial

Primary study design
Interventional

Study type(s)
Quality of life

Health condition(s) or problem(s) studied
Chronic kidney disease

Interventions
Oral sodium bicarbonate 500 mg three times a day, rising to 1 g three times a day or matching placebo

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Sodium bicarbonate

Primary outcome(s)
Change in Short Physical Performance Battery (SPPB) between baseline and 12 months

Key secondary outcome(s))
Current secondary outcome measures as of 10/07/2015:
1. EQ-5D
2. SPPB (baseline, 3, 6, 24 months)
3. Serum sodium, potassium, magnesium, urea, bicarbonate, calcium, phosphate, alkaline phosphatase, creatinine (eGFR calculated by MDRD4 equation), albumin, haemoglobin, thyroid function, HbA1c, lipids
4. Cystatin C
5. Urinary protein/creatinine ratio and urinary albumin/creatinine ratio
6. Height (at screening visit only), weight and anthropometric data (mid arm circumference; triceps skinfold thickness; mid thigh circumference)
7. Handgrip strength measured using dynamometry
8. Six minute walk test
9. KDQoL, a disease-specific quality of life measure
10. Office blood pressure. 3 readings will be taken; the mean of the 2nd and 3rd reading will be used as the outcome
11. Commencement on dialysis
12. All-cause mortality (via General Register Office death records)
13. Death from end-stage renal failure
14. Cardiovascular mortality
15. All hospitalisations (via hospital and GP morbidity records; including heart failure, other cardiovascular and renal-related hospitalisations)
16. Outpatients and general practitioner (GP) visits
17. Changes in medication use, with particular focus on vascular medications and phosphate binders
18. Fractures will be recorded by direct patient report, verified with GP and hospital records
19. Falls will be recorded prospectively using the validated falls diary method
20. Information on side effects (e.g. nausea, indigestion, ankle oedema) will be sought by patient self-report. Adherence to study medication will be assessed by tablet counting.

21. Bone and Vascular Secondary outcomes (measured at baseline, 12 and 24 months)
21.1. Serum markers of bone turnover: bone-specific alkaline phosphatase and tartrate-resistant acid-phosphatase 5b
21.2. Parathyroid hormone (PTH), 25-hydroxy vitamin D (25OHD) and 1,25OHD
21.3. B-type natriuretic peptide
Measured at baseline, 3, 6, 12, and 24 months

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1. EQ-5D
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21. Bone and Vascular substudy - Secondary outcomes (measured at baseline, 12 and 24 months) on up to 150 patients
21.1. Bone mineral density at femoral neck and forearm using DEXA.
21.2. Body composition using DEXA.
21.3. Serum markers of bone turnover: bone-specific alkaline phosphatase and tartrate-resistant acid-phosphatase 5b
21.4. Parathyroid hormone (PTH), 25-hydroxy vitamin D (25OHD) and 1,25OHD
21.5. Arterial stiffness, measured using pulse wave velocity and augmentation index
21.6. B-type natriuretic peptide
Measured at baseline, 3, 6, 12, and 24 months

Completion date
30/09/2018

Eligibility

Key inclusion criteria
Current inclusion criteria as of 10/07/2015:
1. Participant is willing and able to give informed consent for participation in the study
2. Male or female aged 60 years or above
3. Estimated Glomerular Filtration Rate (eGFR) <30 ml/min (i.e. CKD stages 4 and 5) found at screening visit
4. Serum Bicarbonate <22 mmol/L
5. Able (in the Investigators opinion) and willing to comply with all study requirements

Previous inclusion criteria:
1. Participant is willing and able to give informed consent for participation in the study
2. Male or female aged 65 years or above
3. Estimated Glomerular Filtration Rate (eGFR) <30 ml/min (i.e. CKD stages 4 and 5) found at screening visit
4. Serum Bicarbonate <22 mmol/L
5. Able (in the Investigators opinion) and willing to comply with all study requirements

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Senior

Sex
All

Total final enrolment
300

Key exclusion criteria
Current exclusion criteria as of 10/07/2015:
1. Severe cognitive impairment precluding written informed consent
2. Already taking bicarbonate therapy; those taking bicarbonate therapy may be included after a 3 month washout period.
3. Documented renal tubular acidosis (such patients are likely to require bicarbonate, often in very large doses)
4. On renal replacement therapy (haemodialysis or peritoneal dialysis)
5. Anticipated to start renal replacement therapy within 3 months
6. Severe cognitive impairment precluding written informed consent
7. Participant who is terminally ill, as defined as less than 3 months expected survival
8. Decompensated chronic heart failure (to ensure that fluid overload is not exacerbated by the additional sodium load from the intervention)
9. Bisphosphonate therapy (to avoid obscuring bone turnover effects; patients with CKD stages 4 /5 should not usually be taking bisphosphonates as this is a listed contraindication)
10. Uncontrolled hypertension (BP>150/90 despite use of four agents) unless evidence of well controlled blood pressure e.g. 24 hour BP readings or home readings

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7. Participant who is terminally ill, as defined as less than 3 months expected survival
8. Decompensated chronic heart failure (to ensure that fluid overload is not exacerbated by the additional sodium load from the intervention)
9. Bisphosphonate therapy (to avoid obscuring bone turnover effects; patients with CKD stages 4 /5 should not usually be taking bisphosphonates as this is a listed contraindication)
10. Calcium carbonate use (to avoid interaction with bicarbonate)
11. Sevelamer hydrochloride use (to avoid increasing acid load)
12. Uncontrolled hypertension (BP>150/90 despite use of four agents)

Date of first enrolment
01/07/2012

Date of final enrolment
31/03/2016

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Ninewells Hospital
Dundee
United Kingdom
DD1 9SY

Sponsor information

Organisation
Tayside Medical Sciences Centre (UK)

ROR
https://ror.org/000ywep40

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
De-identified participant level data will be available from the Chief Investigator or the Sponsor to bona-fide academic research teams, subject to submission of a proposal for data use, analysis and publication, and approval by a data-sharing committee.

Previous publication and dissemination plan criteria:
Planned publication in high-impact peer reviewed journal, estimated mid to late 2019.

IPD sharing statement
De-identified participant level data will be available from the Chief Investigator or the Sponsor to bona-fide academic research teams, subject to submission of a proposal for data use, analysis and publication, and approval by a data-sharing committee.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2020	09/04/2020	Yes	No
Protocol article	protocol	01/08/2015		Yes	No
Basic results		22/02/2019	22/02/2019	No	No

Basic results			21/04/2020	No	No
Other publications	HTA report	01/06/2020	23/06/2020	Yes	No
Other publications	secondary analysis of associations between frailty, physical performance, and renal biomarkers	01/03/2021	18/03/2021	Yes	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes