ISRCTN14027629 https://doi.org/10.1186/ISRCTN14027629

Multicentre evaluation of sodium bicarbonate in acute kidney injury in critical care (MOSAICC)

Submission date
09/07/2021

Recruitment status
Recruiting

Registration date
27/07/2021

Overall study status
Ongoing

Last Edited
16/01/2025

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Many people who come into intensive care have a sudden worsening in kidney function called acute kidney injury (AKI) that happens as part of their illness. AKI causes more acid than normal to build up in the blood (a process known as acidosis), which can cause further harm. In these patients, kidney replacement therapy (KRT), commonly known as 'dialysis', is the most commonly used treatment but it is invasive, has added risks and requires specialist staff and equipment, making it very expensive.

Another option to treat patients with acidosis is to give an alkali (opposite to acid), such as sodium bicarbonate, to stop the effects of acid build-up and bring the level in the blood to normal. Sodium bicarbonate is a cheap and accessible treatment with the potential to increase survival and avoid KRT, but there is little clinical evidence to support its use in patients with acidosis and AKI.

We want to find out whether using sodium bicarbonate to treat critically ill people with acidosis and AKI improves survival and is cost-effective for the NHS.

Who can participate?
Patients aged 18 years and over with metabolic acidosis and acute kidney injury from about 60 UK NHS ICUs.

What does the study involve?
Eligible patients will be randomly allocated to either receive intravenous sodium bicarbonate or not receive it. The researchers will follow all patients up to 90 days later by 'linking' study data with routinely collected national records. They will also send a questionnaire to all patients at 90 days and one year to find out about their quality of life and use of health services. They will find out if sodium bicarbonate was more effective than no sodium bicarbonate by comparing the number of patients alive in each group at 90 days.
What are the possible benefits and risks of participating? There is no guarantee that patients will benefit directly by taking part in the trial. Sodium bicarbonate is licensed and widely used in the

NHS for the treatment of acidosis. The Medicines and Healthcare products Regulatory Agency (MHRA) have confirmed that the risks of participating in the study are no higher than that of standard medical care.

Like all medicines, sodium bicarbonate can cause side effects, although not everybody gets them. Patients are monitored closely by doctors and nurses. If they feel it is in the participant's best interest to stop the use of sodium bicarbonate, they will do so. Although participants may not directly benefit from taking part, research like this helps to continually improve treatments and care provided to all patients now and in the future.

Where is the study run from?
University Hospitals of Derby & Burton NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
March 2021 to May 2027

Who is funding the study?
National Institute for Health Research (NIHR) – Health Technology Assessment Programme (UK)

Who is the main contact?
Catherine Oversby, MOSAICC@icnarc.org

Study website
https://www.icnarc.org/Our-Research/Studies/Current-Studies/MOSAICC/

Contact information

Type(s)
Scientific

Contact name
Dr Catherine Oversby

Contact details
Intensive Care National Audit & Research Centre
Napier House
24 High Holburn
London
United Kingdom
WC1V 6AZ
+44 (0)20 7831 6878
Catherine.Oversby@icnarc.org

Type(s)
Scientific

Contact name
Prof Lui Forni

Contact details

Department of Clinical & Experimental Medicine
School of Biosciences and Medicine
University of Surrey
Guildford
United Kingdom
GU2 7XH
+44 (0)1483571122
luiforni@nhs.net

Type(s)
Public

Contact name
Dr Study Team

Contact details
-
-
United Kingdom
-
None provided
MOSAICC@icnarc.org

Additional identifiers

EudraCT/CTIS number
2021-002587-44

IRAS number
1003836

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 49697, Grant Codes: NIHR129617, IRAS 1003836

Study information

Scientific Title
Evaluating the clinical and cost-effectiveness of sodium bicarbonate administration for critically ill patients with acute kidney injury and metabolic acidosis

