CLINICAL PRACTICE GUIDELINES

TREATMENT OF ACUTE HYPERKALAEMIA IN ADULTS

UK Renal Association

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Contributors:

Dr Annette Alfonzo – Consultant Nephrologist

Dr Jasmeet Soar – Consultant in Anaesthesia & Intensive Care Medicine; Immediate Past Chairman of Resuscitation Council (UK)

Dr Robert MacTier - Consultant Nephrologist; Former lead of Guidelines Committee of Renal Association

Dr Jonathan Fox – Consultant Nephrologist; Representative of Renal Association

Dr Ilona Shillday – Consultant Nephrologist

Dr Jerry Nolan – Consultant in Anaesthesia & Intensive Care Medicine; Representative of Intensive Care Society

Dr Roop Kishen – Consultant Intensive Care Medicine; Representative of Intensive Care Society

Dr Alistair Douglas – Consultant in Acute Medicine and Nephrology; Representative of Society for Acute Medicine

Dr Bill Bartlett – Representative of Association of Clinical Biochemistry

Mr Martin Wiese – Representative of the College of Emergency Medicine

Mrs Brenda Wilson – Representative of Scottish Resuscitation Group

Mrs Jacqueline Beatson - Representative of Scottish Resuscitation Group

Mrs Lyn Allen – Renal Nurse; Representative of British Renal Society

Mrs Mumtaz Goolam – Renal Nurse; Representative of British Renal Nursing

Mrs Morag Whittle – Representative of UK Renal Pharmacy Group

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Please send feedback to **Dr Annette Alfonzo** at annette.alfonzo@nhs.net.

Posted at www.renal.org/guidelines

This guideline has been endorsed in full by:

This guideline has been endorsed with the following stipulation by:

The Association for Clinical Biochemistry & Laboratory Medicine

The ACB endorses the guidelines submitted for our consideration **as they stand** but would appreciate that the following comments are taken into account on the first review date:

"At the ACB Council we use 7.0 mmol/l as the critical cut-off. However whether it is 7.0 or 6.5 mmol/l is not my main concern. It is acute rises in potassium that are associated with cardiac mortality, and the guidelines from the Renal Association (certainly the flow diagrams anyhow) do not seem to make this distinction. We come across many serum potassiums in the range from 6.1-7.0 mmol/l in patients with CKD and on potassium sparing agents such as ACEI or ARBs which we generally don't tend to treat as acute emergencies unless there are significant ECG changes, which is very rare. Also as you are well aware, delayed separation and processing cause pseudohyperkalaemia and this common scenario is absent as a possible explanation from the flow diagram. The first question that always needs to be asked is whether this is true hyperkalaemia?"

Methods

Purpose

This guideline has been developed to improve the treatment of acute hyperkalaemia and reduce the risk of complications associated with hyperkalaemia and its treatment.

Guideline development

This guideline is a collaboration between the Renal Association and Resuscitation Council (UK). The multidisciplinary writing group consists of nephrologists, intensivists, resuscitation experts, a clinical biochemist, renal nurses and a renal pharmacist. Each contributor was nominated by their organisation to represent their specialist area. The group met in November 2010 in Fife, Scotland to agree the scope for the guideline and critically assess the available evidence for the treatment of acute hyperkalaemia.

This guideline has been reviewed by the Renal Association Clinical Practice Guideline Committee and the Resuscitation Council (UK) Executive Committee. Wider consultation has also been sought via the Renal Association and Resuscitation Council (UK) website.

Review of Evidence

The literature was reviewed using a multiple database search - The Cochrane Library (1995-2013), Ovid MEDLINE (1946-2013), EMBASE (1974-2013), PubMed (1960-2013), Up-to-Date (2011), Web of Knowledge (2001-2013) for all human studies published in english pertaining to the treatment of hyperkalaemia in adults. The keywords used for literature search were – hyperkalaemia, potassium, treatment, arrhythmias, insulin, salbutamol, calcium, dialysis and cardiac arrest.

The hyperkalaemia module comprises of a series of guideline statements accompanied by supporting evidence and audit measures. The recommendations in each guideline statement have been graded using the GRADE system (www.gradeworkinggroup.org) in evaluating the strength of each recommendation (1 = strong, 2 = weak) and quality of evidence (A= high, B = moderate, C= low, D = very low). Each guideline statement begins with a recommendation (Grade 1 evidence) or a suggestion (Grade 2 evidence).

Limitations

Most studies assessing the efficacy of treatment for hyperkalaemia are of patients with end-stage renal disease, are small and have variable designs. Most studies do not assess the

incidence of arrhythmias in clinically significant hyperkalaemia and the evidence for the use of intravenous calcium salts in preventing and treating arrhythmias is limited to case reports and anecdotal evidence. Adverse events, including hypoglycaemia, are not consistently reported.

Scope

This guideline focuses on the recognition and emergency treatment of acute hyperkalaemia in adults in secondary care settings. It is applicable to clinicians in all specialties. This guideline does not comprehensively cover the treatment of hyperkalaemia in out-patient or primary care settings.

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Introduction

Hyperkalaemia occurs when the extracellular potassium ion [K^+] concentration is above the normal value. It is a potentially life-threatening emergency that can be corrected with treatment. It has relevance to all clinicians and is encountered in a variety of clinical settings. Despite this, there is limited evidence to guide treatment. This may account for the observed variability in the treatment of patients with hyperkalaemia, even within the same hospital.[1] Uniform guidance on the treatment of hyperkalaemia based on the best available evidence is therefore needed.

There is no universal definition of hyperkalaemia, but a serum $K^+ \geq 5.5$ mmol/L is widely used.[2,3] In reality, hyperkalaemia is a spectrum with the incidence of complications rising with increasing severity of hyperkalaemia. In addition to the absolute serum K^+ value, the rate of rise of serum K^+ is also important. Co-existing metabolic disturbances can ameliorate (e.g. hypernatraemia, hypercalcaemia, and alkalaemia) or exacerbate (e.g. hyponatraemia, hypocalcaemia or acidosis) the effects of hyperkalaemia.[4]

Hyperkalaemia usually occurs in patients with renal impairment which can be acute or chronic. In patients with chronic kidney disease (CKD), several factors increase susceptibility to hyperkalaemia including reduced glomerular filtration rate (GFR), metabolic acidosis, and a high dietary potassium intake relative to residual renal function.[5] When patients with CKD have other risk factors, e.g. treatment with drugs that interfere with the renin-angiotensin-aldosterone system, the risk of hyperkalaemia is further increased.

Hyperkalaemia causes a rapid reduction in resting membrane potential leading to increased cardiac depolarization, and muscle excitability. This in turn can cause electrocardiographic (ECG) changes.[6,7] The ECG changes with hyperkalaemia do not consistently follow a stepwise, dose-dependent pattern. In reality, many patients have rapid changes in their ECG. The risk of arrhythmias increase with K^+ values > 6.5 mmol/L and even small elevations in K^+ above this concentration can lead to rapid progression from peaked T waves to ventricular fibrillation or asystole.[1] The longer a patient has high K^+ concentrations, the greater the risk of sudden deterioration.[8]

The clinical presentation of hyperkalaemia is highly variable with some patients presenting with an acute illness whilst others may be asymptomatic. The presence of arrhythmias, muscular weakness or paraesthesiae in a patient at risk should raise the clinical suspicion of

hyperkalaemia. The clinical course is unpredictable and sudden death can occur in the absence of premonitory ECG changes.

Recognition of hyperkalaemia depends on laboratory tests and the ECG appearances. Near-patient testing with a blood gas analyser can provide rapid estimation of serum K^+, but this is not always available and there is controversy about the accuracy of the results. Although the ECG is an important tool for assessment and generally correlates with the severity of hyperkalaemia, its utility is limited by interpreter skills[9] and it may be normal even in the presence of severe hyperkalaemia.[10] ECG changes may also be modified by the presence of co-existing metabolic disorders such as metabolic acidosis, calcium concentration, sodium concentration, and the rate of rise of serum K^+.[11]

The threshold for emergency treatment varies, but most guidelines recommend that emergency treatment should be given if the serum K^+ is ≥ 6.5 mmol/L with or without ECG changes.[2,12,13] It is also widely accepted that emergency treatment should be initiated for hyperkalaemia if suspected on clinical grounds or ECG features.[2,3]

There is controversy about the drug treatment of hyperkalaemia. The intravenous calcium salt used (gluconate or chloride) and indications for use are inconsistent and there are no clinical trials on which to base a recommendation. Insulin-glucose infusion is the most effective treatment in lowering serum K^+, but the dose of insulin and concentration of glucose solution vary in published treatment guidelines. Beta-agonists appear to be effective in lowering serum K^+, but some patients are unresponsive. Sodium bicarbonate is often used in clinical practice, but there is little evidence to support its use.[14] Potassium-exchange resins are often used but their place in acute treatment is limited. Although in some clinical scenarios diuretics or intravenous fluids are used in the treatment of hyperkalaemia associated with acute kidney injury, there is no evidence to support this practice.[14]

There are several limitations in the evidence available on the treatment of hyperkalaemia.

1. Study designs vary with few randomised controlled trials (RCTs), small study size and variable statistical analysis.[14]
2. Surrogate markers of efficacy have generally been reported.[14]
3. Adverse events associated with treatment have been poorly documented.

4. Clinically significant complications of hyperkalaemia, such as arrhythmias, are not widely reported in clinical trials; most studies were conducted in stable haemodialysis patients.
5. There are no RCTs on the use of calcium salts for the treatment of hyperkalaemia.
6. Hyperkalaemic cardiac arrest is the worst complication, but the evidence for recommendations is limited to case reports, small case series and clinical experience.
7. There is no evidence-based guideline for the timing of dialysis initiation, but early nephrology or intensive care referral is ideal.

Hyperkalaemic cardiac arrest is uncommon, but potentially reversible even after prolonged resuscitation efforts. All cardiac arrest rhythms have been documented and success has been reported with dialysis during cardiopulmonary resuscitation (CPR).[15] Most nephrologists have little experience in initiating dialysis during cardiac arrest, but it is technically feasible and all modalities have been used.[16] Given that interventions are attempted for other potentially reversible problems in cardiac arrest, e.g. chest drain for tension pneumothorax, cardiopulmonary bypass for hypothermia, pericardiocentesis for cardiac tamponade, it seems reasonable to consider dialysis treatment during CPR for patients with hyperkalaemic cardiac arrest.

This guideline has been developed by a multidisciplinary group to critically assess the literature, address the controversies in treatment and to provide a standardised approach to the treatment of acute hyperkalaemia in adults.

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Summary of Clinical Practice Guideline for Hyperkalaemia

1. Hyperkalaemia (Guidelines Hyperkalaemia 1.1-1.3)

Guideline 1.1 – Hyperkalaemia: Definition, epidemiology and outcomes

We recommend that the European Resuscitation Council Guideline definition of hyperkalaemia be adopted, with hyperkalaemia being stratified as mild (5.5-5.9 mmol/L), moderate (6.0-6.4 mmol/L) or severe (≥6.5 mmol/L). (1C)

Guideline 1.2 – Hyperkalaemia: Definition, epidemiology and outcomes

We recommend that a precipitating cause be considered for all patients presenting with hyperkalaemia. (1B)

Guideline 1.3 – Hyperkalaemia: Definition, epidemiology and outcomes

We recommend that hyperkalaemia is regarded as a medical emergency given its potential for life-threatening consequences. (1A)

2. Hyperkalaemia (Guidelines Hyperkalaemia 2.1-2.2)

Guideline 2.1 – Hyperkalaemia: Clinical Assessment; ABCDE and Early Warning Scoring (EWS) Systems.

We recommend that all patients with known or suspected hyperkalaemia undergo urgent assessment by nursing and medical staff to assess clinical status using the ABCDE approach, an early warning scoring system, and an appropriate escalation plan bearing in mind that the first presentation may be an arrhythmia. (1C)

Guideline 2.2 – Hyperkalaemia: Clinical Assessment; History and examination

We recommend that all patients presenting with hyperkalaemia undergo a comprehensive medical and drug history and clinical examination to determine the cause of hyperkalaemia. (1B)

3. Hyperkalaemia (Guidelines Hyperkalaemia 3.1 - 3.2)

Guideline 3.1 – Hyperkalaemia: ECG

We recommend that all patients with a serum K^+ value ≥ 6.0 mmol/L have an urgent 12-lead ECG performed and assessed for changes of hyperkalaemia. (1B)

Guideline 3.2 – Hyperkalaemia: Cardiac Monitoring: 3-lead ECG

We recommend a minimum of continuous 3-lead ECG monitoring for all patients with a serum K^+ value $\geq$ 6.5 mmol/L, patients with features of hyperkalaemia on 12-lead ECG, and in patients with a serum K^+ value between 6.0-6.4 mmol/L who are clinically unwell or in whom a rapid rise in serum K^+ is anticipated, ideally in a high-dependency setting. (1C)

4. Hyperkalaemia (Guidelines Hyperkalaemia 4.1- 4.3)

Guideline 4.1 – Hyperkalaemia: Laboratory tests

We recommend that lithium heparin anti-coagulated specimens are the sample type of choice when rapid turnaround of urea and electrolytes results is required.(1B)

Guideline 4.2 – Hyperkalaemia: Blood gas analysis

We recommend that in emergencies, K^+ is measured from an arterial or venous blood sample using a point-of-care blood gas analyser whilst awaiting the results from a formal laboratory measurement. (1B)

Guideline 4.3 – Hyperkalaemia: Pseudo-hyperkalaemia

We recommend that urea and electrolytes are measured using paired lithium heparin and clotted serum samples from a large vein using gentle traction, and with prompt laboratory analysis if pseudo-hyperkalaemia is suspected. (1A)

5. Hyperkalaemia (Guidelines Hyperkalaemia 5.1- 5.6)

Guideline 5.1 – Hyperkalaemia: Summary of treatment strategy

We recommend that the treatment of hyperkalaemia follows a logical 5-step approach. (1B)

Guideline 5.2 – Hyperkalaemia: STEP 1 - Protect the heart; intravenous calcium salts

We recommend that intravenous calcium chloride or calcium gluconate, at an equivalent dose (6.8mmol), is given to patients with hyperkalaemia in the presence of ECG evidence of hyperkalaemia. (1A)

Guideline 5.3.1 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; insulin-glucose infusion

We recommend that insulin-glucose (10 units soluble insulin in 25g glucose) by intravenous infusion is used to treat severe ($K^+ \geq$ 6.5 mmol/L) hyperkalaemia. (1B)

Guideline 5.3.2 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; insulin-glucose infusion

We suggest that insulin-glucose (10 units soluble insulin in 25g glucose) by intravenous infusion may be used to treat moderate (K^+ 6.0-6.4 mmol/L) hyperkalaemia. (2C)

Guideline 5.4.1 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; salbutamol

We recommend nebulised salbutamol 10-20mg is used as adjuvant therapy for severe ($K^+ \geq$ 6.5 mmol/L) hyperkalaemia. (1B)

Guideline 5.4.2 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; salbutamol

We suggest that nebulised salbutamol 10-20mg may be used as adjuvant therapy for moderate (K^+ 6.0-6.4 mmol/L) hyperkalaemia. (2C)

Guideline 5.4.3 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; salbutamol

We recommend that salbutamol is not used as monotherapy in the treatment of severe hyperkalaemia. (1A)

Guideline 5.5 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; sodium bicarbonate

We suggest that intravenous sodium bicarbonate infusion is not used routinely for the acute treatment of hyperkalaemia. (2C)

Guideline 5.6 – Hyperkalaemia: STEP 3 – Remove K^+ from body; cation-exchange resins

We suggest that cation-exchange resins are not used in the emergency treatment of severe hyperkalaemia, but may be considered in patients with mild to moderate hyperkalaemia. (2B)

6. Blood monitoring (Guidelines 6.1 - 6.3)

Guideline 6.1 – Hyperkalaemia: STEP 4 - Blood monitoring; serum K^+

We recommend that the serum K^+ is monitored closely in all patients with hyperkalaemia to assess efficacy of treatment and look for rebound hyperkalaemia after the initial response to treatment wanes. (1B)

Guideline 6.2 – Hyperkalaemia: STEP 4 - Blood monitoring; serum K^+

We suggest that serum potassium be assessed at least 1, 2, 4, 6 and 24 hours after identification and treatment of hyperkalaemia. (2C)

Guideline 6.3 – Hyperkalaemia: STEP 4 - Blood monitoring; blood glucose

We recommend that the blood glucose concentration is monitored at regular intervals (0, 15, 30, 60, 90, 120, 180, 240, 300, 360 minutes) for a minimum of 6 hours after administration of insulin-glucose infusion in all patients with hyperkalaemia. (1C)

7. Referral to Renal Services (Guidelines 7.1 - 7.3)

Guideline 7.1 - Hyperkalaemia: Specialist Referral

We suggest that patients with severe hyperkalaemia (serum potassium ≥ 6.5 mmol/L) be referred to their local renal or intensive care team for an urgent opinion, guided by the clinical scenario and its persistence after initial medical treatment. (2C)

