Blood sodium

Study Protocol – February 2024

Study Advisory Group Members

This multidisciplinary and lay group has been convened to guide the development of the study and to identify the primary aim and objectives to be met.

Becky Bonfield	Acute Kidney Injury Lead Advanced Nurse Practitioner
John Dean	Clinical Vice President - Royal College of Physicians
Andrew Gibson	Consultant Neurologist - Royal College of Physicians
Daniel Horner	Royal College Emergency Medicine
David Howell	Consultant in Critical Care Medicine
Mick Kumwenda	Consultant Nephrologist, Royal College of Physicians
Miles Levy	Consultant Endocrinologist
Steve Mathieu	President - Intensive Care Society
Pat McBride	Patient Representative, Pituitary Foundation
Frederick McElewaine	Consultant Endocrinologist, RCP Northern Ireland
Michele Millard	National Quality Improvement Lead – Spire Healthcare
Clare Morlidge	Senior Renal Pharmacist
Nick Murch	Society for Acute Medicine
Dhruv Parekh	Faculty of Intensive Care Medicine
Mayur Patel	Association for Clinical Biochemistry and Lab Medicine
Rob Sayers	Royal College of Surgeons of England
Alastair Scotland	Patient Representative
Mark Sherlock	Consultant Endocrinologist
Helen Simpson	Consultant Endocrinologist
Alexandra Yates	Association for Clinical Biochemistry and Lab Medicine

Clinical Coordinators

John Abercrombie	Clinical Co-ordinator - Surgery
Simon McPherson	Clinical Co-ordinator - Radiology
David Wood	Clinical Co-ordinator - Medicine

Non-clinical staff

Neil Smith	Senior Clinical Researcher
Dee Koomson	Clinical Researcher
Holly Hamilton	Research Assistant
Marisa Mason	Chief Executive

Introduction

Sodium levels in the body are usually carefully controlled. A number of conditions can lead to abnormal sodium levels that the body cannot adjust for which requires corrective action [1-2]. If high levels of sodium levels fall too quickly the brain can swell (cerebral oedema) and this can lead to loss of consciousness, seizures and ultimately death [3]. Conversely if very low sodium levels rise too quickly the brain can shrink, which can lead to an intracranial catastrophe. Moreover, correcting sodium levels too quickly can lead to a devastating irreversible locked-in syndrome called Osmotic Demyelination Syndrome (ODS) which is preventable if managed in the right clinical setting with the appropriate expertise [4]. Therefore, managing alterations in sodium concentrations can be complex and challenging.

Hyponatremia

Hyponatremia is classified into 3 levels, mild: Na^+ 130–135mmol/L, moderate: Na^+ 125–129mmol/L and severe: Na^+ <125mmol/L [1]. Hyponatraemia is primarily a disorder of water balance and is usually associated with a disturbance in the hormone that governs water balance, vasopressin (also called antidiuretic hormone). Even in disorders associated with (renal) sodium loss, vasopressin is generally elevated, which contributes to hyponatraemia [5].

Symptoms of hyponatraemia can vary from mild, non-specific to severe and life-threatening, and are related to both the severity of the hyponatraemia and its rate of onset as well as underlying conditions that may predispose to cerebral oedema (e.g. neurosurgical patients). Rapid changes in serum sodium levels or severe hyponatraemia can cause symptoms of vomiting, headache, drowsiness, seizures, coma, and cardio-respiratory arrest. Chronic hyponatraemia can lead to increased risk of falls, bone fractures, osteoporosis, gait instability, and concentration and cognitive deficit. Symptomatic severe hyponatraemia is a life-threatening condition and needs to be treated as a medical emergency.