Acronym
MOSAICC

Study objectives
MOSAICC is a multi-centre,open,data-enabled randomised clinical trial with internal pilot phase and integrated economic evaluation. The main objective is to evaluate the clinical and cost-effectiveness of IV 8.4% sodium bicarbonate, as compared with no sodium bicarbonate, on 90-

day all-cause mortality (primary clinical effectiveness outcome) and on incremental costs, quality-adjusted life years and net monetary benefit at 90 days (primary economic evaluation outcome) in critically ill patients with metabolic acidosis and acute kidney injury.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 23/09/2021, Manchester Central REC (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8133; gmcentral.rec@hra.nhs.uk), ref: 21/NW/0228

Study design
Interventional randomized controlled trial

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 patient information sheet

Health condition(s) or problem(s) studied
Critically ill patients with metabolic acidosis and acute kidney injury

Interventions
For patients randomised to the intervention group, clinical staff will administer sodium bicarbonate 8.4% weight/volume intravenously, aiming to restore pH to >=7.30. The intervention will continue for the duration of the critical care unit admission or until initiation of kidney replacement therapy. For patients receiving sodium bicarbonate, the starting dose is 50ml administered over 30-60 minutes.
Arterial blood gas analysis should be performed 1-2 hours after each infusion.
Participants should be assessed for response to treatment and repeated doses should be administered depending on subsequent pH readings and clinical status (including haemodynamic monitoring heart rate, blood pressure), as well as blood gas analysis (including pCO2 HCO3 and electrolytes) up to a maximum of 500ml over a 24-hour period.

Patients randomised to the control group will not receive IV sodium bicarbonate.

Once eligible participants have been randomised, indications to commence KRT may subsequently develop and in these situations KRT may be initiated at the discretion of the treating clinician. In both groups, all other care will be provided by the discretion of the treating clinical team according to local routine practice.

Intervention Type
Other

Phase
Phase IV

Primary outcome measure
1. Clinical effectiveness measured by all-cause mortality at 90 days following randomisation using patient records
2. Cost-effectiveness measured using incremental costs, QALYs, and net monetary benefit at 90 days following randomisation using patient records

Secondary outcome measures
1. Mortality at critical care unit discharge, 28 days and 1 year measured using patient records
2. Receipt and duration of respiratory, renal, and advanced cardiovascular organ support, defined according to the Critical Care Minimum Dataset (CCMDS), during the critical care stay measured using patient records
3. Duration of critical care unit and acute hospital stay measured using patient records
4. On-going requirement for KRT at 90 days and 1 year measured using patient records
5. HRQoL at 90 days and 1 year (assessed using the EQ-5D-5L questionnaire)
6. Resource use and costs at 90 days and 1 year measured using patient records
7. Estimated lifetime incremental cost-effectiveness based on the Health Services questionnaire, as well as resource use and costs at 90 days and 1 year and HRQoL

Overall study start date
01/03/2021

Completion date
31/05/2027

Eligibility

Key inclusion criteria
Current inclusion criteria as of 19/12/2022:

1. Adult (aged ≥18 years)
2. Metabolic acidosis (defined by arterial blood gas values of pH <7.30 and PaCO2 <6.5 kPa)
3. AKI – categorised as stage 2 or 3 of the Kidney Disease Improving: Global Outcomes (KDIGO) classification, defined as any one of the following three criteria:
• Serum creatinine ≥2.0 times baseline*
or
• Serum creatinine ≥354 µmol/L, AND
either a rise of ≥27 µmol/L within 48 hours or serum creatinine ≥1.5 times baseline*
or
• Urine output of <0.5 ml/kg/h for ≥12 hours
*For baseline serum creatinine value:
• If available, then use pre-hospitalisation value within 365 days of the current hospital admission date.
• If there are multiple pre-hospitalisation values, then use the one closest to the date of the current hospital admission.

• If a pre-hospitalisation value from the 365 days prior to admission date is not available and there are multiple serum creatinine values from the current hospitalisation, then use the lowest one from the current hospitalisation.
• If no baseline serum creatinine value is available, then estimate it using the provided calculator.