Guideline 7.2 - Hyperkalaemia: Treatment facilities

We recommend that patients with severe hyperkalaemia and problems with airway, breathing and/ or circulation (ABC), be referred to the local ICU team in the first instance. (1C)

Guideline 7.3 - Hyperkalaemia: Treatment facilities

We recommend that stable patients with severe hyperkalaemia be admitted to an area with facilities for cardiac monitoring, ideally in a renal unit, coronary care unit, HDU or ICU depending on local facilities or practice. (2C)

8. Minimum standards for patient transfer (Guidelines 8.1 - 8.2)

Guideline 8.1 - Hyperkalaemia: Transfer to renal services

We suggest that transfer to renal services be considered in clinically stable patients in whom hyperkalaemia cannot be controlled (i.e. serum K <6.5 mmol/L) using medical measures particularly in the presence of advanced or oliguric renal failure (either AKI or CKD). (2C)

Guideline 8.2 - Hyperkalaemia: Minimum standards for safe patient transfer

We suggest that inter- or intra-hospital patient transfer be coordinated by senior clinicians and follows national guidelines. (2B)

9. Indications for escalation of care (Guidelines 9.1-9.5)

Guideline 9.1 – Hyperkalaemia: Escalation of care

We recommend that patients with hyperkalaemia are managed in an area appropriate to their level of clinical need (Level of care 1, 2 or 3). (1B)

Guideline 9.2 – Hyperkalaemia: Escalation of care

We recommend escalation of care, where appropriate, in all patients with problems with airway, breathing, circulation and/ or disability. (1B)

Guideline 9.3 – Hyperkalaemia: Escalation of care – Procedure for referral

We recommend that patients are referred to the ICU team by a senior member of the referring team if escalation of care is required from the outset or if the patient fails to respond to initial treatment. (1B)

Guideline 9.4 – Hyperkalaemia: Escalation of care – Need for RRT and other organ support

We recommend escalation of care in patients with hyperkalaemia requiring renal replacement therapy in addition to other organ support (e.g. ventilation or circulation). (1B)

Guideline 9.5 – Hyperkalaemia: Escalation of care – Method of RRT in ICU

We suggest that the decision to initiate RRT for patients with hyperkalaemia in the ICU and the chosen modality take into account local practice and dialysis facilities. (2C)

10. Hyperkalaemic cardiac arrest (Guidelines 10.1-10.2)

Guideline 10.1 – Hyperkalaemia; Cardiac Arrest; special consideration

We recommend that hyperkalaemia is considered in all patients who have a cardiac arrest as part of identifying and treating a reversible cause using the '4 Hs and 4 Ts' approach. (1A)

Guideline 10.2 – Hyperkalaemia; Cardiac Arrest; dialysis during CPR

We suggest that dialysis is considered for hyperkalaemic cardiac arrest if hyperkalaemia is resistant to medical therapy. (2C)

11. Hyperkalaemia Treatment Algorithms (Guidelines 11.1-11.2)

Guideline 11.1 – Hyperkalaemia; Treatment Algorithm

We recommend a standardised approach to the management of patients with hyperkalaemia using the aid of a treatment algorithm (Appendix 4). (1B)

Guideline 11.2 – Hyperkalaemia; Treatment Algorithm in cardiac arrest

We suggest a standardised approach to the management of patients with hyperkalaemic cardiac arrest using the aid of a treatment algorithm (Appendix 6). (2C)

12. Treatment in Primary Care (Guidelines 12.1-12.6)

Guideline 12.1 – Hyperkalaemia: Treatment in Primary Care; hospital referral

We recommend that all patients with severe hyperkalaemia ($K^+ \geq 6.5$ mmol/L) are referred to secondary care for immediate assessment and treatment. (1B)

Guideline 12.2 – Hyperkalaemia: Treatment in Primary Care; prevention

We recommend that all patients with mild ($K^+ \geq 5.5$-5.9 mmol/L) or moderate (K^+ 6.0-6.4 mmol/L) hyperkalaemia have a review of their medication and diet and regular monitoring of

serum potassium; the urgency of assessment and frequency of potassium monitoring will depend on individual circumstances. (1B)

Guideline 12.3 – Hyperkalaemia: Treatment in Primary Care; prevention

We suggest that renin-angiotensin drugs (ACE-inhibitors, angiotensin II receptor blockers, aliskiren), potassium sparing diuretics, and/ or loop diuretics are stopped during acute illness lasting > 24 hours duration particularly when associated with hypovolaemia or hypotension (e.g. sepsis, diarrhoea and/or vomiting). (1C)

Guideline 12.4 – Hyperkalaemia: Treatment in Primary Care; monitoring

We suggest that renal function is assessed before commencing treatment with drugs that can cause hyperkalaemia and thereafter, renal function and serum potassium be monitored in the community after initiation, after dose adjustments and during acute illness. (2C)

Guideline 12.5 – Hyperkalaemia: Treatment in Primary Care; prescribing

We suggest that non-steroidal anti-inflammatory drugs or trimethoprim, particularly in combination with renin-angiotensin blockade, are avoided in the patients with CKD 4 and 5, and care should also be taken in the elderly. (2B)

Guideline 12.6 – Hyperkalaemia: Treatment in Primary Care; pseudo-hyperkalaemia

We suggest that patients in the community with suspected pseudohyperkalaemia are referred to hospital for verification of hyperkalaemia and appropriate treatment if necessary. (2B)

13. Drug administration and patient safety (Guideline 13.1)

Guideline 13.1 – Hyperkalaemia: Drug safety

We recommend that hospitals adopt standard regimens for drug administration and monitoring in the treatment of hyperkalaemia to reduce adverse events. (1B)

14. Prevention (Guidelines 14.1-14.2)

Guideline 14.1 – Hyperkalaemia: Prevention – STEP 5 - primary

We recommend that measures are taken to prevent hyperkalaemia in patients at risk. (1C)

Guideline 14.2 – Hyperkalaemia: Prevention - STEP 5 - secondary

We recommend that measures are taken to prevent recurrence of hyperkalaemia after acute treatment and appropriate follow-up should be arranged. (1B)

15. Education (Guidelines 15.1-15.2)

Guideline 15.1 – Hyperkalaemia: Education; medical training

We recommend that medical students and junior doctors are educated in the recognition, treatment, potential hazards and prevention of hyperkalaemia. (1C)

Guideline 15.2 – Hyperkalaemia: Education; renal nurses and nurses working in acute care settings

We recommend that nurses working in renal, cardiac or acute care settings are educated in the recognition, treatment, potential hazards and prevention of hyperkalaemia. (1C)

Summary of Audit Measures:

The Renal Association encourages non-renal specialties to record audit measures for all patients diagnosed with hyperkalaemia irrespective of whether or not they are referred to renal services. Hospital laboratories should be capable of providing data to help audit compliance with these guidelines. It is recommended that the following audit measures be recorded for patients with hyperkalaemia.

1. Incidence and outcomes of patients with hyperkalaemia diagnosed:
    a. in the community
    b. in the out-patient clinic
    c. after hospital admission
2. Proportion of patients where there has been a delay of > 24 hours in the recognition of hyperkalaemia.
3. Outcome measures in patients diagnosed with hyperkalaemia:
    a. Length of hospital stay
    b. In-hospital mortality
4. Proportion of patients with a serum K^+ value $\geq$ 6.0 mmol/L who had a 12-lead ECG performed prior to treatment [Audit standard: 100%].
5. Proportion of patients with a serum K^+ value $\geq$ 6.0 mmol/L and an ECG showing features of hyperkalaemia who had their 12-lead ECG repeated following treatment [Audit standard: 100%].
6. Proportion of patients with a serum K^+ value $\geq$6.5 mmol/L who have documented evidence of continuous ECG monitoring [Audit standard: 100%].
7. The average laboratory analysis time to performance K^+ concentration using clotted (serum) and lithium heparin (plasma) samples [Audit standard: within 60 minutes].
8. The frequency of ECG changes in patients treated with intravenous calcium salts.
9. Adverse events as a result of treatment with intravenous calcium salts.
10. The proportion of patients with severe hyperkalaemia ($K^+ \geq$ 6.5 mmol/L) treated with insulin-glucose infusion [Audit Standard: 100%].
11. The proportion of patients who develop adverse effects of salbutamol (e.g. tachycardia, arrhythmia).

12. The proportion of patients with severe hyperkalaemia treated with resins [Audit Standard; 0%].
13. The frequency of bowel complications with the use of cation-exchange resins.
14. The proportion of patients in whom serum K^+ was measured at least once within 2 hours of treatment for severe hyperkalaemia [Audit Standard: 100%].
15. The proportion of patients in whom a serum K^+ was not performed within 6 hours of identification of hyperkalaemia [Audit Standard: 0%].
16. The proportion of patients who have at least one blood glucose test performed with 1 hour of completion of insulin-glucose infusion [Audit Standard: 100%].
17. Appropriateness and timeliness ICU referral.
18. Seniority of ICU personnel from whom advice was sought.
19. All cardiac arrests should be audited [Audit Standard 100%] – hospital participation in the National Cardiac Arrest Audit is encouraged as part of quality improvement and benchmarking (https://ncaa.icnarc.org).
20. The proportion of acute hospitals in the UK implementing the hyperkalaemia treatment algorithms.
21. Adverse events in relation to treatment of hyperkalaemia.
22. The frequency of prescribed drugs potentially contributing to hyperkalaemia.
23. The frequency of recurrence of hyperkalaemia beyond 48 hours after an acute episode.
24. The availability of guidelines and/ or education on hyperkalaemia in renal unit, intensive care unit, emergency department or general ward [Audit Standard: 100%].

Future Research:

There are numerous unanswered questions about the treatment of patients with hyperkalaemia. Areas for future research include:

1. The incidence of hyperkalaemia in patients with AKI.
2. The incidence of hyperkalaemia in patients with ESRD (i.e. eGFR < 15 ml/min).
3. The severity of illness at presentation of hyperkalaemia as represented by EWS.
4. The correlation between potassium measurements using a blood gas analyser versus the laboratory.
5. The incidence of pseudo-hyperkalaemia in the community compared with hospital patients.
6. The proportion of patients with documented hypoglycaemia (blood glucose < 4.0 mmol/L) after treatment with insulin-glucose infusion.
7. The proportion of acute hospital admissions referred to Renal Services for treatment of hyperkalaemia in a single centre annually.
8. The proportion of patients requiring inter-hospital transfer for treatment of hyperkalaemia.
9. The incidence and outcome of hyperkalaemic cardiac arrest.
10. The frequency of dialysis initiation for hyperkalaemic cardiac arrest.

1. Hyperkalaemia (Guidelines Hyperkalaemia 1.1-1.3)

Guideline 1.1 – Hyperkalaemia: Definition, epidemiology and outcomes

We recommend that the European Resuscitation Council Guideline definition of hyperkalaemia be adopted with hyperkalaemia being defined as mild (5.5-5.9 mmol/L), moderate (6.0-6.4 mmol/L) or severe (≥6.5 mmol/L). (1C)

Audit measures:

1. Incidence and outcomes of patients with hyperkalaemia diagnosed:
    - in the community
    - in the out-patient clinic
    - after hospital admission
2. Proportion of patients where there has been a delay of > 24 hours in the recognition of hyperkalaemia.

Rationale

Electrolyte abnormalities are a recognised cause of cardiac arrhythmias, cardiac arrest and sudden death. The disturbance associated with the most immediately life-threatening consequences is hyperkalaemia. The importance of emergency treatment for hyperkalaemia and other electrolyte disorders has been acknowledged in the European Resuscitation Council (ERC) Guidelines.[1]

The published electrolyte values used to define hyperkalaemia and its severity vary. Although there is no universal definition of hyperkalaemia, a serum K^+ of ≥ 5.5 mmmol/L is widely accepted.[1-4] It can be further classified as mild (5.5-5.9 mmol/L), moderate (6.0-6.4 mmol/L) or severe (≥ 6.5 mmol/L).[1] This classification provides a guide to clinical decision-making and in practice, the precise values that trigger treatment decisions will depend on the patient's clinical condition and rate of change in the serum K^+ concentration.[1]

Other sources have used a threshold of ≥ 7.0 mmol/L to define severe hyperkalaemia.[2,6,7] The ERC has adopted a lower threshold (i.e. ≥ 6.5 mmol/L) for several reasons. Firstly, treatment for hyperkalaemia is frequently delayed. In patients presenting to an Emergency Department, the median time to treatment was 117 minutes (IQR 59-196 minutes).[8] In hospital patients, the mean time to first treatment was 2.1 hours in patients with a serum K^+ ≥ 6.5 mmol/L and was significantly longer in patients with a serum K^+ of 6.0-6.4 mmol/L at 2.8

hours.[9] Secondly, most patients manifest ECG changes of hyperkalaemia at a serum $K^+ \geq$ 6.7mmol/L.[10] Thirdly, there is usually a time delay in obtaining laboratory results by which time the serum K^+ may have risen further. Lastly, the threshold used to define 'severe' hyperkalaemia is likely to influence speed and intensity of treatment.

References

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Guideline 1.2 – Hyperkalaemia: Definition, epidemiology and outcomes

We recommend that a precipitating cause be considered for all patients presenting with hyperkalaemia. (1B)

Rationale

The incidence of hyperkalaemia in hospital patients is between 1.1% and 10%.[1-3] In a study of hospital patients, the most common causes were renal failure (77%), drugs (63%) and hyperglycaemia (49%).[4] In clinical practice, there may be a combination of factors contributing to hyperkalaemia.

Drugs are an important cause of hyperkalaemia, especially following the widespread use of renin-angiotensin-aldosterone blocking drugs in the treatment of heart failure and for renal protection. These drugs predispose to hyperkalaemia because they impair aldosterone secretion and reduce renal perfusion resulting in decreased K^+ excretion in the distal tubule. Renin-angiotensin-aldosterone blocking drugs have been implicated in hyperkalaemia in approximately 10% of outpatients within a year of starting treatment [4-7] and in 10-38% of patients admitted to hospital with hyperkalaemia.[8]

Hyperkalaemia is common among patients with end-stage renal disease (ESRD) on dialysis and has been reported in 10% of pre-dialysis samples.[9] Clinically significant hyperkalaemia is seen in 5-10% of patients requiring regular haemodialysis.[10] The risk increases with the length of the inter-dialytic interval, recirculation on dialysis and with dietary non-adherence. Among haemodialysis patients, hyperkalaemia is the reason for emergency dialysis in 24% of cases[11] and is responsible for 3-5% of deaths.[12,13] The perception that long-term haemodialysis patients develop some tolerance to hyperkalaemia is debatable.

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Guideline 1.3 – Hyperkalaemia: Definition, epidemiology and outcomes

We recommend that hyperkalaemia is regarded as a medical emergency given its potential for life-threatening consequences. (1A)

Audit measure:

1. Outcome measures in patients diagnosed with hyperkalaemia:
    a. Length of hospital stay
    b. In-hospital mortality

Rationale

Hyperkalaemia is unpredictable and arrhythmias and cardiac arrest can occur at any time. The mortality caused by hyperkalaemia in the general population is unknown, but in patients with

ESRD, it accounts for 1.9% of mortality.[1] In patients with CKD, hyperkalaemia increases the odds of mortality within 1 day of the event.[2]

Hyperkalaemia is usually fatal at potassium concentrations greater than 10 mmol/L, but survival has been reported in patients with extreme hyperkalaemia.[3-5] In one of these reports, the patient recovered completely despite a serum K^+ of 14 mmol/L.[3]

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2. Hyperkalaemia (Guidelines Hyperkalaemia 2.1 - 2.2)

Guideline 2.1 – Hyperkalaemia: Clinical Assessment; ABCDE and Early Warning Scoring (EWS) Systems.

We recommend that all patients with known or suspected hyperkalaemia undergo urgent assessment by nursing and medical staff to assess clinical status using the ABCDE approach, an early warning scoring system, and an appropriate escalation plan bearing in mind that the first presentation may be an arrhythmia. (1C)

Rationale

The most significant consequences of hyperkalaemia are arrhythmias and cardiac arrest, therefore early recognition, cardiac monitoring and prompt treatment are essential. Early

identification of hyperkalaemia, with or without adverse clinical signs, enables specific interventions, specialist referral (if required) and appropriate escalation of care.

Approach:

1. Use the 'Chain of Prevention'[1] which incorporates five key steps – staff education, monitoring, recognition, the 'call for help' and the 'response', as a basis for structuring the response to patient deterioration and prevention of cardiorespiratory arrest.

2. Ensure that your institution has an education programme that is focused on the prevention of patient deterioration for ward staff and responding clinical personnel. Staff should attain the necessary competences identified in the Department of Health document "Competencies for recognising and responding to acutely ill patients in hospital."