In recent years, there have been increasing guidelines to recommend the use of hypertonic saline to correct hyponatraemia in patients with clinical signs of cerebral oedema. This has been shown to be both safe and effective if performed in a controlled and monitored environment. Inappropriate initial management by giving 0.9% saline which may not lead to the requisite improvement in sodium can be harmful as cerebral oedema may worsen with resultant adverse neurological outcome and death. Conversely, over-rapid correction of sodium within the first 24-48 hours may lead to ODS and irreversible, preventable harm. Overcorrection of sodium and ODS can be prevented by frequent monitoring of plasma sodium and the use of hypotonic solution (e.g. 5% dextrose) and/or desmopressin to prevent the over-correction of sodium. It is therefore vital that this group of patients have early specialist input because most generalists will not be comfortable with the idea of clamping the kidney with vasopressin in cases of over-correction.

Hypernatraemia

High sodium is classified as, mild: Na+ 145-150mmol/L, moderate: Na+ 150-155mmol/L and severe: Na+ > 155 mmol/L. High sodium is less common than hyponatraemia but is associated with a worse prognosis and is a sign of profound water depletion. This is both incredibly distressing for patients who are desperately thirsty, and dangerous in patients who are unable to communicate their thirst if they are obtunded. This leads to high mortality if not recognised or treated quickly.

Diabetes Insipidus

Diabetes insipidus (AVP-Deficiency or AVP-resistance), if not managed appropriately can lead to both hyponatraemia (over-treatment with desmopressin and fluids) and hypernatraemia (under-treatment). Importantly, prescribing of desmopressin and access to free water or appropriate

intravenous fluids is vital in the management of these patients in hospital. This is of particular importance in patients with reduced levels of consciousness who are unable to ask for water and patients who are fasting for procedures.

References

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Guidelines and standards

The Society for Endocrinology, European Society for Endocrinology and American Endocrine Society have all published guidelines on the acute management of severe symptomatic hyponatraemia in adult patients.

Society for endocrinology endocrine emergency guidance: Emergency management of severe symptomatic hyponatraemia in adult patients
https://ec.bioscientifica.com/view/journals/ec/5/5/G4.xml

European Society of Endocrinology Clinical guideline for the management of hyponatraemia

https://www.ese-hormones.org/publications/guidelines/european-society-of-endocrinology-clinical-guideline-for-the-management-of-hyponatraemia/

The Society for Endocrinology has also published guidelines on the inpatient management of cranial Diabetes Insipidus.
https://www.endocrinology.org/media/scplexuf/guidelines-for-the-inpatient-management-of-cranial-diabetes-insipidus.pdf

The Pituitary Foundation has emergency sick-day rules for the management of desmopressin in Diabetes Insipidus, as well as a Diabetes Insipidus Safety card.
https://www.pituitary.org.uk/information/publications/diabetes-insipidus/sick-day-rules-advice-for-diabetes-insipidus-patients/

There has been a BMJ editorial (2019) on the investigation and management of Diabetes Insipidus (https://www.bmj.com/content/364/bmj.l321) as well as a BMJ podcast entitled 'The dangers of Diabetes Insipidus' which is widely available. There is NICE Health topic on Hyponatraemia: Hyponatraemia. https://cks.nice.org.uk/topics/hyponatraemia/

Despite these national guidelines written by specialists, there is no national quality standard.

Aims and objectives

Overall aim:
To identify and explore the avoidable and modifiable factors in the care of adults with abnormal levels of blood sodium in hospital.

Objectives
Organisational
To review the structures and systems in place to deliver a high-quality service to patients with abnormal levels of sodium.

- Acute hospital care pathways (acute medicine/ ambulatory care/ same day emergency care) and surgical admission with sodium complications
- Guidelines/ protocols in existence and use for the management of abnormal sodium levels
    - Hydration policy
    - Clinical lead for IV fluid management
- Access to investigations
- Laboratory capabilities and reporting
- Involvement of specialist teams
- Multidisciplinary team working (including members of the MDT)
- Staffing
- Treatments (including variation in treatment choice)
- Current medication review
- Severity assessment
- Discharge and follow-up arrangements
- Serious adverse events
- Audit, QI, coding
    - Participation in national audits
    - Active local audits and quality improvement