_____

Previous inclusion criteria:

1. Adult (aged ≥18 years)
2. Metabolic acidosis (defined by arterial blood gas values of pH <7.25, PaCO2 <6.5 kPa and bicarbonate ≤20 mmol/L)
3. AKI – categorised as stage 2 or 3 of the Kidney Disease Improving: Global Outcomes (KDIGO) classification, defined as any one of the following three criteria:
• Serum creatinine ≥2.0 times baseline*
or
• Serum creatinine ≥354 µmol/L, AND either a rise of ≥27 µmol/L within 48 hours or serum creatinine ≥1.5 times baseline*
or
• Urine output of <0.5 ml/kg/h for ≥12 hours
*For baseline serum creatinine value:
• If available, then use pre-hospitalisation value within 365 days of the current hospital admission date.
• If there are multiple pre-hospitalisation values, then use the one closest to the date of the current hospital admission.
• If a pre-hospitalisation value from the 365 days prior to admission date is not available and there are multiple serum creatinine values from the current hospitalisation, then use the lowest one from the current hospitalisation as the baseline value.
• If no baseline serum creatinine value is available, then estimate it using the provided calculator.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 2,250; UK Sample Size: 2,250

Key exclusion criteria
Current exclusion criteria as of 16/01/2025:

1. Respiratory acidosis (acute or chronic)
2. Kidney replacement therapy (KRT) planned to start within 3 hours and treating clinician(s) unwilling to defer if randomised to sodium bicarbonate

3. Deemed unsuitable for KRT
4. High output stoma/ileostomy
5. Percutaneous biliary drainage
6. End stage kidney failure defined as documented eGFR<15 ml/min/1.73m² prior to onset of this acute illness or end stage kidney disease (ESKD) on dialysis
7. Known renal tubular acidosis
8. Diabetic ketoacidosis
9. High anion gap acid poisoning (e.g. polyethylene glycol (PEG), aspirin, methanol)
10. Symptomatic hypocalcaemia (Ionised calcium <1.05 mmol/L) †
11. Hypernatraemia (Plasma sodium >150 mmol/L) †
12. Severe hypokalaemia (Potassium <3.0 mmol/L) †
13. Death perceived as imminent
14. Known hypersensitivity to sodium bicarbonate or to any of the excipients listed in section 6.1 of the SmPC
15. Previously randomised into MOSAICC
† Exclusion criteria 10-12 are dynamic, and if corrected, patient may be reconsidered for the trial.

———

Previous exclusion criteria as of 19/12/2022:

1. Respiratory acidosis (acute or chronic)
2. Kidney replacement therapy (KRT) immediately indicated and treating clinician(s) unwilling to defer if randomised to sodium bicarbonate
3. Deemed unsuitable for KRT
4. High output stoma/ileostomy
5. Percutaneous biliary drainage
6. End stage kidney failure defined as documented eGFR<15 ml/min/1.73m² prior to onset of this acute illness or end stage kidney disease (ESKD) on dialysis
7. Known renal tubular acidosis
8. Diabetic ketoacidosis
9. High anion gap acid poisoning (e.g. polyethylene glycol (PEG), aspirin, methanol)
10. Symptomatic hypocalcaemia (Ionised calcium <1.05 mmol/L) †
11. Hypernatraemia (Plasma sodium >150 mmol/L) †
12. Severe hypokalaemia (Potassium <3.0 mmol/L) †
13. Death perceived as imminent
14. Known hypersensitivity to sodium bicarbonate or to any of the excipients listed in section 6.1 of the SmPC
15. Previously randomised into MOSAICC
† Exclusion criteria 10-12 are dynamic, and if corrected, patient may be reconsidered for the trial.

———

Previous participant exclusion criteria as of 28/04/2022:

1. Respiratory acidosis (acute or chronic)
2. Clinical decision already in place to start patient on kidney replacement therapy (KRT)
3. Deemed unsuitable for KRT
4. High output stoma/ileostomy
5. Percutaneous biliary drainage
6. Documented eGFR<15 ml/min/1.73 m² or end stage kidney disease (ESKD) on dialysis
7. Known renal tubular acidosis

8. Diabetic ketoacidosis
9. High anion gap acid poisoning (e.g. polyethylene glycol (PEG), aspirin, methanol)
10. Symptomatic hypocalcaemia (Ionised calcium <1.05 mmol/l)†
11. Hypernatraemia (Plasma sodium >150 mmol/l)†
12. Severe hypokalaemia (Potassium <3.0 mmol/l)†
13. Death perceived as imminent
14. Known hypersensitivity to sodium bicarbonate or to any of the excipients listed in section 6.1 of the SmPC
15. Previously randomised into MOSAICC
† Exclusion criteria 10-12 are dynamic, and if corrected, the patient may be reconsidered for the trial.