3. Develop a clear policy for the monitoring of patient's vital signs, based on the guidance in the National Institute for Health and Clinical Excellence clinical guideline 50 (Acutely ill patients in hospital: recognition of and response to acute illness in adults in hospital).[2]

4. Use an early warning scoring system based on the Royal College of Physicians National Early Warning Score (NEWS)[3] to identify patients who are deteriorating and therefore at risk of cardiorespiratory arrest.[4]

5. Use a patient charting system that facilitates the regular measurement and recording of early warning scores.[2,5]

6. Ensure that your institution has a clear universally known and understood, mandated, unambiguous, graded, activation protocol for escalating monitoring or summoning a response to a deteriorating patient.[2]

7. Ensure that your institution has a standardised method for communicating information about a deteriorating patient (e.g., SBAR, RSVP) between staff members.[6]

8. Check if your institution has a designated outreach service or rapid response team (e.g., Medical Emergency Team [MET]) capable of responding to acute clinical crises identified by clinical triggers or other indicators.[7]

9. Ensure that your institution has a clear and specific policy that requires a clinical response to 'calling criteria' or early warning systems ('track and trigger').[2,4,8] This should include the specific responsibilities of senior medical and nursing staff, including consultants and should identify the maximum response times.

10. Ensure staff are trained in and encouraged to use structured communication tools (e.g. SBAR – Situation, Background, Assessment, Recommendation).[6]

Clinical assessment using the ABCDE approach is well-established in the care of acutely ill patients[4] and allows identification of potentially life-threatening problems. A summary of this approach including clinical indicators relevant to hyperkalaemia is given below:

ABCDE APPROACH

A – **Airway** – Recognise and treat airway obstruction.

B – **Breathing** – Assess adequacy of ventilation: clinical examination, respiratory rate, O_2 saturation, arterial blood gas. Give oxygen aiming for 'normal' oxygen saturation and provide ventilatory support if necessary.

C – **Circulation** – Assess cardiovascular status: colour, pulse, BP, volume status, peripheral circulation, urine output (check for palpable bladder), cardiac rhythm (ECG, cardiac monitor), electrolytes (Urea and electrolytes, Mg^{2+}, Ca^{2+}, Phosphate). Establish intravenous access, take bloods. Consider fluid bolus (with care), vasopressors, inotropes treatment of arrhythmia, correct electrolyte abnormalities.

D – **Disability** – Assess neurological function: AVPU or GCS score and blood glucose - support ABC and correct underlying cause.

E – **Exposure** – Head to toe assessment and look for evidence of cause, e.g., signs of injuries, compartment syndrome, palpable bladder, skin rashes, dialysis access (central venous catheter, AV fistula, peritoneal dialysis catheter). Check temperature – do not let the patient get cold, and maintain the patient's dignity at all times.

Table 1: The ABCDE approach to assess and treat the deteriorating patient.

Most hospitals in the UK use EWS systems to assess and detection and monitoring of acutely ill patients.[2-4] The EWS uses a combination of several vital signs and mental status abnormalities to help detect acutely ill patients who are seriously ill and likely to deteriorate. In practice, a baseline assessment and serial monitoring of vital signs are useful in assessing the response to treatment. EWS or calling criteria help to identify the need for more frequent monitoring, when to call for expert help and the need for escalation of care. Hospitals should ensure that the system used is validated for their specific patient population to identify those at increased risk of serious clinical deterioration or death on admission and during hospital stay.[2] The Royal College of Physicians (London) has developed a National Early Warning Scoring System (NEWS) for use in the UK.[3]

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Guideline 2.2 – Hyperkalaemia: Clinical Assessment; History and examination

We recommend that all patients presenting with hyperkalaemia undergo a comprehensive medical and drug history and clinical examination to determine the cause of hyperkalaemia. (1B)

Rationale

A careful medical history may reveal the cause of hyperkalaemia.[1] It is important to elicit any background of kidney disease. Hyperkalaemia may occur in the context of pre-existing chronic kidney disease (CKD) or acute kidney injury (AKI). If this is unclear from the medical history or cannot be provided by the family, access to previous medical records and

biochemistry results can establish the patient's baseline renal function. Drugs, including over-the-counter medications, are an important cause of hyperkalaemia. Therefore knowledge of current medication and any recent changes to medication is very useful.

Evaluation of the presenting illness usually helps to determine the cause of hyperkalaemia. The cause may be volume depletion (e.g. diarrhoea and vomiting) on a background of kidney disease and/or nephrotoxic drugs. The clinical presentation may be over-shadowed by the primary illness, but some symptoms (e.g. muscle weakness, paraesthesiae, palpitations) may suggest severe hyperkalaemia.[1,2] In patients receiving haemodialysis, it is useful to establish duration since last dialysis, type of dialysis access (e.g. central venous catheter or AV fistula), recent problems on dialysis (e.g. poor blood flow via dialysis access, recent access interventions), medication, and any recent dietary indiscretions. Non-compliance with diet or dialysis regimen is an important and preventable cause of hyperkalaemia.[2,3] If dialysis patients present with hyperkalaemia to the emergency department or a non-renal ward, the local renal team should be informed urgently as medical interventions will only temporarily control hyperkalaemia. Some patients are particularly at risk of hyperkalaemia and there should be a high index of suspicion of hyperkalaemia if these patients become unwell.

Risk factors for Hyperkalaemia:

- Dialysis dependency (haemodialysis or peritoneal dialysis)
- Chronic Kidney Disease Stages 4 & 5 (CKD, eGFR < 30 ml/min/1.73m^2)
- Nephrotoxic medications (e.g. renin-angiotensin drugs, non-steroidal anti-inflammatory drugs)
- Cardiac failure (e.g. renin-angiotensin drugs)
- Diabetes mellitus (e.g. renin-angiotensin drugs, diabetic keto-acidosis)
- Liver disease (e.g. spironolactone, hepato-renal failure)
- Adrenal insufficiency

Table 2: Factors associated with an increased risk of hyperkalaemia.

References:

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3. Hyperkalaemia (Guidelines Hyperkalaemia 3.1 - 3.2)

Guideline 3.1 – Hyperkalaemia: ECG

We recommend that all patients with a serum K^+ value ≥ 6.0 mmol/L have an urgent 12-lead ECG performed and assessed for changes of hyperkalaemia. (1B)

Audit measures:

1. Proportion of patients with a serum potassium value ≥ 6.0 mmol/L who had a 12-lead ECG recorded before treatment [Audit Standard 100%].
2. Proportion of patients with a serum potassium value ≥ 6.0 mmol/L and an ECG showing features of hyperkalaemia who had their 12-lead ECG repeated following treatment [Audit Standard 100%].

Rationale

The ECG is used to assess cardiac toxicity and risk of arrhythmias, and should be recorded promptly during the assessment of patients with known or suspected hyperkalaemia. Most patients show ECG changes when the serum K^+ is greater than 6.7 mmol/L.[1] When the diagnosis of hyperkalaemia can be established based on the ECG, treatment can be initiated even before serum biochemistry is available. The typical ECG features of hyperkalaemia are shown in Figure 1.

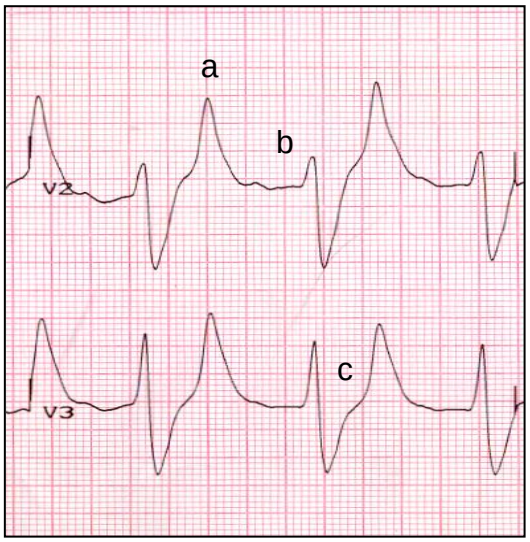

Figure 1: ECG in a patient with severe hyperkalaemia (serum K^+ 9.1 mmol/L) illustrating peaked T waves (a), diminished P waves (b) and wide QRS complexes (c).

The ECG changes associated with hyperkalaemia are attributable to the physiological effect of a raised serum potassium on myocardial cells. The atrial myocardium is more sensitive

than the ventricular myocardium to the effects of hyperkalaemia and the specialised tissue (sinoatrial node and bundle of His) is the least sensitive.[2] Hyperkalaemia is associated with depression of conduction between adjacent cardiac myocytes, manifesting in prolongation of the PR interval and QRS duration. The P wave amplitude is diminished in the early stages as T wave amplitude increases.

Suppression of sinoatrial function results in sinus bradycardia or standstill, and escape beats or rhythms may maintain some output in these circumstances. Suppression of atrioventricular (AV) conduction will give rise to varying degrees of AV block and in the event of complete AV block, a ventricular escape rhythm may maintain some output. When escape rhythms do not maintain output in these settings, asystolic cardiac arrest ensues. The ECG changes of hyperkalaemia usually follow a progressive pattern (Figure 2).

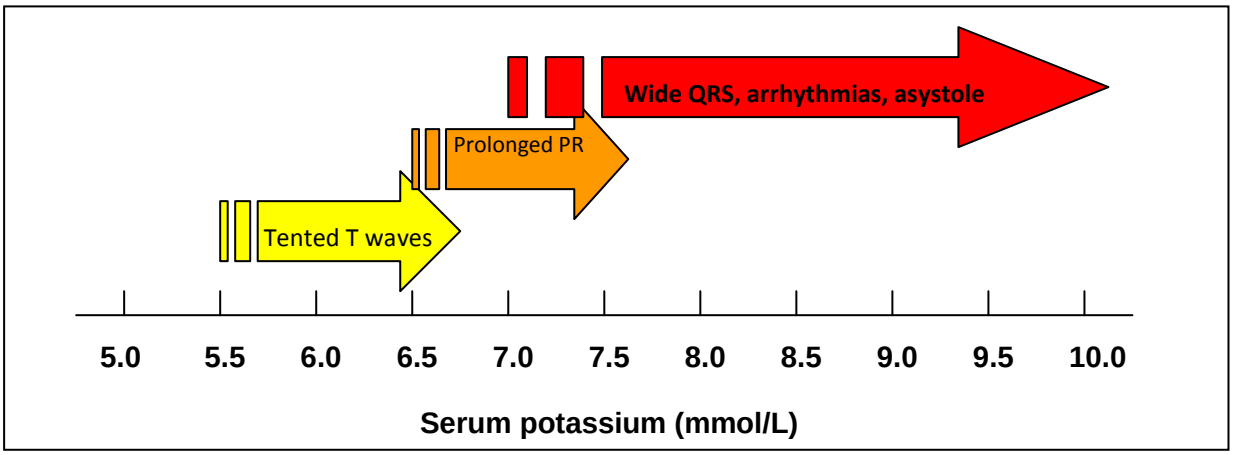

Figure 2: Progressive changes in ECG with increasing severity of hyperkalaemia.

Although the ECG is useful in assessing patients with hyperkalaemia, there are some shortfalls. Firstly, the value of the ECG is dependent on the skill of the interpreter. Physician interpretation of the ECG results in the diagnosis of hyperkalaemia with a sensitivity of just 0.34-0.43.[3] Secondly, the ECG may be normal even in the presence of severe hyperkalaemia.[4] Thirdly, ECG changes may be minimal even in patients (i.e. haemodialysis patients) most at risk of hyperkalaemia.[5] Fourthly, the ECG appearance may be atypical in patients with hyperkalaemia associated with diabetic ketoacidosis. In this setting there are reports showing ECG changes suggestive of myocardial ischaemia or pseudoinfarction.[6,7] Finally, the first presentation with severe hyperkalaemia may be ventricular fibrillation or asystole.[8]

Hyperkalaemia can affect the function of both temporary[9,10] and permanent pacemakers.[11-14] Hyperkalaemia causes two important clinical abnormalities in patients with pacemakers – widening of the paced QRS complex and increased atrial and ventricular pacing thresholds with or without increased latency (an increase in the interval between the pacemaker stimulus artefact and the onset of the paced beat).[15]

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Guideline 3.2 – Hyperkalaemia: Cardiac Monitoring: 3-lead ECG

We recommend a minimum of continuous 3-lead ECG monitoring for all patients with a serum K^+ value $\geq$ 6.5 mmol/L, patients with features of hyperkalaemia on 12-lead ECG, and in patients with a serum K^+ value between 6.0-6.4 mmol/L who are clinically unwell or in whom a rapid rise in serum K^+ is anticipated, ideally in a high-dependency setting. (1C)

Audit measure:

1. Proportion of patients with a serum K^+ value $\geq$ 6.5 mmol/L who have documented evidence of continuous ECG monitoring [Audit standard: 100%].

Rationale

Patients with hyperkalaemia are at increased risk of arrhythmias. Continuous ECG monitoring will enable early recognition and prompt treatment to prevent life-threatening arrhythmias. In general terms, the greater the severity of hyperkalaemia, the higher the incidence of ECG abnormalities and risk of arrhythmias.[1] Therefore the first step in assessing the hyperkalaemic patient is assessing this risk and taking immediate action.

Hyperkalaemia causes arrhythmias by causing hyperpolarisation of cells, making them less able to depolarise when necessary.[1] Arrhythmias can occur at any time in the patient's presentation without prior toxic ECG changes.[2] Some of the typical arrhythmias are shown in Figure 3. All arrhythmias have been reported in patients with hyperkalaemia – narrow complex tachycardias including atrial fibrillation,[3] bradycardia,[4-7] ventricular tachycardia[8] and

idioventricular rhythms.[9] Given the unpredictable nature of hyperkalaemia and the variable threshold for arrhythmias from patient-to-patient, vigilance is the best approach.

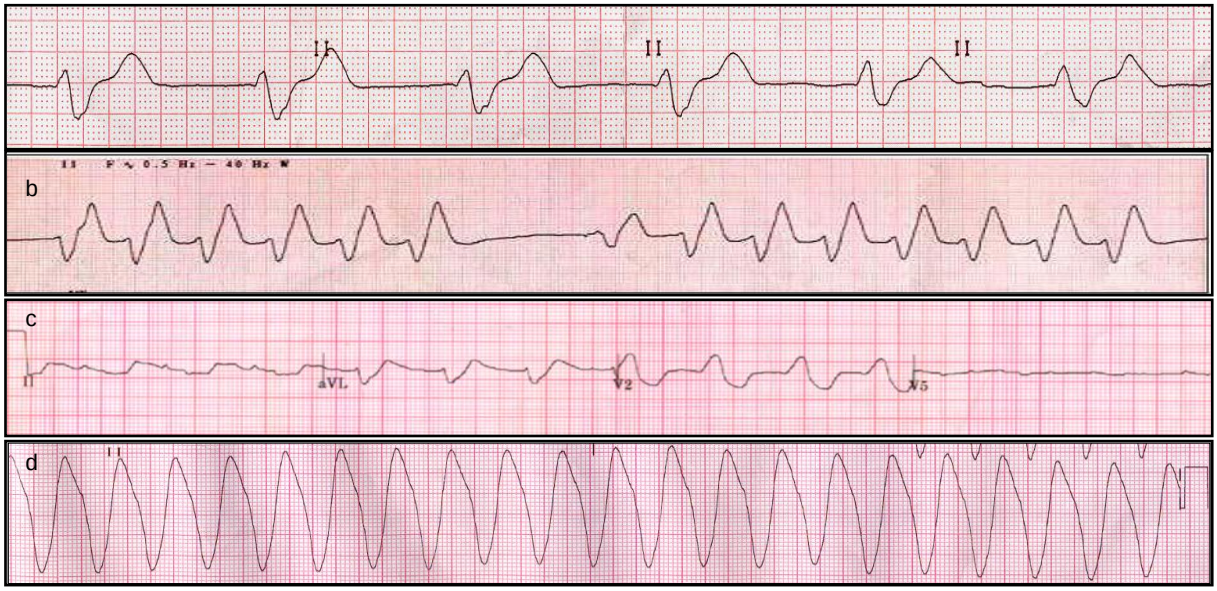

Figure 3: Arrhythmias in patients with severe hyperkalaemia illustrating bradycardia with wide QRS [K^+ 9.6 mmol/L] (a), sine wave with pause [K^+ 9.3 mmol/L] (b) and sine wave without pause [K^+ 8.4 mmol/L] (c) and ventricular tachycardia [K^+ 9.1 mmol/L] (d).

Bradycardia associated with severe hyperkalaemia may be resistant to conventional treatment and is enhanced in patients taking negatively chronotropic drugs (e.g beta-blockers). In many instances, the ECG is available before serum biochemistry and may show complete heart block. Although bradycardia is documented to be a potential adverse effect of intravenous calcium salts, calcium can increase the heart rate in patients with hyperkalaemia-induced bradycardia.[6,7] Atropine[7] may be ineffective in the presence of hyperkalaemia. Temporary pacing may be ineffective, may induce arrhythmias and delays definitive treatment; it is not recommended for treating hyperkalaemia-induced bradycardia.[2] External pacing methods may be useful whilst treatment for hyperkalaemia is underway.

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4. Hyperkalaemia (Guidelines Hyperkalaemia 4.1 - 4.3)

Guideline 4.1 – Hyperkalaemia: Laboratory tests

We recommend that lithium heparin anti-coagulated specimens are the sample type of choice when rapid turnaround of urea and electrolytes results is required. (1B)

Audit Measure:

1. The average laboratory analysis time for K^+ concentration using clotted (serum) and lithium heparin (plasma) samples [Audit standard: within 60 minutes].