Clinical

To explore remediable factors in the process of care of patients with abnormal sodium levels throughout the pathway, with a focus on the following areas:

- Identification of abnormal sodium levels
- Delays in diagnosis, referrals to specialists
- Access to and involvement of specialist teams
- Appropriate clinical setting
- Treatment
- Investigations and Imaging
- Sharing of any treatment escalation plans
- Post-operative complications
- Serious adverse events to highlight areas of care for improvement
- Medication management, including review of current medications
- Discharge and follow up
- Readmissions
- Examples of good practice
- Remediable factors in the quality of care received and produce recommendations for improvement

Methods

Participating hospitals

Data will be collected from all hospitals in England, Wales and Northern Ireland, which admit and treat patients with abnormal sodium levels.

Population

All patients aged 18 or over who were admitted to hospital between 1st October 2023 and 31st December 2023 and diagnosed with Hypernatremia or Hyponatraemia will be included in the initial patient identification. Retrospective ICD10 coding and/or laboratory sodium data will be used to identify patients. Patients who develop abnormal sodium levels after a surgical procedure during our study period will also be included.

The following ICD10 codes (in any position), will be used to identify patients.

E87.0	Hyperosmolality and hypernatraemia
E87.1	Hypo-osmolality and hyponatraemia
E27.2	Addisonian crisis
E23.2	Diabetes insipidus (AVP-deficiency and AVP-resistance)
G37.9	Demyelinating disease of central nervous system, unspecified

Up to 8 cases per hospital will be included for questionnaire completion and peer review.

Incidence and prevalence

Hyponatraemia is estimated to occur in 15–20% of all hospital inpatients [1] and is the commonest electrolyte disorder observed in clinical settings [6–10].

Hospital Episode Statistics (HES) for England data, 2021-2022

Primary diagnosis: 4-character code and description		**Finished consultant episode**	**Admissions**	**Emergency**	**Planned**
E87.0	Hyperosmolality and hypernatraemia	2,924	1,363	1,304	15

E87.1	Hypo-osmolality and hyponatraemia	44,066	23,711	22,285	547
E27.2	Addisonian crisis	2,060	1,181	1,120	25
E23.2	Diabetes insipidus	381	287	91	94
G37.9	Demyelinating disease of central nervous system, unspecified	1,091	843	238	174

Patient Episode Database for Wales (PEDW)

Primary diagnosis: 3-character code and description		Finished consultant episode	Admissions	Emergency
E87.0	Hyperosmolality and hypernatraemia	121	63	58
E87.1	Hypo-osmolality and hyponatraemia	2,054	1,309	1,201
E27.2	Addisonian crisis	106	64	59
E23.2	Diabetes insipidus	12	9	2
G37.9	Demyelinating disease of central nervous system, unspecified	25	23	7

Case identification

Within each Trust/Health Board NCEPOD has a Local Reporter (usually employed in clinical audit) who is responsible for providing the details of cases for inclusion to NCEPOD. At the start of the study the Local Reporter will be contacted and advised to set-up a study contact who can interrogate laboratory biochemistry results so patients with abnormalsodium levels can be identified retrospectively. In addition to laboratory sodium results, ICD10 code data as detailed above will be used to identify a cohort of patients coded and other selected data from central hospital records will be collected via completion of a spreadsheet. This will include patient details (NHS number, hospital number, date of birth), admission/discharge dates, source of admission, procedure details, if available, critical care admission, whether the patient died in hospital and discharge location.

Method of data collection

Clinician questionnaire

A questionnaire will be sent to the named consultant responsible for the patient's care when they were treated in hospital with abnormal sodium levels. Within this there will be instruction to pass the questionnaire on to most appropriate clinician should it not be the named person.

Data collected will include information on the hospital admission including discharge and follow up, the involvement of the specialist teams, treatments and investigations the patient received in hospital, specialist reviews and readmissions, use of protocols and clinical pathways.

