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MOSAICC – Multicentre evaluation Of Sodium bicarbonate in Acute kidney Injury in Critical Care

Overview

Background

Around 184,000 adults are admitted to critical care each year in the UK, around half of whom have a sudden worsening in kidney function (acute kidney injury or 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. Over half of patients with acidosis and AKI will not survive.

One way to treat patients with acidosis is to give an alkali (opposite to acid) to stop the effects of acid build-up and bring the level of acid in the blood to normal. Sodium bicarbonate is often used and is a cheap and accessible treatment, but there is little evidence to support its use. As a result, there is variation in practice. Doctors and nurses have to decide if a patient should get sodium bicarbonate or progress to more invasive support known as kidney replacement therapy (KRT), which has added risks and requires specialist staff and equipment, making it very expensive.

So far, only one study has looked at the benefits of sodium bicarbonate in critically ill patients with acidosis, and found that it was not an effective treatment. However, in a small subgroup of patients who had acidosis and AKI, results pointed to possible benefits of sodium bicarbonate, with fewer patients dying and fewer patients needing KRT. However, to know with certainty, this needs to be tested thoroughly in a randomised clinical trial (RCT) specifically designed to address this question.

Our research question: in critically ill adults with metabolic acidosis and acute kidney injury (AKI), is treatment with intravenous (IV) sodium bicarbonate 8.4% weight/volume (w/v) superior to no IV sodium bicarbonate in terms of all-cause mortality at 90 days (clinical effectiveness) and incremental costs, quality-adjusted life years (QALYs) and net monetary benefit at 90 days (cost-effectiveness)?

Aim

To evaluate the clinical and cost-effectiveness of IV sodium bicarbonate 8.4% w/v, as compared with no sodium bicarbonate, in critically ill adults with metabolic acidosis and AKI in the UK.

Design

MOSAICC is a pragmatic multi-centre, open, data-enabled randomised clinical trial (RCT) with an internal pilot phase and integrated economic evaluation.

Objectives

Primary objectives

To evaluate the effect of IV sodium bicarbonate 8.4% w/v versus no sodium bicarbonate on:

- 90-day all-cause mortality (clinical effectiveness)
- Incremental costs, quality-adjusted life years and net monetary benefit at 90 days (cost-effectiveness).

Secondary objectives

To evaluate the effect of IV sodium bicarbonate 8.4% w/v versus no sodium bicarbonate on:

- Mortality at critical care unit discharge, 28 days and one year
- Receipt and duration of respiratory, renal, and advanced cardiovascular organ support during the critical care stay
- Duration of critical care unit and acute hospital stay
- On-going requirement for KRT at 90 days and one year
- Health-related quality of life (HrQoL) at 90 days and one year
- Resource use and costs at 90 days and one year
- Estimated lifetime incremental cost-effectiveness.

Site eligibility criteria

- Active participation in the Case Mix Programme (CMP) or equivalent national clinical audit
- Routine stock of IV sodium bicarbonate 8.4% w/v
- Identify a local Principal Investigator
- Identify a MOSAICC research nurse responsible for day-to-day local trial coordination
- Agree to incorporate MOSAICC into routine critical care clinical practice, highlighting the importance of systematic screening for potential eligible patients and prompt randomisation
- Agree to adhere to patient randomisation allocations and ensure adherence to the protocol
- Agree to randomise, where possible, all eligible patients and maintain a Screening Log
- Agree to data collection requirements.

Patient eligibility criteria

Inclusion criteria

1. Adult (aged ≥18 years);
2. Metabolic acidosis (pH <7.30 and $PaCO_2$ <6.5 kPa); and
3. AKI KDIGO stage 2 or 3

Exclusion criteria

1. Respiratory acidosis (acute or chronic)
2. KRT immediately indicated and treating clinician(s) unwilling to defer
3. Deemed unsuitable for KRT
4. High output stoma/ileostomy
5. Percutaneous biliary drainage
6. Documented eGFR<15 ml/min/1.73m^2 or end stage kidney disease on dialysis
7. Known renal tubular acidosis
8. Diabetic ketoacidosis
9. High anion gap acids poisoning (e.g. 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 excipients listed in section 6.1 of the SmPC
15. Previously randomised into MOSAICC

Co-enrolment will be permitted with observational studies (including those collecting samples) without prior agreement needed. Co-enrolment agreements will be put in place on a case-by-case basis with other interventional trials.

Sample size

- 2,250 patients
- 60 NHS adult critical care units
- Recruitment period: 12/04/2022 to 30/06/2024

Randomisation

Patients will be randomised 1:1 between the intervention and control groups using a deferred consent model.

Intervention group: IV sodium bicarbonate 8.4% w/v

- Aiming to achieve pH ≥7.30 for the duration of critical care stay or until commencement of KRT.
- Starting dose of 50ml infusion (over 30-60 minutes), repeated doses depending on clinical status, up to a maximum daily dose of 500ml/24hrs.
- Arterial blood gas analysis should be done 1-2 hours after each infusion.
- All other care will be at the discretion of the treating clinical team.

Control group: No sodium bicarbonate

- All care will be at the discretion of the treating clinical team.
- An open trial is preferred over placebo controlled as with frequent blood gas measurements required as part of routine critical care practice it is impossible to blind the effects of sodium bicarbonate.