Rationale

The treatment of hyperkalaemia requires timely access to accurate serum K^+ measurements. Potassium measurement can be undertaken in the laboratory or at the point of care using a variety of techniques. Laboratory measurements of K^+ focus on those in blood plasma or serum. This provides an advantage over whole blood measurements from blood gas analysers because haemolysis can be identified by visual inspection after centrifugation or by spectrophotometric analysis of the specimen for the presence of haemoglobin. In-vitro

haemolysis of blood samples can cause a variable increase in K^+ concentrations leading to misclassification of normokalaemic patients as hyperkalaemic, and hypokalaemic patients as normokalaemic.[1]

The choice of specimen sent to the laboratory will depend on the tests requested and the urgency. Routine samples for measurement of urea and electrolytes are usually requested in a clotted serum sample. In emergencies where hyperkalaemia is suspected, specimens collected in a lithium heparin tube can be analysed more rapidly as there is no requirement to wait for the sample to clot before centrifugation. Laboratories may differ in their requirements for other tests and different reference intervals may also apply.

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Guideline 4.2 – Hyperkalaemia: Blood gas analysis

We recommend that in emergencies, K^+ is measured from an arterial or venous blood sample using a point-of-care blood gas analyser whilst awaiting the results from a formal laboratory measurement. (1B)

Rationale

Blood gas analysers (BGA) are increasingly available at the point of care with analytical repertoires that include electrolyte measurements. Haemolysis is an important confounding factor in the measurement of K^+, especially when using whole blood specimens via BGA. A greater concordance has been reported between BGA and the laboratory results when the K^+ concentration is greater than 3 mmol/L.[1] A larger blood sample (i.e. more than 1mL) can reduce the extent of haemolysis and improve accuracy.[2]

BGA potassium measurement has been compared with central laboratory venous analysis in many clinical settings with variable recommendations.

1. During cardiac arrest, the use of BGA analysis was not recommended as the limits of agreement between the results were wide (95% limits of agreement ranging from -1.182 to 1.394 mmol/L), although the mean differences in K^+ values between the 50

paired specimens was low at 0.106 mmol/L.[3] However, in this study none of the patients were hyperkalaemic and in this setting time is crucial.

2. In the ICU, two large studies found small differences in mean K^+ values using these methods (0.03 mmol/L with a 95% confidence interval of 0.011 to 0.056 in 529 paired samples)[4] and (0.156 mmol/L with a 95% confidence interval of 0.42 to 0.62 in 200 paired samples).[5] They both concluded that there is sufficient agreement between the results to use the BGA analyser to guide clinical decisions.

3. In the emergency department, one study reported the difference between BGA and laboratory K^+ to be 0.49 mmol/L (95% CI of agreement 0.839 to 0.943) in 53 paired samples.[6] This study concluded that BGA machines can be used to guide treatment. In clinical practice, early identification has the potential benefits of ensuring appropriate triage, safe patient transfer and appropriate ward placement.

The benefits in achieving a rapid measurement of serum K^+ level using a BGA is only utilised if it influences clinical decisions. Interestingly, a survey of 60 doctors, including 24 consultants, showed that 51.6% would wait for laboratory confirmation and 48.4% would base clinical decisions on results obtained from the BGA.[4] This highlights the need for guidance on the application of BGA machines in the management of hyperkalaemia.

Local laboratory medicine specialists should ensure that the all methods used for measurement of potassium are fit for purpose and that the methods are appropriately quality controlled and quality assessed. Point of care testing systems and processes, used for the measurement of potassium, should follow best practice as identified by the MHRA (Medicines and Healthcare Regulatory Agency, 2010).[7] Local risk assessments of the relative value and safety of point of care *verus* laboratory delivery of potassium measurements should form part of the development process.

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Guideline 4.3 – Hyperkalaemia: Pseudo-hyperkalaemia

We recommend that urea and electrolytes are measured using paired lithium heparin and clotted serum samples from a large vein using gentle traction with prompt laboratory analysis if pseudo-hyperkalaemia is suspected. (1A)

Rationale

Ideally, the laboratory measurement will reflect the K^+ concentration in the extra-cellular fluid *in vivo.* Pseudo-hyperkalaemia describes the finding of a raised *serum* (clotted blood) K^+ value concurrently with a normal *plasma* (non-clotted blood) potassium value. The clotting process releases K^+ from cells and platelets, which increases the serum K^+ concentration by an average of 0.4 mmol/L. The most common cause of pseudo-hyperkalaemia is a prolonged transit time to the laboratory or poor storage conditions.

Other causes of pseudo-hyperkalaemia include a high platelet count, haemolysis, erythrocytosis, difficult venepuncture, prolonged storage time of clotted samples, or cold storage conditions. When using evacuated tubes for blood collection, if the order of draw is wrong, the sample can be contaminated with potassium EDTA (for full blood count).[1,2] Another common cause of contamination is sampling from the arm into which potassium-containing fluids are being infused. An inverse relationship between ambient temperature and

potassium concentration has been reported with higher K^+ values in the winter months and has been termed 'seasonal' pseudo-hyperkalaemia.[3]

Pseudo-hyperkalaemia can be excluded by performing simultaneous measurements of plasma potassium in a lithium heparin anti-coagulated specimen and in a clotted sampled.[4] This will provide two values with the lower being in the heparinised specimen. Pseudo-hyperkalaemia is detected when the serum potassium concentration exceeds that of the plasma by more than 0.4 mmol/L.[1,5] The difference in results may be in the order of several mmol/L. A full blood count should also be performed to exclude a haematological disorder.[1]

Laboratories have developed standard protocols to reduce the risks of pseudo-hyperkalaemia and pseudo-*normo*kalaemia. Labelling the time of collection on specimens, reducing transit times, and optimising storage conditions (i.e. avoiding wide fluctuations in temperature) for specimens from primary care are important strategies. These measures may in turn reduce out-of-hours calls to deputising services and admissions to acute medicine units for the investigation of hyperkalaemia.

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5. Hyperkalaemia (Guidelines Hyperkalaemia 5.1 - 5.5)

Guideline 5.1 – Hyperkalaemia: Summary of treatment strategy

We recommend that the treatment of hyperkalaemia follows a logical 5-step approach. (1B)

Rationale

The treatment of hyperkalaemia currently varies considerably. A systematic approach taking into account clinical priorities may reduce this variability, enhance patient outcome and reduce adverse events related to hyperkalaemia and its treatment (Figure 4).[1] This process begins with an assessment of the risk of arrhythmias, followed by action to reduce the serum potassium concentration by shifting potassium back into cells and removing it from the body. Treatment effectiveness is assessed by monitoring the serum K^+, and hypoglycaemia is avoided or detected and treated promptly by frequent monitoring of the blood glucose. Treatment is not complete until the cause is identified and steps taken to prevent recurrence. The hyperkalaemia treatment algorithm outlines this sequential approach [Guideline 11.1].

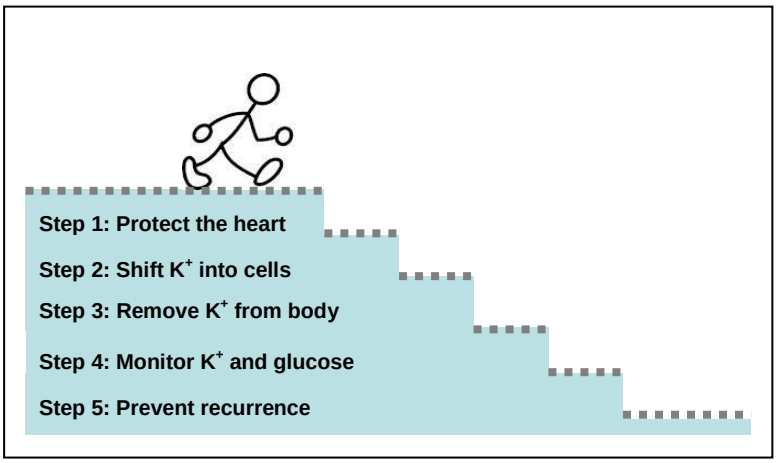

Figure 4: There are five key steps in the treatment of hyperkalaemia (*never walk away without completing all of these steps*).

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Guideline 5.2 – Hyperkalaemia: STEP 1 - Protect the heart; intravenous calcium salts

We recommend that intravenous calcium chloride or calcium gluconate, at an equivalent dose (6.8mmol), is given to patients with hyperkalaemia in the presence of ECG evidence of hyperkalaemia. (1A)

Audit Measures

1. The frequency of ECG changes in patients treated with intravenous calcium salts.
2. Adverse events as a result of treatment with intravenous calcium salts.

Rationale

The use of intravenous (IV) calcium in the treatment of hyperkalaemia is well established in clinical practice, but is based on sparse evidence. The toxic effects of K^+ on the heart and their antagonism by calcium were first demonstrated in an animal model in 1883,[1] and later confirmed in 1939.[2] IV calcium was shown to be effective in treatment and prophylaxis in patients with acute kidney injury during the Korean War.[3] Although much of the evidence to support its use arises from case reports and anecdotal experience,[4] there remains little doubt of the importance of IV calcium in emergency treatment of hyperkalaemia even when the serum calcium is normal.

The electrophysiological effect of K^+ on the heart is dependent on its extracellular concentration, direction of change (hypokalaemia or hyperkalaemia) and rate of change. The effect of K^+ on the resting membrane potential of cardiac myocytes is modulated by the simultaneous calcium concentration such that an elevated calcium concentration decreases the depolarisation effect of an elevated K^+ concentration.[5]

IV calcium antagonises the cardiac membrane excitability thereby protecting the heart against arrhythmias. It is effective within 3 minutes as shown by an improvement in the ECG appearance (e.g. narrowing of the QRS complex). The dose should be repeated if there is no effect within 5-10 minutes. The duration of action is only 30-60 minutes, so further doses may be necessary if hyperkalaemia remains uncontrolled. As IV calcium does not lower serum K^+, other interventions are urgently required.

10 ml 10% Calcium Chloride = 6.8 mmol Ca^{2+}
10 ml 10% Calcium Gluconate = 2.26 mmol Ca^{2+}

Table 3: Calcium content of IV calcium salts used in treatment of hyperkalaemia.

The choice of calcium salt, chloride or gluconate, has largely been guided by practicalities such as availability, local practice and the clinical condition of the patient. There are some

important differences between the two available solutions. Both preparations, calcium chloride and calcium gluconate, are available in the form of 10ml of 10% solution (Table 3). Calcium chloride contains approximately three times more calcium (6.8 mmol/ 10ml) as compared with calcium gluconate (2.26mmol/ 10ml). There is conflicting evidence on the bioavailability of ionised calcium in the two preparations. It has been suggested that calcium gluconate has limited bioavailability because of chelation and the reliance on hepatic metabolism,[6] but in contrast, no difference in availability of ionised calcium was shown in the anhepatic stage of liver transplantation.[7] Given the uncertainty, the chloride salt has been recommended in the setting of haemodynamic instability, including cardiac arrest. This also raises some doubt about the efficacy of the gluconate salt in patients with acute kidney injury, which is often associated with haemodynamic compromise.

The main adverse effect of IV calcium is tissue necrosis if extravasation occurs. For this reason, many guidelines have recommended the use of calcium gluconate, which is regarded as less toxic on peripheral veins. Although adverse event reporting is likely to be incomplete, tissue necrosis has been reported to the MHRA following the use of both IV calcium salts [Guideline 13.1]. Therefore, the key preventative strategy is to ensure adequate venous access prior to administration. Other potential adverse effects are peripheral vasodilation, hypotension, bradycardia, syncope and arrhythmias. Interestingly, in the historical case series by Chamberlain in 1964, up to 60ml 10% calcium gluconate and 90ml 10% calcium chloride were used with no serious adverse events documented.[4]

Caution with administration of IV calcium has historically been advised in patients with known or suspected digoxin toxicity. As hypercalcaemia may potentiate digoxin toxicity, a slower rate of administration, over 30 minutes, has been recommended in these patients.[8-10] To date, there have been five case reports of death in this context.[11-13] These reports illustrate a temporal association, but lack evidence of a cause-and-effect relationship. In contrast, there are reports in the literature showing no adverse effects in patients given IV calcium in the presence of unrecognised digoxin toxicity.[14-15] In reality, the digoxin level is usually unknown at presentation. Furthermore, a recent study has shown no increased risk of arrhythmias or mortality in patients treated with IV calcium in the presence of digoxin intoxication.[16]

In clinical practice, there are several pitfalls in the administration of IV calcium.

1. A single dose of 10ml 10% calcium gluconate is often administered irrespective of the response which is often inadequate.

2. The 12-lead ECG is frequently not repeated after administration to assess response. A response may be seen with a narrowing of the QRS complex (Figure 5), reduction in T wave amplitude (Figure 5), increase in heart rate in bradycardic patients or reversal of arrhythmia.
3. IV calcium can cause bradycardia, therefore there may be reluctance to administer if the patient's heart rate is already slow.
4. The relatively short duration of action of IV calcium (30-60 minutes) may not be considered in patients with prolonged hyperkalaemia.
5. IV calcium may not be deemed necessary in patients in whom emergency dialysis is planned or being initiated for severe hyperkalaemia.

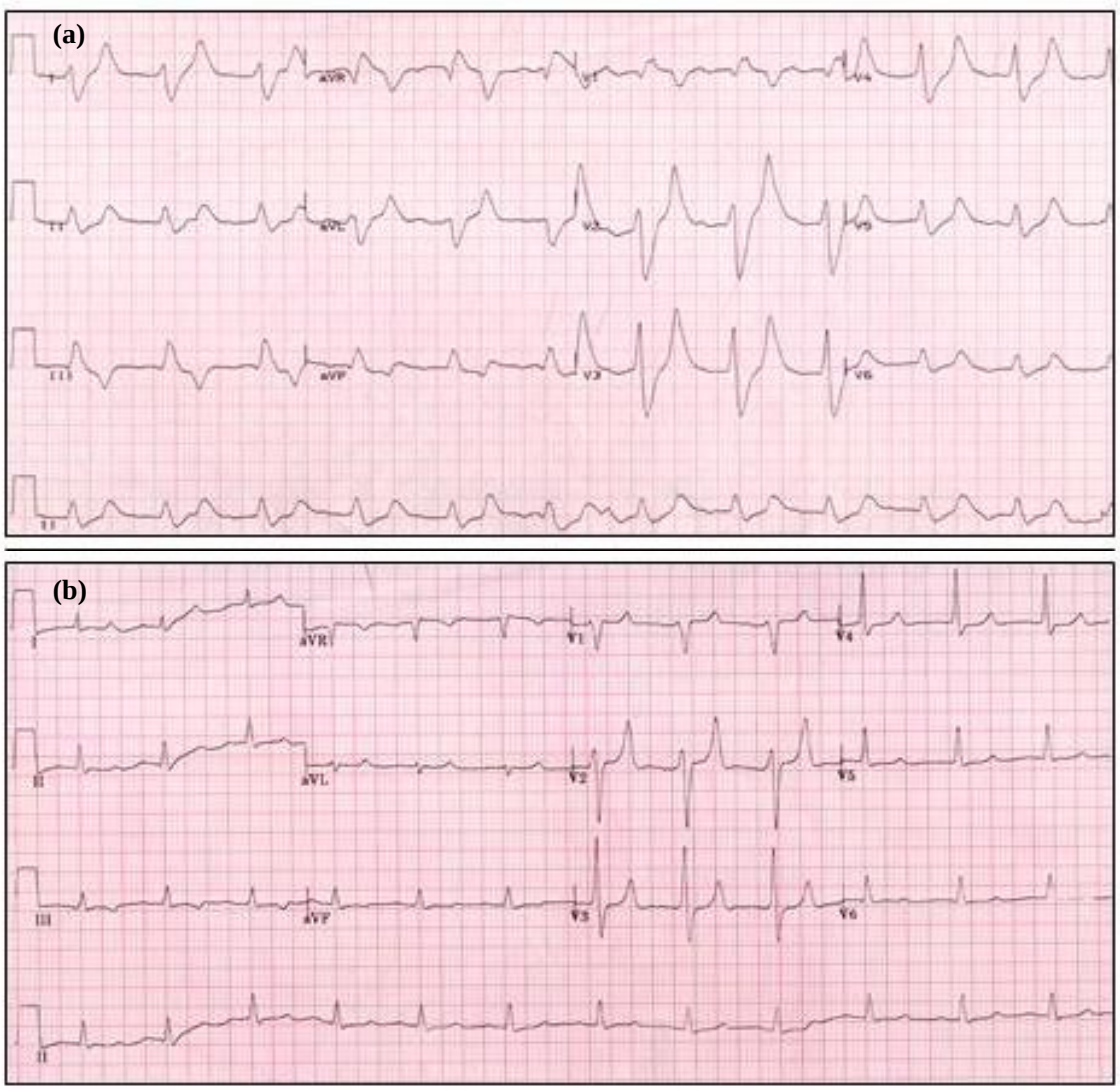

Figure 5: ECG on admission (a) and following 20ml 10% calcium gluconate IV (b) in a patient with serum K^+ 9.3 mmol/L who presented with generalised weakness.