_____

Previous participant exclusion criteria as of 02/11/2021:

1. Respiratory acidosis (acute or chronic)
2. Clinical decision already in place to start the patient on kidney replacement therapy (KRT)
3. Deemed unsuitable for KRT
4. Acute diarrhoea, including high output stoma/ileostomy
5. Percutaneous biliary drainage
6. Documented Stage 4 chronic kidney disease (CKD) [eGFR <30 ml/min/1.73m2] or end-stage kidney disease (ESKD) on dialysis
7. Known renal tubular acidosis
8. Diabetic ketoacidosis
9. High anion gap acid poisoning (e.g. polyethylene glycol (PEG), aspirin, methanol)
10. Known to be pregnant
11. Symptomatic hypocalcaemia (Ionised calcium <1.05 mmol/L)†
12. Hypernatraemia (Plasma sodium >150 mmol/L)†
13. Severe hypokalaemia (Potassium <3.0 mmol/L)†
14. Solid organ transplant
15. Death perceived as imminent
16. Known hypersensitivity to sodium bicarbonate or to any of the excipients listed in section 6.1 of the SmPC
†Exclusion criteria 11-13 are dynamic, and if corrected, the patient may be reconsidered for the trial

Previous exclusion criteria:
1. Respiratory acidosis (acute or chronic)
2. Clinical decision already in place to start the patient on kidney replacement therapy (KRT)
3. Acute diarrhoea, including high output stoma/ileostomy
4. Percutaneous biliary drainage
5. Documented stage 4 chronic kidney disease (CKD) [eGFR <30ml/min/1.73m^2] or end-stage kidney disease (ESKD) on dialysis
6. Known renal tubular acidosis
7. Diabetic ketoacidosis
8. High anion gap acid poisoning (e.g. polyethylene glycol (PEG), aspirin, methanol)
9. Known to be pregnant
10. Symptomatic hypocalcaemia (Ionised calcium <1.05 mmol/L)
11. Hypernatraemia (Plasma sodium >150 mmol/L)
12. Solid organ transplant
13. Death perceived as imminent

Date of first enrolment
12/04/2022

Date of final enrolment
31/08/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal Surrey County Hospital
Egerton Road
Guildford
United Kingdom
GU2 7XX

Study participating centre
Royal Derby Hospital
University Hospitals of Derby and Burton NHS Foundation Trust
Uttoxeter Road
Derby
United Kingdom
DE22 3NE

Study participating centre
Worthing Hospital
Lyndhurst Road
Worthing
United Kingdom
BN11 2DH

Sponsor information

Organisation
University Hospitals of Derby and Burton NHS Foundation Trust

Sponsor details

Royal Derby Hospital
Uttoxeter Road
Derby
England
United Kingdom
DE22 3NE
+44 (0)1332 724710
teresa.grieve@nhs.net

Sponsor type
Hospital/treatment centre

Website
https://www.uhdb.nhs.uk/

ROR
https://ror.org/04w8sxm43

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC)

Funder Name
National Institute for Health Research (NIHR) (UK)

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan

The results of MOSAICC will be disseminated actively and extensively. This will cover both progress during the trial period and the results at the end of the study. Outputs will include, but will not be limited to, the following areas:
• meeting and conference presentations (international and national) of study progress and results;
• publication of study (1) protocol (2) statistical analysis plan (3) primary results, and (4) longer-term outcomes, including economic evaluation; and
•incorporation into clinical guidelines

Intention to publish date

31/05/2028

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request (MOSAICC@icnarc.org)

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 4.2	21/08/2023	11/12/2023	No	No
Protocol file	version 5.0	04/09/2024	16/01/2025	No	No