Data collection

To ensure an efficient design, data collection is nested within the Case Mix Programme and will utilise additional routinely collected data from other national NHS sources.

Funding and resources

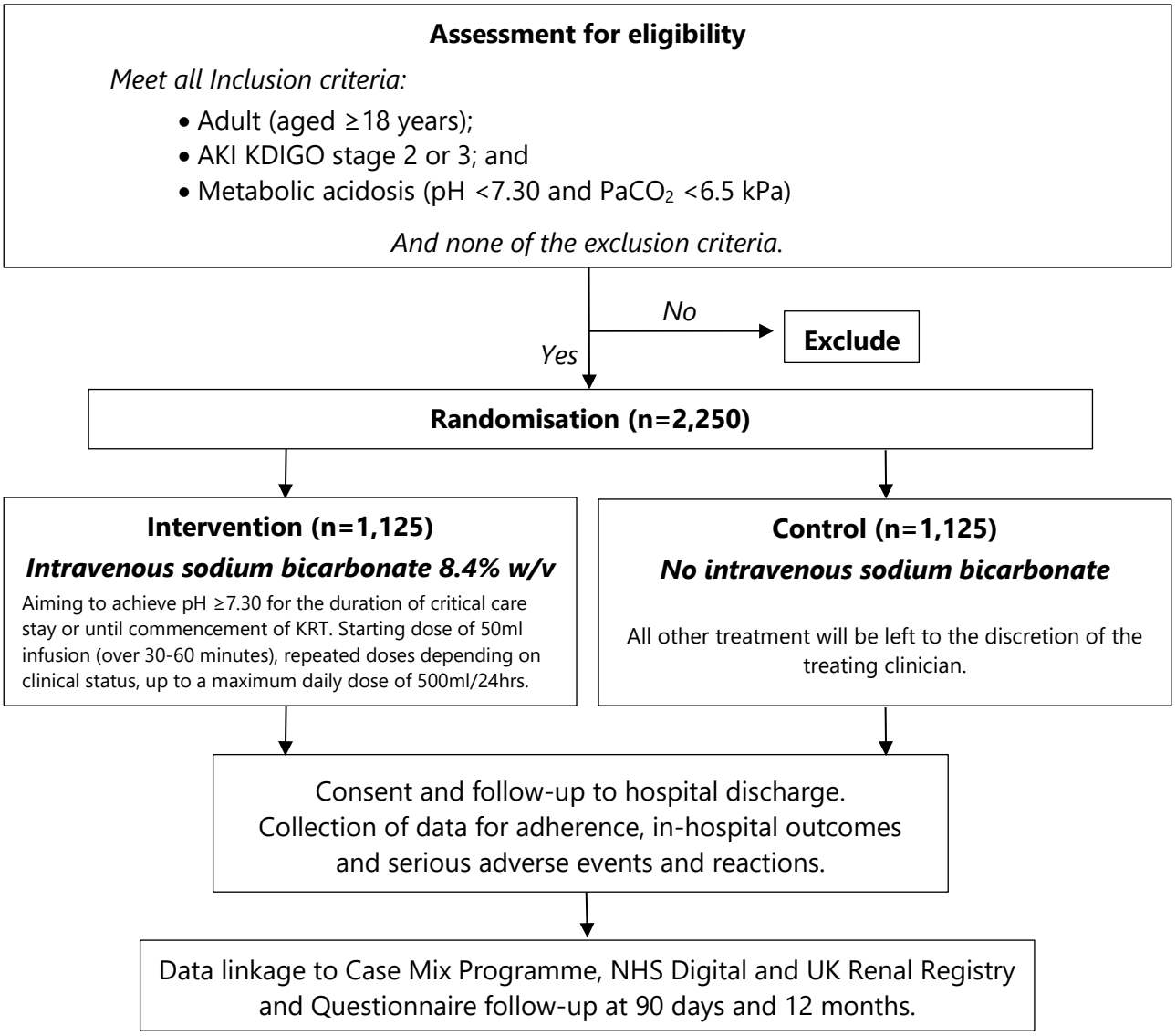
This trial is funded by the National Institute for Health and Care Research (NIHR) – Health Technology Assessment (HTA) Programme (Project number: 129617).

The trial is eligible to receive NIHR CRN support (CPMS 49697).

The following direct research costs from the grant will be available from ICNARC:

- Study start-up: £250
- Per eligible patient recruited: £175
- Study close-down: £250

Trial flow



Trial Management and Investigator team

Chief Investigators	Professor Lui Forni, University of Surrey Professor Nick Selby, University of Nottingham
Co-Investigators	Dr Manu Shankar-Hari, University of Edinburgh Mrs Kelly Wright, King's College Hospital NHS Foundation Trust Professor Kathryn Rowan, ICNARC Professor David Harrison, ICNARC Dr Douglas Gould, ICNARC Dr James Doidge, ICNARC Dr Zia Sadique, London School of Hygiene and Tropical Medicine Dr Luke Hodgson, University Hospitals Sussex NHS Trust Mr Michael Wise, Patient and Public Involvement (PPI) representative
Trial Management	ICNARC Clinical Trials Unit
Sponsor	University Hospitals of Derby and Burton NHS Foundation Trust