There is general agreement that IV calcium salts should be used in the presence of life-threatening ECG changes (absent P waves, wide QRS, sine-wave pattern)[8,17-20] or in the presence of arrhythmias or cardiac arrest.[20-21] More controversially, some reports have also recommended their use in patients with isolated peaked T waves.[9,22] This approach seems reasonable as the transition time from peaked T waves to broad QRS complex is unknown and is likely to be highly variable from patient to patient.[23] Additionally, as peaked T waves are a frequently recollected sign of hyperkalaemia, it may also prompt earlier recognition and treatment.[23]

There is no consensus on the use of IV calcium in hyperkalaemic patients with a normal ECG. Some authors suggest that IV calcium should not be injected in the absence of ECG changes regardless of the serum K^+ concentration.[22] The rationale being that the ECG may be a better indicator of immediate danger than the serum K^+ value itself.[4] Other authors highlight the insensitivity of the ECG in assessing the severity of hyperkalaemia.[10,24-25] This issue is compounded by the variability in ECG interpretation.[26-27] Given that the ECG is the best tool for assessing cardiac toxicity, the effect of IV calcium is assessed by an improvement in ECG appearance, and IV calcium is not without risk, then IV calcium should be reserved for patients with ECG changes of hyperkalaemia.

In summary, IV calcium has been widely recommended for the treatment and prophylaxis of arrhythmias in patients with hyperkalaemia. The use of IV calcium buys time for other interventions to take effect in lowering the serum K^+. Both preparations can be given safely if venous access is adequate. When 10% calcium gluconate is used, sequential doses of 10ml solution are often required whereas a single dose of calcium chloride is more likely to be effective. Therefore, we recommend an equivalent dosage of calcium chloride or gluconate (6.8 mmol) for initial therapy.

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Guideline 5.3.1 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; insulin-glucose infusion

We recommend that insulin-glucose (10 units soluble insulin in 25g glucose) by intravenous infusion is used to treat severe ($K^+ \geq 6.5$ mmol/L) hyperkalaemia. (1B)

Guideline 5.3.2 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; insulin-glucose infusion

We suggest that insulin-glucose (10 units soluble insulin in 25g glucose) by intravenous infusion may be used to treat moderate (K^+ 6.0-6.4 mmol/L) hyperkalaemia. (2C)

Audit measure:

1. The proportion of patients with severe hyperkalaemia ($K^+ \geq 6.5$ mmol/L) treated with insulin-glucose infusion [Audit Standard: 100%].

Rationale (Guidelines 5.3.1 – 5.3.2)

Insulin is the most reliable agent for shifting K^+ into cells in patients with hyperkalaemia.[1] Notably, most studies on the efficacy of insulin-glucose have included predominantly patients with ESRD.[2]

Insulin and catecholamines shift K^+ into cells.[3] Insulin lowers serum potassium by activating Na^+-K^+ ATPase and by recruitment of intracellular pump components into the plasma membrane.[4] Insulin binding to specific membrane receptors results in extrusion of Na^+ and cellular uptake of K^+. This effect is independent of its hypoglycaemic action.[5]

STUDY	N	Dose of Soluble Insulin	Dose of Glucose	Mean initial K^+ (mmol/L)	Peak reduction in K^+ (mmol/L)	Time of max action	Duration of Effect (min)	Hypoglycaemia (%)
Lens[13] 1989	10	10 units	40g	6.7	1.0	60	>360	20
Allon[7] 1990	12	10 units	25g	5.48	0.65	45	>60	75
Ljutic[11] 1993	9	10 units	25g	6.33	0.76	60	>60	11
Allon[8] 1996	5	5 mU/kg/min	60g	4.28	0.85	60	>60	0
Duranay[12] 1996	20	10 units	30g	>6.0	0.98	180	>360	0
Kim[14] 1996	8	5 mU/kg/min	40g	6.3	0.7	60	>60	0
Ngugi[10] 1997	70	10 units	25g	6.9	0.9	60-120	>360	20
Mahajan[9] 2001	30	12 units	25g	6.59	0.83	180	>360	3.3

Table 4: Efficacy of insulin-glucose monotherapy.

The administration of hypertonic glucose alone is not recommended for the treatment of hyperkalaemia as endogenous insulin production is unlikely to be sufficient for a therapeutic effect and there is a risk of exacerbating the hyperkalaemia by inducing hypertonicity.[6] In

hyperglycaemic patients, e.g. diabetic ketoacidosis, insulin should be given without dextrose as the cause of hyperkalaemia is likely to be the hyperglycaemia itself. Potassium concentration starts to decrease within 15 minutes of starting an insulin-glucose infusion,[7,8] with the peak reduction (ranging from 0.65-1.0 mmol/L) occurring between 30-60 minutes[7-14] (Table 4). The reduction in serum K^+ may be sustained for up to two hours after administration following which there is usually a gradual rebound.[15]

The efficacy of insulin-glucose is increased if given in combination with salbutamol. The peak K^+ lowering effect with combination therapy at 60 minutes was found to be 1.5 mmol/L with intravenous beta-agonist therapy[13] and 1.2 mmol/L with nebulised beta-agonist therapy.[7]

The main risk of insulin-glucose therapy is hypoglycaemia. This risk is associated with the dose of glucose administered, but studies show conflicting results with the incidence of hypoglycaemia ranging from 11-75% when 25g glucose is administered (Table 4). Uraemia is known to attenuate the hypoglycaemic response to insulin although this does not affect its hypokalaemic action.[5] Patients with renal failure may experience delayed hypoglycaemia, up to 6 hours after infusion,[16] therefore close monitoring is required for several hours. Some experts advocate a continuous infusion of glucose following insulin-glucose treatment to avoid the occurrence of hypoglycaemia.[7]

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Guideline 5.4.1 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; salbutamol

We recommend nebulised salbutamol 10-20mg is used as adjuvant therapy for severe ($K^+ \geq$ 6.5 mmol/L) hyperkalaemia. (1B)

Guideline 5.4.2 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; salbutamol

We suggest that nebulised salbutamol 10-20mg may be used as adjuvant therapy for moderate (K^+ 6.0-6.4 mmol/L) hyperkalaemia. (2C)

Guideline 5.4.3 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; salbutamol

We recommend that salbutamol is not used as monotherapy in the treatment of severe hyperkalaemia. (1A)

Audit Measure:

1. The proportion of patients who develop adverse effects of salbutamol (e.g. tachycardia, arrhythmia).

Rationale (Guidelines 5.4.1 – 5.4.3)

Salbutamol is a beta-2 adrenoceptor agonist and promotes the intracellular shift of K^+ by activation of the Na-K ATPase pump. Salbutamol and other beta-agonists are equally effective given intravenously or by nebuliser.[1-3] The nebulised route is easier to administer and causes fewer side-effects.[4] Tremor, palpitations (increase in heart rate >15 per minute) and headache are the most frequently reported adverse effects. Mild hyperglycaemia (2-3 mmol/L increase) has also been reported[5-7] and this may partly protect against insulin-induced hypoglycaemia.[8] There are no studies to assess the safety of salbutamol in patients with cardiac disease, therefore cautious use is recommended with cardiac monitoring.

The effect of salbutamol is dose-dependent[9] and the onset of action is within 30 minutes with its peak effect within 60 minutes. Nebulised salbutamol 10mg decreases serum K^+ by 0.53-0.88 mmol/L[1,9,10] and 20mg decreases serum K^+ by 0.66-0.98 mmol/L [5,9] (Table 5). The effects of salbutamol last for at least 2 hours. In one study, a small transient paradoxical increase in serum K^+ ($\geq$ 0.1 mmol/L) was observed in 59% of patients within one minute of completion of inhaled salbutamol therapy, but serum K^+ returned to baseline within 3 minutes.[7]

The combination of salbutamol with insulin-glucose is more effective than either treatment alone.[5,11] The peak K^+ lowering effect with combination therapy at 60 minutes was 1.5 mmol/L with intravenous beta-agonist therapy[11] and 1.2 mmol/L with nebulised beta-agonist therapy.[5]

STUDY	N	Dose of Salbutamol	Mean initial K^+ (mmol/L)	Peak reduction in K^+ (mmol/L)	Time of max action	Duration of Effect (min)
Allon[9] 1989	10	10 mg	5.93	0.62	90	>120
Allon[10] 1996	8	10 mg	4.29	0.53	60	>60
Liou[1] 1994	17	10 mg	5.8	0.88	90	>60
Montoliu[6] 1990	10	15 mg	6.5	0.9	30	>360
Kim[14] 1997	9	15 mg	5.99	0.57	60	> 60
Allon[9] 1989	10	20 mg	5.81	0.98	90	>120
Allon[5] 1990	12	20 mg	5.56	0.66	60	>60
McClure[2] 1994	11	2.5/ 5 mg*	5.9	0.61	30	>300
Mandelberg[7] 1999	17	1200μg (via MDS-I)	5.5	0.4	60	ns

Table 5: Studies investigating efficacy of *nebulised* salbutamol in hyperkalaemia.

***children (aged 5-18 years)**
ns – not stated

Salbutamol may be ineffective in some patients with hyperkalaemia. Non-selective beta-blockers may prevent the hypokalaemic response to salbutamol.[12] Up to 40% of patients with ESRD do not respond to salbutamol, even in the absence of beta-blocker therapy, and the mechanism for this resistance is unknown.[5,9] The degree of potassium lowering is variable and 20-40% of patients have a decline in serum $K^+ < 0.5$ mmol/L.[13] Given that there is no way to predict which patients will respond to salbutamol or to what extent and there is a potential risk of an early rise in serum K^+ after administration, salbutamol should not be used as monotherapy.

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Guideline 5.5 – Hyperkalaemia: STEP 2 – Shift K^+ into cells; sodium bicarbonate

We suggest that intravenous sodium bicarbonate infusion is not used routinely for the acute treatment of hyperkalaemia. (2C)

Rationale

There is currently insufficient evidence to support the use of intravenous sodium bicarbonate for the acute treatment of hyperkalaemia. Almost all of the available evidence comes from

studies performed in stable chronic haemodialysis patients. When compared with other potassium-lowering regimens, sodium bicarbonate monotherapy failed to lower K^+ acutely.[1,2] Prolonged administration of sodium bicarbonate may lower K^+, but at the expense of a large sodium load.[2] Hypertonic saline (5% solution) has been reported to reverse the cardiotoxicity induced by hyperkalaemia in a small series,[3] but concludes that this approach may be life-saving only in selected cases. There remains no supporting evidence for this approach.

There is little evidence to suggest that sodium bicarbonate enhances the efficacy of other potassium-lowering regimens. In stable non-diabetic dialysis patients the addition of sodium bicarbonate to intravenous insulin and dextrose or nebulised salbutamol made no difference to the decrease in serum K^+.[1] One study showed that a combination of insulin and dextrose, intravenous salbutamol and intravenous sodium bicarbonate was more effective at lowering K^+ than any of the possible two regimen combinations.[4]

There is no evidence to suggest that sodium bicarbonate is more effective at lowering serum K^+ as the severity of metabolic acidosis increases. Changes in serum K^+ did not correlate with basal values of plasma bicarbonate or blood pH.[5,6] There is also no evidence to suggest that sodium bicarbonate is more effective in patients as the severity of hyperkalaemia increases.[5]

Overall, the available evidence is limited and mainly comes from stable patients with ESRD on haemodialysis. This may not reflect the clinical response in patients with hyperkalaemia in the context of acute kidney injury. However the use of sodium bicarbonate comes with the risk of sodium and fluid overload and the risks may outweigh any potential (unproven) benefits in this patient group. The use of sodium bicarbonate in hyperkalaemic cardiac arrest will be discussed in Guideline 10.

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Guideline 5.6 – Hyperkalaemia: STEP 3 – Remove K^+ from body; cation-exchange resins

We suggest that cation-exchange resins are not used in the emergency management of severe hyperkalaemia, but may be considered in patients with mild to moderate hyperkalaemia. (2B)

Audit Measures:

1. The proportion of patients with severe hyperkalaemia treated with resins [Audit Standard; 0%].

2. The frequency of bowel complications with the use of cation-exchange resins.

Rationale

Cation-exchange resins are cross-linked polymers with negatively charged structural units which can exchange bound sodium (Kayexalate) or calcium (calcium resonium) for cations including K^+. Their onset of action is slow which limits their use in emergencies.

Evidence in support for the use of cation-exchange resins in the treatment of hyperkalaemia is limited. Studies in favour of their use also highlighted that multiple doses were required over several days with the effect on lowering the serum K^+ noted over 1 to 5 days.[1,2] In these studies, it was also unclear whether the effect in K^+ lowering was attributable to the resin or induction of diarrhoea by cathartics. In the Cochrane Review,[3] only one study met the criteria for inclusion and did not show any serum K^+ lowering after a single dose of resin and/or cathartic within four hours when compared with placebo in patients with ESRD.[4]

The most serious adverse effect of resins is intestinal necrosis. This can occur when given orally[5] or as an enema.[6] Constipation is common; therefore, resins are usually given in combination with a cathartic.

In summary, resins play no role in the emergency management of hyperkalaemia. However, they may have a role in mild to moderate hyperkalaemia where control over a longer period of time may be acceptable and in circumstances where dialysis is delayed or inappropriate.

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6. Hyperkalaemia (Guidelines Hyperkalaemia 6.1 - 6.3)

Guideline 6.1 – Hyperkalaemia: STEP 4 - Blood monitoring; serum K^+

We recommend that the serum K^+ is monitored closely in all patients with hyperkalaemia to assess efficacy of treatment and look for rebound hyperkalaemia after the initial response to treatment wanes. (1B)

Guideline 6.2 – Hyperkalaemia: STEP 4 - Blood monitoring; serum potassium

We suggest that serum potassium be assessed at least 1, 2, 4, 6 and 24 hours after identification and treatment of hyperkalaemia. (2C)

Audit measures:

1. The proportion of patients in whom serum K^+ was measured at least once within 2 hours of treatment for severe hyperkalaemia [Audit Standard: 100%].
2. The proportion of patients in whom a serum K^+ was not performed within 6 hours of identification of hyperkalaemia [Audit Standard: 0%].

Rationale (Guidelines 6.1 – 6.2)

Insulin-glucose infusion and nebulised salbutamol are the most effective treatments in reducing serum K^+ values. The timing for blood monitoring after medical treatment is influenced by their rate of onset of action, time to achieve peak serum K^+ lowering and the duration of their action.

Insulin-glucose and nebulised salbutamol are effective within 30-60 minutes and last for up to 4-6 hours. The time to maximal effect with insulin-glucose ranges from 45-180 minutes and for nebulised salbutamol from 30-90 minutes.[1] Therefore, the effect of these drugs can be assessed between 60-180 minutes after treatment. The reduction in serum K^+ is approximately 1.0 mmol/L if insulin-glucose or nebulised salbutamol is used alone or 1.2 mmol/L if used in combination.

The aim of treatment is to achieve a serum K < 6.0 mmol/L within 2 hours of initiation of treatment. Therefore, measure the serum K^+ at 1, 2, 4 and 6 hours after initial treatment to determine if the K^+ value has decreased sufficiently and to detect any rebound in serum K^+ as the effects this therapy lasts 4-6 hours. Measure the serum K^+ at 24 hours to ensure that control of hyperkalaemia has been maintained.

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Guideline 6.3 – Hyperkalaemia: STEP 4 - Blood monitoring; blood glucose

We recommend that the blood glucose concentration is monitored at regular intervals (0, 15, 30, 60, 90, 120, 180, 240, 300, 360 minutes) for a minimum of 6 hours after administration of insulin-glucose infusion in all patients with hyperkalaemia. (1C)

Audit measure:

1. The proportion of patients who have at least one blood glucose test performed within 1 hour of completion of insulin-glucose infusion [Audit Standard: 100%].

Rationale

Hypoglycaemia, defined as a blood glucose of < 4.0 mmol/L,[1] is the most common adverse reaction following insulin-glucose infusion for the treatment of hyperkalaemia. Symptomatic, severe hypoglycaemia, is defined as a blood glucose of < 2.8 mmol/L or hypoglycaemia requiring assistance from another person or medical personnel.[2]

The clinical manifestations of hypoglycaemia tend to be progressive, but the early signs are not always detected. Mild hypoglycaemia often presents with sweating, palpitations, tremor and hunger. Severe hypoglycaemia results in more serious symptoms including confusion, coma or even death.[2] Hypoglycaemia is a significant patient safety event and should be anticipated with regular blood glucose monitoring following insulin-glucose infusion.