The questionnaires will be disseminated via the NCEPOD online questionnaire system which is accessed by NCEPOD local reporters. The local reporters will then be able email the relevant clinician, granting them access to the online questionnaire. Reminder emails will be sent at six and ten weeks where the data are outstanding. The Local Reporter will be asked to return copied extracts of the patient's case notes to NCEPOD alongside the completed questionnaires.

Hospital organisational questionnaire

An organisational questionnaire will be sent to all hospitals that admit and treat patients with abnormal sodium levels. Data collected will include information around the organisation of services in the process of identifying, screening, assessing, treating severe hypo- and hypernatraemia, networks of care, multidisciplinary team working, the use of guidelines/protocols and training. The questionnaires will be disseminated via the online questionnaire system. Local reporters will be able to invite multiple clinicians to complete the questionnaire.

Case note review
Case note review will be undertaken for a sample of patients who were treated patients with abnormal sodium levels.

Case notes
Photocopies of the case notes of each included patient will be requested at the time of questionnaire dissemination. A list detailing the required case note extracts will be circulated to local reporters. Upon receipt at NCEPOD the case notes will be anonymised removing patient identifiable information.

Reviewer assessment form
A multidisciplinary group of reviewers (details below) will be recruited to assess the case notes and questionnaires and give their opinions on the quality of care via the reviewer assessment form.

Anonymous online clinician survey
An anonymous online survey for healthcare professionals who treat patients with abnormal sodium levels. This questionnaire will be targeted at, but not limited to, clinicians and allied health professionals working in hospitals who treat patients with abnormal sodium levels. The survey will collect data on the views of healthcare professionals regarding their own confidence and training level in providing care to this cohort of patients. The data will not be linked to any other aspects of data collection.

Anonymous online patient survey
An anonymous online survey will gather data on the patient views on the care received following an admission with abnormal sodium levels. The data will not be linked to any other aspects of data collection.

Below are the anticipated sample sizes of each type of data collected:

Data Source	**Target Number**
Hospital organisational questionnaire	~200
Clinician questionnaire	~500
Case note review	~500
Clinician survey	~100
Patient survey	~100

Study method test
The data collection methods and data collection tools will be tested to ensure they are robust.

Analysis and Review of Data
Case Reviewers
A multidisciplinary group of reviewers will be recruited to assess the case notes and questionnaires and provide their opinion on the care the patients received.

An advert will be sent to Local Reporters to disseminate throughout the relevant departments. It will also be placed on the NCEPOD website. Successful applicants will be asked to attend a training day where they will work through anonymised case notes with the case reviewer form. A number of meeting dates will be arranged, and each reviewer will then be asked to attend a further 4 meetings. NCEPOD staff will ensure there is a mix of specialties at each meeting from across the UK. Each meeting will be chaired by an NCEPOD clinical coordinator who will lead discussion around the cases under review. Meetings will be held virtually if COVID-19 restrictions prevent clinicians from

attending. This method has been set up and approved by CAG. Towards the end of the study the reviewers will be invited to attend a meeting where the data will be presented to and discussed with them. The reviewers will also be sent two copies of the draft report for their comment as this is developed.

Confidentiality and data protection
All electronic data are held in password protected files and all paper documents in locked filing cabinets. As soon as possible after receipt of data NCEPOD will encrypt electronic identifiers and anonymise paper documents. Section 251 approval has been obtained to perform this study without the use of patient consent in England and Wales.

Study promotion
Prior to data collection, NCEPOD will contact all hospitals that admit and treat patients with patients with abnormal sodium levels.

The study will also be promoted to via patient groups, NCEPOD Local Reporters (sending the study poster on to the relevant departments), via study contacts recruited as part of the case identification strategy, and via the relevant Colleges and Associations.

Dissemination
On completion of the study a report will be published and widely disseminated.

Data sharing
Post-publication of the study there is the potential to share anonymised data sets with interested parties working in the same field. This will be undertaken following a strict process and will ensure the data does not become identifiable in their nature due to small numbers.

Timeline