Hypoglycaemia is associated with significant morbidity and mortality.[1,3] The impact of hypoglycaemia is independent of diabetic status and adverse outcomes have been shown in patients with diabetes mellitus[1,2] and in those without diabetes.[1] One mechanism by which hypoglycaemia may be detrimental is by reducing myocardial blood flow and this has been shown in patients with diabetes and in healthy adults.[4]

The reported incidence of hypoglycaemia is variable, but is likely to be influenced by the dose of glucose administered, the dose of soluble insulin administered, and the diabetic status of the patient. Comparison of studies using 10 units of soluble insulin showed variable occurrence of hypoglycaemia even when the same concentration of glucose was used. In three of these studies using 25g glucose, the incidence of hypoglycaemia ranged from 11-75%.[5-7] When 30g glucose was administered, there were no episodes of hypoglycaemia reported,[8] but in another study using 40g glucose the incidence of hypoglycaemia was 20%.[9] Although

these differences may reflect the small number of participants involved in each study, it may also reflect the duration and frequency over which the blood glucose was monitored.

These studies provide little evidence to base a definitive frequency and duration of blood glucose monitoring following insulin-glucose infusion; however, the impact of insulin-glucose on serum K^+ lowering may be a reasonable surrogate marker. The effect of insulin-glucose on the serum K^+ is apparent within 15 minutes, is maximal at 45-180 minutes, is maintained for approximately two hours and lasts for up to 4-6 hours. This prolonged effect of insulin on controlling serum K^+ has also been shown on blood glucose with hypoglycaemia reported as late as 5-6 hours after infusion.[10] Therefore assess the blood glucose at 0, 15, 30, 60, 90, 120, and then hourly for up to 6 hours post-infusion.

Treat hypoglycaemia with a bolus of 25-50g glucose. Consider a continuous infusion of glucose to avoid a further episode unless volume overload is a potential concern. If a further infusion of insulin-glucose is required to treat uncontrolled hyperkalaemia, then reduce the dose of insulin and monitor blood glucose closely.

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7. Hyperkalaemia (Guidelines Hyperkalaemia 7.1 – 7.3)

Guideline 7.1 - Hyperkalaemia: Specialist Referral

We suggest that patients with severe hyperkalaemia (serum potassium ≥ 6.5 mmol/L) be referred to their local renal or intensive care team for an urgent opinion, guided by the clinical scenario and its persistence after initial medical treatment. (2C)

Guideline 7.2 - Hyperkalaemia: Treatment facilities

We recommend that patients with severe hyperkalaemia and problems with airway, breathing and/ or circulation (ABC), be referred to the local ICU team in the first instance. (1C)

Guideline 7.3 - Hyperkalaemia: Treatment facilities

We recommend that stable patients with severe hyperkalaemia be admitted to an area with facilities for cardiac monitoring, ideally in a renal unit, coronary care unit, HDU or ICU depending on local facilities or practice. (2C)

Rationale (Guidelines 7.1 – 7.3)

Hyperkalaemia may be present on hospital admission or develop during the course of admission due to acute illness or alterations in medications. It may be feasible to manage most cases of mild to moderate hyperkalaemia on a non-renal ward. In many of these cases, hyperkalaemia resolves after the discontinuation of a drug (e.g. ACE-inhibitor). However, patients with moderate hyperkalaemia who are at risk of further rise (e.g. oliguria, rhabdomyolysis) and those with severe hyperkalaemia should be assessed by a senior

clinician (i.e. registrar or consultant grade). Referral to the renal or intensive care team should be guided by the cause of hyperkalaemia, condition of the patient, response to initial medical treatment and availability of services locally.

To facilitate specialist referral, information on the patient history, haemodynamic status, EWS, medication, biochemistry and ECG findings should be readily available. Urine output in patients with AKI is very valuable if available. A history of advanced kidney disease or dialysis-dependency will allow appropriate triage to an area with dialysis facilities. This information is outlined on the Hyperkalaemia Algorithm [Guideline 11.1] which can be used to assist referral.

Following referral, the nephrologist and/ or intensivist is tasked with optimising medical management whilst considering the need for urgent RRT to avoid potentially life-threatening arrhythmias. If dialysis is deemed appropriate, then suitability for this to be carried out in the renal or intensive care unit has to be considered. Prior to transfer to the renal unit, the need for escalation of care [Guidelines 9.1-9.2] and safety of patient transfer [Guidelines 8.1-8.2] must also be considered. The management plan, ceiling of care (i.e. ward, HDU or ICU) and resuscitation status should be documented early in the course of admission for all patients.

Clinical judgement is necessary in determining the appropriate level of care for individual patients. Given the risk of arrhythmias, patients with severe hyperkalaemia require continuous cardiac monitoring and need to be triaged to an area with these facilities.[1,2] The decision on patient triage will be guided by the need for basic or advanced organ support. Patients requiring acute renal replacement therapy (e.g. haemodialysis or haemofiltration) meet the criteria for Level 2 care,[3] and this can be delivered in a renal high dependency unit or ICU. Patients receiving a minimum of two organ support (e.g. renal and cardiovascular or respiratory) meet the criteria for Level 3 care.[3] Early discussion with the ICU team will allow decisions on suitability for ICU and timing of escalation of care.

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8. Hyperkalaemia (Guidelines Hyperkalaemia 8.1 - 8.2)

Guideline 8.1 - Hyperkalaemia: Transfer to renal services

We suggest that transfer to renal services be considered in clinically stable patients in whom hyperkalaemia cannot be controlled (i.e. serum K <6.5 mmol/L) using medical measures particularly in the presence of advanced or oliguric renal failure (either AKI or CKD). (2C)

Guideline 8.2 - Hyperkalaemia: Minimum standards for safe patient transfer

We suggest that inter- or intra-hospital patient transfer be coordinated by senior clinicians and follows national guidelines. (2B)

Rationale (Guidelines 8.1 – 8.2)

The most important aspect of patient transfer is ensuring safety. There are three key steps in optimising patient transfer - firstly, to decide if transfer is absolutely necessary; secondly, to stabilise the patient prior to transfer; and thirdly, to coordinate the transfer itself.[1]

The decision to transfer the patient with hyperkalaemia will be guided by the availability of renal services locally. Intra-hospital patient transfer from a ward or emergency department to a high dependency area, renal unit or ICU within the referring hospital is less complicated. In other cases, definitive management will require inter-hospital transfer to the nearest renal unit or ICU. The decision to transfer a patient to another hospital, must be made by a responsible consultant, in conjunction with consultant colleagues from relevant specialities in both the referring and receiving hospitals. The decision to accept a transferred patient should be made by a consultant in the receiving unit.[2]

Pre-transfer stabilisation is essential for all patients. Following appropriate medical therapy for hyperkalaemia, the response to treatment should be assessed with repeat biochemistry and ECG prior to transfer. We suggest that a patient should not, in general, be transferred

between hospitals if the serum K^+ is ≥ 6.5 mmol/L, though other factors (in particular, the location of intensive care and dialysis facilities) will occasionally over-ride this consideration. All observations, including blood glucose, should be closely monitored prior to transfer. Intensive care review is necessary for patients with any concern regarding oxygenation or haemodynamic instability.

The organisation of the patient transfer itself requires a coordinated approach and liaison with the receiving team to ensure that they are prepared for the patient's arrival. The timing and urgency of transfer should be decided by the nephrologist and/or intensivist. Every hospital should have suitable arrangements in place for providing patient transfer including trained personnel, equipment, and drugs to treat the specific problem.[1,2] Cardiac monitoring and resuscitation equipment are essential for the transfer of patients with hyperkalaemia, either within or between hospitals.

Summary of requirements for safe patient transfer:
[Adapted from CREST 2006, Dunn, 2006, AAGBI Guidelines 2009, ICS 2011]:

1. Decision regarding need for patient transfer
2. Review of investigations and treatment and ensure clear management plan
3. Pre-transfer assessment and stabilisation
4. Good communication between referring team, renal and on-call services
5. Arrangement of ambulance for inter-hospital transfer
6. Consider staff (medical, nursing,), drugs (calcium gluconate or chloride, 20% dextrose in event of hypoglycaemia) and equipment (cardiac monitor/ defibrillator, blood glucose monitor) required for safe transfer
7. Ensure medical and nursing records are complete and are kept confidential as governed by the Data Protection Act 1998
8. Inform patient's relatives of transfer
9. Provide ongoing treatment and care on route as necessary
10. Maintaining patient dignity
11. Hand-over to receiving team
12. Return of transfer staff

Table 6: Minimum standards for safe patient transfer.

Record keeping is a legal requirement for all patient transfers. Clear records should be maintained at all stages of transfer including the patient's condition, reason for transfer, names of referring and accepting consultants, clinical status prior to transfer, during and on arrival. Arrangements should be in place for the return of staff after transfer. The procedure for safe patient transfer[1-4] is summarised in Table 6.

References

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9. Hyperkalaemia (Guidelines Hyperkalaemia 9.1 - 9.5)

Guideline 9.1 – Hyperkalaemia: Escalation of care

We recommend that patients with hyperkalaemia are managed in an area appropriate to their level of clinical need (Level of care 1, 2 or 3). (1B)

Guideline 9.2 – Hyperkalaemia: Escalation of care

We recommend escalation of care, where appropriate, in all patients with problems with airway, breathing, circulation and/ or disability. (1B)

Guideline 9.3 – Hyperkalaemia: Escalation of care – Procedure for referral

We recommend that patients are referred to the ICU team by a senior member of the referring team if escalation of care is required from the outset or if the patient fails to respond to initial treatment. (1B)

Audit measures:

1. Appropriateness and timeliness ICU referral.
2. Seniority of ICU personnel from whom advice was sought.

Rationale (Guidelines 9.1 - 9.3)

Escalation of care to a high dependency area or intensive care unit is not always appropriate. Inappropriate admission to a critical care area may create false hope and unrealistic expectations for patients and their families. It is important to consider factors including aetiology of acute illness, pre-morbid functional status, quality of life and the wishes of the patient. Notably, the views of patients and their families may be influenced by the media.[1] The outcome of patients with ESRD is reflected by the extent of comorbidity.[2]

The decision to refer for escalation of care should take place only after the initial resuscitation measures are underway, the response to treatment has been assessed and after consultation with senior medical staff. This decision should take into account the likelihood of survival (e.g. reversible illness), extent of comorbidity, accurate assessment of pre-morbid functional status, and the patient's wishes.

Consultation between senior physician/ surgeon and the intensive care team should be individualised and undertaken promptly to avoid further clinical deterioration. Although admission criteria to the ICU may vary across the country, patients should not be denied escalation of care simply on the basis of age. Similarly, patients should not be denied ICU admission simply in the presence of ESRD as many patients on long-term dialysis live productive lives and may be awaiting renal transplantation.

Postoperative patients, especially after major surgery, may exhibit acidosis and/or fluid and electrolyte shifts. They are better monitored in HDU or ICU according to local protocols. Trauma victims may require blood transfusion, especially when major limb fractures are involved. Significant haemorrhage and need for massive blood transfusion increases risk of hyperkalaemia,[5] among other abnormalities, and these patients are best cared for in a higher care level area. Rhabdomyolysis may be associated with significant metabolic acidosis and hyperkalaemia warranting care of these patients in HDU/ICU environment.

Guideline 9.4 – Hyperkalaemia: Escalation of care – Need for RRT and other organ support

We recommend escalation of care in patients with hyperkalaemia requiring renal replacement therapy in addition to other organ support (e.g. ventilation or circulation). (1B)

Guideline 9.5 – Hyperkalaemia: Escalation of care – Method of RRT in ICU

We suggest that the decision to initiate RRT for patients with hyperkalaemia in the ICU and the chosen modality take into account local practice and dialysis facilities. (2C)

Rationale (Guidelines 9.4 - 9.5)

The provisional of RRT in renal units and ICUs varies across the country with respect to the timing of initiation and modality of RRT available. Conventional intermittent haemodialysis (IHD) is thought to be the most effective method for K^+ removal,[6,7] but continuous veno-venous haemofiltration (CVVH) and continuous veno-venous haemodiafiltration (CVVHDF) are more commonly available in ICUs in the UK.[8] The severity of critical illness has been shown to lead to inadequate dialysis in ICU patients with acute kidney injury.[9]

Traditionally, it has been thought that haemofiltration (HF) is not as efficient as IHD at removing K^+ and therefore is not generally recommended as the first line extracorporeal therapy in hyperkalaemic patients.[10] However, these opinions are based on HF with low effluent (filtration) volumes produced during the procedure. Evidence is scarce, mainly in the form of case reports, and there are no large or controlled trials.

Overall, HF is an acceptable RRT technique for emergency management of hyperkalaemia. It has been suggested that CVVHDF and not CVVH is the strategy of choice,[10] however in one study, no difference could be found in K^+ removal with either of the RRT modalities.[11] Therefore the mode chosen should be guided by local availability and experience.

The main advantages of haemofiltration (HF) methods are their potential benefits in haemodynamically unstable patients, lower risk of rebound hyperkalaemia given its continuous nature and kinetics of solute removal, ability to tailor dialysate potassium according to serum K^+ measurements and importantly its wide availability in ICUs. Nearly 90% of UK ICUs have facilities for RRT.

HF should be able to remove significant quantities of K^+ from blood provided certain criteria are met.

These can be summarised as follows:

- Maintain effluent volumes $\geq$ 20 $ml.kg^{-1}.hr^{-1}$. It has been suggested in the past that CVVH has poor creatinine clearance (low Kt/V). However, when adequate effluent volumes are produced, comparable Kt/V can be obtained; with an effluent volume of about 30 $ml.kg^{-1}.hr^{-1}$, a creatinine clearance of about 35 $ml.min^{-1}$ is observed[12] and with effluent rate of 35 $ml.kg^{-1}.min^{-1}$ a Kt/V of 1.6 is obtained.[13]

- Blood flows should be adequate to keep a filtration fraction of <25%.[13]
- Predilution fluid replacement reduces efficiency of the system; predilution, if used at all, should be kept to minimum, ideally <20% of overall replacement.[14]
- Initially, HF should be carried out with K^+ free replacement fluid; frequent K^+ monitoring is essential to prevent hypokalaemia. This can be easily monitored in most ICUs as most blood gas machines now measure electrolytes.

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10. Hyperkalaemia (Guidelines Hyperkalaemia 10.1 - 10.2)

Guideline 10.1 – Hyperkalaemia; Cardiac Arrest - special consideration

We recommend that hyperkalaemia is considered in all patients who have a cardiac arrest as part of identifying and treating a reversible cause using the '4 Hs and 4 Ts' approach. (1A)

Guideline 10.2 – Hyperkalaemia; Cardiac Arrest - dialysis during CPR

We suggest that dialysis is considered for hyperkalaemic cardiac arrest if hyperkalaemia is resistant to medical therapy. (2C)

Audit Measure:

1. All cardiac arrests should be audited – hospital participation in the National Cardiac Arrest Audit is encouraged as part of quality improvement and benchmarking.

Rationale (Guidelines 10.1 – 10.2)

Hyperkalaemia is an uncommon, but potentially reversible cause of cardiac arrest. The ECG changes in hyperkalaemia have been traditionally described as progressive, but ventricular fibrillation (VF) may occur at any time and the first presenting sign of hyperkalaemia may be cardiac arrest. Severe hyperkalaemia causes a progressive decrease in myocardial conductivity and excitability, thereby blocking cardiac conduction globally and maintaining cardiac standstill.[1] The probability of cardiac arrest is likely to correlate with the severity of hyperkalaemia, but the threshold for VF in hyperkalaemia appears to vary from patient to patient[2]. For these reasons, arrhythmias should be anticipated and cardiac monitoring is essential for all patients with severe hyperkalaemia or in the presence of ECG changes.

	PEA/Asystole			VF/VT		
Study	**Events %**	**ROSC Achieved n (%)**	**Survival to D/C n (%)**	**Events %**	**ROSC Achieved n (%)**	**Survival to D/C n (%)**
Davis 2008[3] (US HD patients in HD facilities) n= 102	35	37	11	65	51	31
Meaney 2010[5] (US, all in-hospital cardiac arrests) n= 51,919	76	42	11	24	64	37

Table 7: Outcome of cardiac arrest in patients receiving haemodialysis (HD) in an out-patient dialysis facility versus all in-hospital cardiac arrests.

The presenting cardiac arrest rhythm associated with hyperkalaemia may be shockable (pulseless ventricular tachycardia (VT) or VF) or non-shockable (pulseless electrical activity (PEA) or asystole). Shockable rhythms have been reported to be more common in the dialysis population than non-shockable rhythms.[3,4] Additionally, shockable rhythms are associated with a higher incidence of return of spontaneous circulation (ROSC) and survival to hospital discharge in the general population[5] as well as in patients with ESRD.[3] Non-shockable cardiac arrest rhythms are associated with a poor outcome, irrespective of the aetiology (Table 7).

There have been several reports of successful resuscitation following hyperkalaemic cardiac arrest (Table 8). Survival after pulseless VT or VF[6-12] and asystole or PEA cardiac arrest[13-19] has been reported. In many of these reports, patients were refractory to defibrillation until the potassium was controlled. Resuscitation efforts were frequently prolonged. Interestingly, in one report, a patient who presented in PEA followed by asystole, made a spontaneous recovery 8 minutes after resuscitation was terminated whilst being prepared for transfer to the mortuary.[17] This could suggest that the effects of medical therapy may be delayed in the context of hyperkalaemic cardiac arrest. Care also needs to be taken in diagnosing death after cessation of unsuccessful CPR efforts.[20]

Study	**Age (yrs)**	**Arrest Rhythm**	**[K] at arrest (mmol/L)**	**CPR pre-RRT (min)**	**Dialysis modality**	**Dialysis duration (min)**	**[K] at ROSC (mmol/L)**	**Outcome**
Torricella[14] 1989	53	Asystole	10.2	10	CVVH	90	6.5	Full recovery
Lin[7] 1994	27	VT	9.6	55	HD	25	7.6	Full recovery
	58	VF	8.5	35	HD	30	7.2	Full recovery
	77	VT	8.5	105	HD	35	5.2	Died
Costa[15] 1994	57	Asystole	9.6	15	HD	95	7.2	Survived (3 days)
Jackson[16] 1996	16	Asystole	9.8	165	PD	60	4.3	Full recovery
Kao[9] 2000	68	VT	8.3	100	HD	40	5.1	Full recovery
Schummer[27] 2000	68	ns	9.0	ns	HDF	10	ns	Full recovery
Iwanczuk[28] 2008	53	ns	8.5	ns	HD	40	5.4	Full recovery

Table 8: Outcome of hyperkalaemic cardiac arrest with dialysis during CPR.

The universal ALS algorithm applies to all patients and the initial steps of recognition of cardiac arrest, initiating high-quality CPR with minimal interruption, and attempting defibrillation if required, are independent of the cause of cardiac arrest.[21] During CPR, reversible causes should be considered and treated. If the serum potassium is $\geq$ 6.5 mmol/L early in the resuscitation attempt, then hyperkalaemia may be responsible for the cardiac arrest. Hyperkalaemia occurring late in the resuscitation attempt may be the consequence of progressive acidosis and hypoxia, and may not be the precipitant of the cardiac arrest or require specific intervention.[22]

Initiate medical treatment for hyperkalaemia and seek expert help early during the resuscitation attempt.[23] If hyperkalaemia is suspected (e.g. dialysis patient), treat even before the serum potassium is known. However, in the absence of hyperkalaemia, intravenous calcium has deleterious effects in cardiac arrest with coronary vasospasm and worsening cerebral hypoxic damage.

There is little evidence for the use of specific medical interventions in hyperkalaemic cardiac arrest - calcium chloride, dextrose-insulin infusion and sodium bicarbonate; however, these remain standard practice and form the basis of the treatment algorithm - Appendix 6. Calcium chloride (10 mL 10% Calcium Chloride) may be repeated after 10-15 minutes if there is no ROSC and should be repeated if CPR is prolonged as its effects last only 30-60 minutes. Monitor blood glucose and serum K^+ every 15 minutes to assess for hypoglycaemia and response to treatment. There is no evidence that sodium bicarbonate lowers serum potassium, but metabolic acidosis exacerbates the effect of hyperkalaemia; therefore, in the context of cardiac arrest, the use of sodium bicarbonate remains justifiable.

Medical therapy may be insufficient in controlling hyperkalaemia and there are many reports of successful outcomes with dialysis during CPR.[6,7,9,14-16,24-28] There were no neurological sequelae in most of these cases despite prolonged resuscitation attempts. Success has been reported using all modes of haemodialysis (HD), haemofiltration (CVVH),[26] haemodiafiltration (HDF),[27] as well as peritoneal dialysis (PD)[16]. Dialysis has also been used successfully for re-warming in hypothermic cardiac arrest[29,30] and in one of these cases, manual CPR was used for 5.5 hours with a good neurological outcome.[30]

The timing for consideration of dialysis in hyperkalaemic cardiac arrest is not well established, but some useful information can be derived from the above reports (Table 8). The mean serum K^+ at the time of cardiac arrest was 9.0 mmol/L (range 8.3-10.2 mmol/L). The mean serum K^+ at ROSC was 6.3 mmol/L in patients who received a haemodialysis modality (range 5.1-7.6 mmol/L). Therefore, the mean reduction in K^+ required to achieve ROSC was 2.7 mmol/L (range 1.3-3.7 mmol/L) and this would be difficult to achieve with drugs alone. The mean duration of CPR before initiation of dialysis was 53 minutes (range 10-105 minutes). The mean duration of dialysis to achieve ROSC was 45 minutes (range 10-95 minutes). There was an inverse relationship between duration of CPR and duration of dialysis required to achieve ROSC. Given that dialysis initiation will require some planning, it is reasonable to start preparations early. Although this provides little evidence to guide practice, it is reasonable to consider initiating dialysis if ROSC is not achieved within 15-30

minutes of CPR if ongoing resuscitation is deemed appropriate and dialysis facilities are available. During prolonged resuscitation attempts, the use of mechanical devices to perform chest compressions (e.g. LUCAS, Autopulse) should be considered.

The ERC Guidelines have acknowledged dialysis initiation for hyperkalaemic cardiac arrest.[23] This recommendation was based on several considerations. Firstly, the reports of successful outcomes of hyperkalaemic cardiac arrest have demonstrated that it is technically feasible to dialyse during CPR, although there may be some publication bias in the literature. With the aid of the blood pump, a blood flow rate of up to 200 ml/min can be achieved with a chest compression rate of 100/min.[8,30] Secondly, the evidence base for other interventions for hyperkalaemia, particularly calcium salts, is also limited, but has become standard medical practice. Thirdly, it seems logical to utilise the most effective intervention for the most serious complication of hyperkalaemia, particularly when medical therapies may be less effective. Lastly, other invasive procedures are recommended for other special circumstances of cardiac arrest - cardiopulmonary bypass for hypothermia, chest drain insertion for tension pneumothorax and pericardiocentesis for cardiac tamponade, therefore the most effective therapy for hyperkalaemia should be also be considered.

In summary, there appears to be growing evidence over the last two decades that chest compression can support adequate blood flow for dialysis during CPR. Given that defibrillation is frequently unsuccessful until the serum K^+ is controlled, analogous to warming during resuscitation for hypothermia, dialysis should be considered in refractory hyperkalaemic cardiac arrest. Early liaison with renal and intensive care teams is essential.

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11. Hyperkalaemia (Guidelines Hyperkalaemia 11.1 - 11.2)

Guideline 11.1 – Hyperkalaemia: Treatment Algorithm

We recommend a standardised approach to the management of patients with hyperkalaemia using the aid of a treatment algorithm [Appendix 4]. (1B)

Guideline 11.2 – Hyperkalaemia: Treatment Algorithm in cardiac arrest

We suggest a standardised approach to the management of patients with hyperkalaemic cardiac arrest using the aid of a treatment algorithm [Appendix 6]. (2C)

Audit Measure:

1. The proportion of acute hospitals in the UK implementing the hyperkalaemia treatment algorithms.

Rationale (Guidelines 11.1 – 11.2)

Treatment algorithms are well established for many acute medical emergencies, including acute asthma, anaphylaxis and cardiac arrest. Algorithms provide evidence-based and step-by-step guidance to simplify management. Importantly, algorithms facilitate consistency in medical management if adopted into practice.

Algorithms have previously been designed for the management of potassium disorders.[1] The current guidelines have been extended to include a timeline for treatment, documentation of clinical parameters and monitoring in patients presenting with hyperkalaemia [Appendix 4]. The approach to resuscitation in hyperkalaemia cardiac arrest is also outlined [Appendix 6]. Use these documents for specialty referral and file as a permanent record of the event.

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12. Hyperkalaemia (Guidelines Hyperkalaemia 12.1 - 12.6)

Guideline 12.1 – Hyperkalaemia: Management in Primary Care; hospital referral

We recommend that all patients with severe hyperkalaemia ($K^+ \geq 6.5$ mmol/L) are referred to secondary care for immediate assessment and treatment. (1B)

Guideline 12.2 – Hyperkalaemia: Management in Primary Care; prevention

We recommend that all patients with mild ($K^+ \geq 5.5$-5.9 mmol/L) or moderate (K^+ 6.0-6.4 mmol/L) hyperkalaemia have a review of their medication and diet and regular monitoring of serum potassium; the urgency of assessment and frequency of potassium monitoring will depend on individual circumstances. (1B)

Guideline 12.3 – Hyperkalaemia: Treatment in Primary Care; prevention

We suggest that renin-angiotensin drugs (ACE-inhibitors, angiotensin II receptor blockers, aliskiren), potassium sparing diuretics, and/ or loop diuretics are stopped during acute illness lasting > 24 hours duration particularly when associated with hypovolaemia or hypotension (e.g. sepsis, diarrhoea and/or vomiting). (1C)

Guideline 12.4 – Hyperkalaemia: Management in Primary Care; monitoring

We suggest that renal function is assessed before commencing treatment with drugs that can cause hyperkalaemia and thereafter, renal function and serum potassium be monitored in the community after drug initiation, after dose adjustments and during acute illness. (2C)

Guideline 12.5 – Hyperkalaemia: Treatment in Primary Care; prescribing

We suggest that non-steroidal anti-inflammatory drugs or trimethoprim, particularly in combination with renin-angiotensin blockade, are avoided in the patients with CKD 4 and 5, and care should also be taken in the elderly. (2B)

Guideline 12.6 – Hyperkalaemia: Management in Primary Care; pseudo-hyperkalaemia

We suggest that patients in the community with suspected pseudohyperkalaemia are referred to hospital for verification of hyperkalaemia and appropriate treatment if necessary. (2B)

Rationale (Guidelines 12.1 - 12.6)

There is very little evidence on which to base guidelines for management of hyperkalaemia in primary care. However as severe hyperkalaemia is unpredictable and potentially life threatening, all patients found to have severe hyperkalaemia ($K^+ \geq 6.5$ mmol/L) should be referred immediately for assessment and treatment.

Most cases of hyperkalaemia in the community occur in the context of treatment for hypertension, diabetes and/ or heart disease. Many of these patients also have pre-existing chronic kidney disease which increases the risk of hyperkalaemia. Drugs that interfere with the renin-angiotensin system (ACE inhibitors and angiotensin receptor blockers) often in combination with potassium sparing diuretics (aldosterone antagonists and amiloride) increase the risk of hyperkalaemia. Indeed, the increased use of spironolactone for severe heart failure has resulted in a significant increase in hyperkalaemic episodes.[1-4] The risk of adverse events with renin-angiotensin blocking drugs is increased in the elderly and in those with peripheral vascular disease as these patients are likely to have renovascular disease.[5]

Anticipate hyperkalaemia in patients at risk - monitoring of serum potassium in the community is essential. Assess renal function before initiation of renin-angiotensin drugs, after every dose adjustment and during acute illness; in practice, community monitoring has been found to be sub-optimal.[6] Mild or moderate hyperkalaemia may resolve after stopping or reducing the dose of these drugs. Advise patients to withhold these drugs during acute illness, especially when there is hypovolaemia, dehydration or hypotension (e.g. sepsis, diarrhoea and/or vomiting).[7]

Trimethoprim is a commonly used antibiotic in hospital and general practice, however its potential to cause hyperkalaemia is not widely recognised. Risk factors for hyperkalaemia in association with trimethoprim use include older age, pre-existing renal impairment, and concomitant use of renin-angiotensin drugs.[8,9]

Salt Substitutes
Lo Salt
Also Salt
Morton Salt Substitute
NoSalt
Nu-Salt

Table 9: Salt Substitutes containing Potassium Chloride

In patients with chronic kidney disease, dietary modification to avoid or reduce intake of high potassium foods may also be of benefit. . Patients are often unaware that salt substitutes that contain potassium (Table 9) can cause severe hyperkalaemia,[10,11] therefore patients at risk of hyperkalaemia should be advised against using these products. Patients with CKD 4 and 5 referred to the renal clinic should be assessed by a renal dietician.[12]

Some cases of hyperkalaemia in primary care may be spurious. A long transit time to the laboratory is often implicated. When this is suspected paired serum and plasma potassium samples should be performed simultaneously and sent to the laboratory urgently as described in Guideline 3.2. In practice, this may not be technically feasible to achieve in primary care and referral to secondary care would be appropriate.

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13. Hyperkalaemia (Guidelines Hyperkalaemia 13.1)

Guideline 13.1 – Hyperkalaemia: Drug safety

We recommend that hospitals adopt standard regimens for drug administration and monitoring in the treatment of hyperkalaemia to reduce adverse events. (1B)

Audit measure:

1. Adverse events in relation to treatment of hyperkalaemia.

Rationale

Many hospitals have developed treatment guidelines for the treatment of hyperkalaemia, but there is considerable variation in the recommendations on drug dosage and method of delivery. The administration of drugs used to treat hyperkalaemia is outlined in Appendix 2.

Adverse events in relation to hyperkalaemia and its treatment appear to be under-reported.[1] Data were obtained from the Medicines and Healthcare products Regulatory Agency (MHRA) Adverse Drug Reaction (ADR) database for UK spontaneous 'suspected' ADR reports received by the MHRA through the Yellow Card Scheme associated with intravenous calcium salts.[2] The data obtained specifically looked at ADR reports where the suspect drug was intravenous (including intravenous infusion or intravenous bolus) calcium chloride and calcium gluconate or reports where the specific calcium salt is not stated by the reporter (excluding multi-constituent products with ingredients that include both calcium chloride and calcium gluconate).

To date, the MHRA has received 11 UK suspected ADR reports following administration of intravenous calcium salts via the Yellow Card Scheme.[2] Unfortunately, the indication for use was only stated in 4 out of 11 reports and was hyperkalaemia in 2 of these. Notably, skin necrosis or other cutaneous reaction was reported in only 5 out of 11 cases. The other adverse effects reported included allergic reaction, gait disturbance, blurred vision, sweating and dyspnoea.[2] It is important to note that the Yellow Card Scheme is voluntary, therefore these data do not necessarily reflect the true incidence of complications or provide strong evidence for a causal relationship between the reported complications and the use of intravenous calcium salts. Other factors such as the underlying disease or other medicines may contribute to suspected adverse reactions.

Hypoglycaemia is the most common complication of the treatment of hyperkalaemia. The reported incidence of hypoglycaemia ranges from 0-75% and appears to correlate with the dosage of glucose rather than the dosage of insulin used.[3]

The current hyperkalaemia guideline emphasises the need for secure venous access, careful drug preparation and administration and close monitoring of blood glucose.

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14. Hyperkalaemia (Guidelines Hyperkalaemia 14.1 - 14.2)

Guideline 14.1 – Hyperkalaemia: STEP 5 - Prevention - primary

We recommend that measures are taken to prevent hyperkalaemia in patients at risk. (1C)

Guideline 14.2 – Hyperkalaemia: STEP 5 - Prevention - secondary

We recommend that measures are taken to prevent recurrence of hyperkalaemia after acute treatment and appropriate follow-up be arranged. (1B)

Audit Measures:

1. The frequency of prescribed drugs potentially contributing to hyperkalaemia.
2. The frequency of recurrence of hyperkalaemia beyond 48 hours after an acute episode.

Rationale (Guidelines 14.1 – 14.2)

Given the potentially life-threatening consequences of hyperkalaemia, it is ideally avoided, but if it does occur, steps should be taken to avoid further episodes. Patients with impaired renal function are most at risk, but hyperkalaemia may occur in patients with previously normal renal function during an acute illness or initiation of potentially nephrotoxic medication.

The main measures in primary prevention in patients with CKD are regular blood monitoring, careful drug prescribing and dietary advice. Patient information and education may reduce the risk of inadvertent hyperkalaemia.

Drugs are frequently implicated in hyperkalaemia (Table 10). In patients with known renal disease, drugs that impair potassium elimination (e.g. potassium-sparing diuretics, angiotensin converting enzyme (ACE)-inhibitors, angiotensin receptor blockers and non-steroidal anti-inflammatory drugs (NSAIDS) should be used cautiously or avoided.

Drugs that alter transmembrane potassium movement
β blockers
Digoxin
Potassium-containing drugs
Potassium supplements
Salt substitutes
Hyperosmolar solutions (mannitol, glucose)
Suxamethonium
Intravenous cationic amino acids
Stored red blood cells (haemolysis releases potassium)
Herbal medicines (such as alfalfa, dandelion, horsetail, milkweed, and nettle)
Drugs that reduce aldosterone secretion
ACE inhibitors; Angiotensin II receptor blockers
NSAIDs
Heparins
Antifungals (ketoconazole, fluconazole, itraconazole)
Ciclosporin
Tacrolimus
Drugs that block aldosterone binding to mineralocorticoid receptor
Spironolactone
Eplerenone
Drospirenone
Drugs that inhibit activity of epithelial sodium channel
Potassium sparing diuretics (amiloride, triamterene)
Trimethoprim
Pentamidine

Table 10: Drugs commonly associated with hyperkalaemia (adapted from Nyrienda et al, BMJ 2009).[4]

Assess renal function before initiation of these drugs, at one week afterwards, and after every dose titration, even in patients with normal renal function. Take particular care if these drugs are prescribed in combination. Consider stopping these medicines in acute illness, especially when there is hypovolaemia, dehydration or hypotension (e.g. diarrhoea and vomiting).[1] Trimethoprim is a commonly prescribed antibiotic, but its association with hyperkalaemia is not widely appreciated. Avoid it in patients with an eGFR < 30ml/min (i.e. CKD 4 and 5).[2,3]

In dialysis patients, many factors can contribute to the development of hyperkalaemia. Sub-optimal dialysis may result from inappropriate dialysis prescription, poor vascular access, or non-compliance with dialysis attendance or duration. Adherence to a low-potassium diet is notoriously poor in dialysis patients and can cause life-threatening hyperkalaemia. Prolonged fasting without hydration or constipation can predispose dialysis patients to hyperkalaemia.[5]

Secondary prevention is essential for all patients presenting with hyperkalaemia. Assess risk factors for the development of hyperkalaemia and remove any potential precipitants. Nephrotoxic drugs, alone or in combination, are potentially modifiable risk factors. Recommencing these drugs after the acute episode requires a balanced risk assessment by a senior physician. A follow-up plan and liaison with primary care is essential.

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15. Hyperkalaemia (Guidelines Hyperkalaemia 15.1-15.2)

Guideline 15.1 – Hyperkalaemia: Education - medical training

We recommend that medical students and junior doctors are educated in the recognition, treatment, potential hazards and prevention of hyperkalaemia. (1C)

Guideline 15.2 – Hyperkalaemia: Education - renal nurses, and nurses working in acute care settings

We recommend that nurses working in renal, cardiac or acute care settings are educated in the recognition, treatment, potential hazards and prevention of hyperkalaemia. (1C)

Audit Measure:

1. The availability of guidelines and/ or education on hyperkalaemia in renal unit, emergency department or general ward [Audit Standard: 100%].

Rationale (Guidelines 15.1 – 15.2)

Hyperkalaemia is a common medical emergency and all doctors should be familiar with its recognition and treatment. Education on hyperkalaemia should start during pre-registration medical training and continue in the foundation program and beyond. A standardised approach and implementation of a hyperkalaemia algorithm will assist junior doctors and reduce variability in treatment. Some top tips are summarised in Table 11.

All nurses working in an acute care setting should be aware that hyperkalaemia is a life-threatening condition that requires prompt treatment. The need for close monitoring of serum K^+, blood glucose and cardiac rhythm should be emphasised in nursing education and practice. Renal nurses are frequently involved in caring for patients with hyperkalaemia in the renal ward and dialysis unit. Therefore, renal nursing education programs should include hyperkalaemia, its management and potential complications.[1]

Clinical staff must be trained in cardiopulmonary resuscitation. If cardiorespiratory arrest occurs, all clinical staff must be able to:

- recognise the cardiorespiratory arrest;
- summon help;
- start CPR;

- attempt defibrillation within 3 minutes of collapse using an automated external defibrillator or manual defibrillator.

References:

1. Stover, J. Non-dietary causes of hyperkalaemia. Nephrology Nursing Journal 2006; 33: 221-222.
2. Resuscitation Council (UK). Resuscitation Guidelines 2010. http://www.resus.org.uk/pages/guide.htm

Top tips

Who is at risk?

- Dialysis patients – non-compliance, missed dialysis session, access problems
- Patients with AKI
- Patients with chronic heart failure
- Patients taking drugs that affect K^+ regulation (ACE-inhibitors, angiotensin II receptor blockers, potassium-sparing diuretics, aliskiren, etc)
- Any acutely ill patient

Warning signs?

- Arrhythmia
- ECG showing signs of hyperkalaemia
- Patient complaining of paraesthesiae or limb weakness

What to do next?

- Send bloods urgently (use lithium-heparin tube)
- Check K^+ using BGA (arterial or venous sample) for quick K^+ value
- Perform 12-lead ECG
- Cardiac monitoring if $K^+ \geq 6.5$ mmol/L or acutely unwell with K > 6.0 mmol/L
- Get IV access (if not already available)
- Start medical treatment (use 5-step approach)
- Refer for renal or ICU opinion early

Dialysis patient with hyperkalaemia?

- Treat medically unless dialysis immediately available
- Protect the heart (dialysis will take time to be initiated and to lower potassium)
- Inform renal team urgently
- Prevent recurrence
    - review dialysate fluid and prescription
    - check dialysis access and recirculation
    - review diet

Pitfalls in treating hyperkalaemia

Do I wait for laboratory result or can I act on K^+ from BGA? BGA gives good estimation of serum K^+ value and treatment should not be delayed.

Is the serum potassium really that high? If in doubt, check on BGA and assess ECG.

What if the ECG is normal? ECG may be normal even in severe hyperkalaemia, so treat according to guidelines based on severity of hyperkalaemia.

How do I recognise a sine wave ECG? ECG has a sinusoidal pattern with no recognisable P or T waves (see example in Appendix 3).

Table 11: Top tips for treatment of hyperkalaemia.

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CONFLICT OF INTEREST STATEMENTS

Dr Annette Alfonzo

No conflicts of interest.

Consultant in Nephrology
Victoria Hospital NHS Fife
Hayfield Road, Kirkcaldy. KY2 5AH.

Dr Jasmeet Soar

No conflicts of interest.

Consultant in Anaesthesia & Intensive Care Medicine
North Bristol NHS Trust
Bristol BS10 5NB

Dr Jerry Nolan

No conflicts of interest.

Consultant in Anaesthesia Intensive Care Medicine
Royal United Hospital Bath NHS Trust
Combe Park, Bath. BA1 3NG.

Dr Robert Mactier

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Consultant in Nephrology
Greater Glasgow and Clyde NHS Trust
Western Infirmary, Dumbarton Road, Glasgow. G11 6NT.

Dr Jonathan Fox

No conflicts of interest.

Consultant in Nephrology and Representative of Renal Association
Greater Glasgow and Clyde NHS Trust
Western Infirmary, Dumbarton Road, Glasgow. G11 6NT.

Dr Ilona Shilliday

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Consultant in Nephrology and Internal Medicine
Monklands Hospital
Monkscourt Avenue, Airdrie. ML6 0JS.

Dr Alaistair Douglas

No conflicts of interest.

Consultant in Acute Medicine and Nephrology
Vice-President of The Society for Acute Medicine
Ninewells Hospital and Medical School
Dundee. DD1 9SY

Roop Kishen

I have received honoraria in the past from Gambro. I am the main author: Standards and Recommendations for the Provision of Renal Replacement Therapy on Intensive Care Units in the United Kingdom 2009. Prepared on behalf of the Standards and Safety Committee, Intensive Care Society.

Consultant in Intensive Care Medicine & Anaesthesia (retired)
Salford Royal NHS Foundation Trust
Salford, Manchester. M6 8HD

Dr Bill Bartlett

No conflicts of interest.

Consultant Clinical Scientist
Joint Clinical Director Diagnostics
Access Directorate, Clinical Lead
Dept of Blood Sciences
Ninewells Hospital & Medical School
Dundee. DD1 9SY

Mr Martin Wiese

No conflicts of interest.

Consultant in Emergency Medicine
Leicester Royal Infirmary
Leicester. LE1 5WW.

Mrs Brenda Wilson

No conflicts of interest.

Resuscitation Officer
Victoria Hospital NHS Fife
Hayfield Road, Kirkcaldy. KY2 5AH.

Mrs Jackie Beatson

No conflicts of interest.

Resuscitation Officer
Victoria Hospital NHS Fife
Hayfield Road, Kirkcaldy. KY2 5AH.

Mrs Lyn Allen

No conflicts of interest.

Renal Nurse and Senior Clinical Educator
Royal Derby Hospital
Uttoxeter Road
Derby. DD22 3NE.

Ms Mumtaz Goolam

No conflicts of interest.

Senior Nurse
Glaxo Renal Unit
Heartlands Hospital
Heart of England NHS Foundation Trust
Birmingham
B9 5SS

Mrs Morag Whittle

No conflicts of interest.

Senior Renal Pharmacist
Greater Glasgow and Clyde NHS Trust
Western Infirmary
Dumbarton Road, Glasgow. G11 6NT.

Appendix 1: Stages of Chronic Kidney Disease

Appendix 2: Drug administration and safety

A. Calcium Gluconate and Calcium Chloride

B. Insulin-glucose infusion

C. Salbutamol

D. Calcium resonium

Appendix 3: ECG in Hyperkalaemia – sine wave.

Appendix 4: Algorithm – Management of Hyperkalaemia in Adults.

Appendix 5: Universal ALS Algorithm.

Appendix 6: Algorithm – Management of Hyperkalaemic Cardiac Arrest in Adults.

Appendix 1: Stages of CKD (KDOQI Guidelines)[1]

Stage	eGFR	Description
1	**≥ 90**	**Kidney damage with normal or ↑GFR**
2	**60-89**	**Kidney damage with mild ↓GFR**
3	**30-59**	**Moderate ↓GFR**
4	**15-29**	**Severe ↓GFR**
5	**<15 (or dialysis)**	**Kidney failure**

eGFR – estimated glomerular filtration rate.

Notes:

Patients in stages 1 and 2 must have evidence of kidney damage identified on imaging studies (e.g. structural abnormality) or abnormalities in blood or urine (e.g. haematuria and/or proteinuria).

Reference:

1. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification. Am J Kidney Dis 2002; 39: S1-S266.

Appendix 2A: Drug administration and safety

Calcium Gluconate 10% Injection (10 ml contains 2.26 mmol/L calcium)

Calcium Chloride 10% Injection (10 ml contains 6.8 mmol/L calcium)

Administration

Draw up 10 ml 10% Calcium chloride and give intravenously over 5-10 minutes.

OR

Draw up 30 ml 10% Calcium gluconate and give intravenously over 5-10 minutes.

Continuous cardiac monitoring is essential during infusion.

12-lead ECG is required before and after administration.

Administer via large peripheral vein or central venous catheter.

Dose can be repeated after 5-10 minutes if hyperkalaemic changes persist.

Action

Effective within 3 minutes and duration of action is 30-60 minutes.

Safety

Intravenous calcium salts are irritant to veins and can cause tissue necrosis if extravasation occurs. Therefore ensure access is patent and watch for signs of irritation.

Do not administer sodium bicarbonate simultaneously via same access due to risk of formation of insoluble calcium salts.

Do not mix with any drugs due to incompatibilities.

A yellow card should be completed for all adverse events.

Appendix 2B: Drug administration and safety

Insulin and Glucose

Administration

Dosage: 10 units soluble insulin (e.g. Actrapid) in 25g glucose (50ml 50% glucose or 125 ml 20% glucose) given intravenously over 15-30 minutes into a large vein.

Preparation: Measure 10 units soluble insulin using an ***insulin syringe*** (10 units is 0.1ml)

Inject insulin into 25g glucose (50 ml 50% glucose or 125 ml 20% glucose), invert and mix.

Withdraw contents of vial into 50ml syringe.

Dose may be repeated if necessary.

Action

Effective within 15-30 minutes and duration of action is 4 -6 hours.

Safety

Incorrect measurement of insulin can be fatal.

Blood glucose monitoring is essential for at least 6 hours post administration.

Hyperosmolar glucose (i.e. 50%) should not be used for hyperkalaemia in association with diabetic ketoacidosis.

Appendix 2C: Drug administration and safety

Salbutamol

Administration

Give 10-20 mg nebulised salbutamol.

Use mouthpiece or close fitting mask.

Action

Onset of action is 30-60 minutes and duration of action is 4-6 h.

Safety

Caution with ischaemic heart disease (give only 10 mg).

Caution if tachyarrhythmia present.

Tremor and tachycardia are most common adverse effects.

Caution in open angle glaucoma.

Up to 40% of patients will not respond to treatment. Therefore salbutamol should not be used as monotherapy.

Appendix 2D: Drug administration and safety

Calcium Resonium

Administration

Oral

15g orally 3-4 times daily.

Add to water 3-4 ml/ g of resin. Can be added to syrup or milk for greater palatability.

Regular laxative is recommended.

Rectal

Add 30g to 150 ml water. Enema should be retained for at least 9 hours then colon irrigated to remove resin.

Use if patient vomiting or has upper gastrointestinal problems.

Can be used in combination with oral for more rapid initial results.

If both routes used do not continue with rectal administration after oral dose has reached the rectum.

Action

Slow onset of action (more than 4 hours), therefore not recommended for emergency management.

Safety

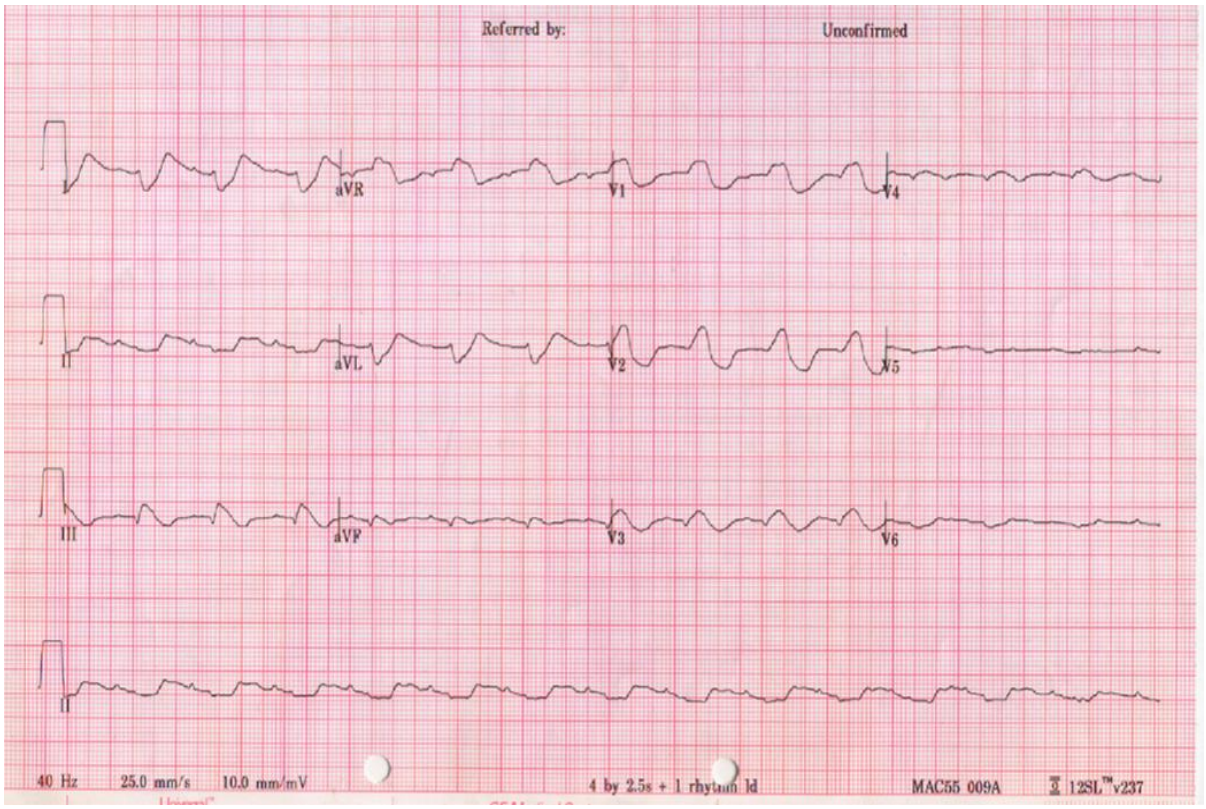
Contraindicated in obstructive bowel disease.

Intestinal necrosis is most severe adverse effect and risk increases with the concomitant use of sorbitol.

Constipation is common with resins.

Prolonged use can cause hypomagnesaemia and hypercalcaemia.

Appendix 3 – Sine wave ECG



Appendix 4: ALS Algorithm

Appendix 5: Algorithm – Management of Hyperkalaemia in Adults.

(see attachment)

Appendix 6: Algorithm – Management of Hyperkalaemic Cardiac Arrest in Adults.

(see attachment)

Abbreviations

AAGBIG	Association of Anaesthetists of Great Britain and Ireland Guideline
ABCDE	Airway – Breathing – Circulation – Disability - Exposure
ACE	Angiotensin converting enzyme
AKI	Acute Kidney Injury
ARDS	Adult respiratory distress syndrome
AV	Artero-venous
AVPU	Alert – Verbal – Pain - Unresponsive
BGA	Blood gas analyser
BP	Blood pressure
Ca^{2+}	Calcium ion
CKD	Chronic kidney disease
CPR	Cardiopulmonary resuscitation
CVVH	Continuous veno-venous haemofiltration
CVVHDF	Continuous veno-venous haemodiafiltration
ECG	Electrocardiogram
ERC	European Resuscitation Council
ESRD	End-stage renal disease
EWS	Early warning score
GCS	Glasgow coma scale
GFR	Glomerular filtration rate
HDF	Haemodiafiltration
HDU	High dependency unit
HF	Haemofiltration
ICS	Intensive Care Society
ICU	Intensive Care Unit
IHD	Intermittent haemodialysis

IV	Intravenous
K^+	Potassium ion
MET	Medical emergency team
MHRA	Medicines and Healthcare products Regulatory Agency
Na^+	Sodium ion
PEA	Pulseless electrical activity
RCT	Randomised controlled trial
ROSC	Return of spontaneous circulation
RRT	Renal replacement therapy
SBAR	Situation – Background – Assessment - Recommendation
VF	Ventricular fibrillation
VT	Ventricular tachycardia