The management of acute hyperkalaemia in neonates and children

Kavitha Masilamani, Judith van der Voort

ABSTRACT
This review article describes the pathophysiology and common aetiologies of hyperkalaemia including pseudohyperkalaemia, renal impairment, medication, rhabdomyolysis and aldosterone deficiency. Two clinical cases are used to describe symptoms (mainly muscle weakness and arrhythmias) and illustrate different management options. An approach to management including relevant investigations and interpretation of ECG changes is described. Emergency drug treatments are outlined and the effectiveness of individual therapeutic methods in reducing the potassium concentration described. Chronic management is mentioned but is outside the scope of this article. Hyperkalaemia is a rare but potentially life threatening emergency. It is a manifestation of a disease and therefore the incidence in children is not known. Quick and effective intervention may be necessary and clinicians must be adept at managing this condition. This overview provides two clinical scenarios and summarises aetiologies, investigations and management.

INTRODUCTION
Potassium (K⁺) is predominantly an intracellular cation (with concentrations between 100–150 mmol/l) with a small fraction present in the extracellular compartment. Potassium homeostasis is vital for cellular and neuromuscular functions and essential for the regulation of cell volume, pH and enzyme function.¹ ²

Hyperkalaemia is defined as a potassium level greater than 5.5 mmol/l in children and more than 6 mmol/l in newborns. Elevated levels of potassium constitute a medical emergency due to the concentration-dependent effect on cardiac myocyte membrane potentials, resulting in potential arrhythmias. Hence treatment must be prompt and preferably sustained.

CASE 1
A 16-year-old patient with stage 5 chronic kidney disease (CKD) secondary to Alport syndrome was incidentally found to have a serum potassium level of 7.7 mmol/l during a routine clinic visit. The diagnosis of Alport syndrome had been confirmed on renal biopsy at the age of 6 years. The patient had been on renal replacement therapy (continuous cycling peritoneal dialysis) since the age of 14. His older and younger brothers both had Alport syndrome. Previous episodes of moderately elevated potassium had led to initiation of a low potassium diet, but there was a long history of non-compliance with the diet, medication and fluid restriction. His urine output had gradually reduced preceding this episode of hyperkalaemia. He had poorly controlled hypertension, necessitating the use of four antihypertensive medications, including enalapril. His blood results at the time of admission are given in table 1.

An urgent ECG showed tented t-waves. The hyperkalaemia was treated with intravenous calcium gluconate, nebulised salbutamol three times within 1 h, oral calcium resonium given twice and the immediate start of peritoneal dialysis. Enalapril was discontinued and the serum potassium concentration fell within 4 h to 5.3 mmol/l. End stage renal failure, complicated by the recent reduction in urine output, non-compliance with diet and enalapril, were thought to be the causes of the hyperkalaemia. The patient has since had a successful cadaveric renal transplant.

CASE 2
A 22-month-old girl presented to hospital with a 5-day history of generalised oedema and oliguria. She had been fit and well apart from a preceding viral illness. There was no history of diarrhoea. On admission she was found to be weak and profoundly hypertensive (160/100 mm Hg), oedematous and pale with minimal urine output (0.4 ml/kg/h). The results of her blood investigations are given in table 2.

Initial management of hyperkalaemia included intravenous calcium gluconate, nebulised salbutamol, oral calcium resonium, intravenous sodium bicarbonate and an insulin and glucose infusion. Her hypertension was managed with frusemide, labetalol and hydralazine infusions. The potassium fell to 6.9 mmol/l and her blood pressure reduced to 140/100 mm Hg, but the haemoglobin fell further to 5.9 g/dl. A haemodialysis line was inserted without a blood transfusion due to the risk of further hyperkalaemia and hypertension. Haemodialysis was commenced, with a concomitant blood transfusion, allowing for simultaneous potassium and fluid removal. Further investigations showed low complement levels (C3 and C4), elevated lactic dehydrogenase and reticulocyte count and a further drop in platelet count, confirming a diagnosis of atypical haemolytic uraemic syndrome (HUS). Renal function recovered completely after a period of haemodialysis and plasma exchange.

REGULATION OF POTASSIUM BALANCE: PHYSIOLOGY
Almost 98% of the total body potassium is intracellular, whereas sodium (Na⁺) is predominantly
an extracellular cation. The distribution of these cations in the different compartments is maintained by the sodium and potassium activated adenosine triphosphatase (Na⁺/K⁺-ATPase) pump, determining cellular resting membrane potential. The resting potential, essential for normal neurological function, is generated by the diffusion of K⁺ out of the cell, making the interior electrically negative compared to the extracellular fluid.¹

Normal potassium homeostasis is achieved by a balance between potassium intake, intra- and extracellular distribution and urinary excretion by the cortical collecting ducts. Under normal circumstances, an increase in potassium intake will lead to an increase in the serum potassium concentration and redistribution intracellularly, facilitated by insulin and β-adrenergic receptors, followed by a stimulus for the collecting duct to increase excretion in the urine within 6–8 h.

### AETIOLOGY OF HYPERKALAEMIA

The aetiology of hyperkalaemia can be categorised into the three groups listed below.

#### Increased intake

- Increased potassium intake alone does not lead to hyperkalaemia as long as the ability to excrete potassium is maintained as described above. Rarely, an extremely high intake of potassium can lead to significant hyperkalaemia and arrhythmia, for example, following intravenous or oral potassium penicillin,³ ⁴ or a blood transfusion, especially when the blood is not fresh.⁵

#### Redistribution of potassium from the intracellular to extracellular compartment

- Pseudohyperkalaemia due to cell breakdown following venepuncture or capillary sampling is the most frequent reason for a raised serum potassium result in children. A red tinge may be noted in the serum, caused by the release of haemoglobin from the cell. Spontaneous cell breakdown in patients with very high white cell or platelet counts after venepuncture can cause leaking of potassium into the serum.⁶ A repeat free-flowing sample should be performed immediately to ensure the true potassium concentration is normal.

- Metabolic acidosis results in the movement of hydrogen ions into the intracellular space in order to buffer the intracellular pH. To maintain electroneutrality, potassium moves out of the cell resulting in hyperkalaemia.

- Insulin promotes movement of potassium into the cells, therefore insulin deficiency, as in diabetic ketoacidosis, can lead to hyperkalaemia. The severity of hyperkalaemia in diabetic ketoacidosis is mitigated by potassium losses in the stool and urine: the increased flow in the distal tubule creates a low urinary K⁺ concentration, favouring K⁺ excretion; increased sodium delivery and absorption in the collecting duct also enhances K⁺ excretion.

- Intravascular hyperosmolality will cause water movement out of cells, dragging potassium with it (solvent drag) followed by an increase in the intracellular potassium concentration, creating a favourable gradient for potassium movement out of cells.

- Tissue breakdown can cause the release of potassium from the cells into the extracellular fluid. Clinical examples include trauma or severe hypothermia, causing rhabdomyolysis. Chemotherapy, causing the breakdown of lymphoma cells in bulky lymphoma and of white cells in high-count leukaemia, can lead to tumour lysis syndrome. Significant haemolysis can cause hyperkalaemia.⁷

- Strenuous exercise can cause the release of potassium from cells. Higher potassium concentrations cause a mild degree of physiological vasodilatation, which improves blood supply to the tissues.

- Hyperkalaemic periodic paralysis is an autosomal dominant uncommon condition in children. It presents with episodes of muscle weakness, triggered by periods of exercise or fasting, associated with hyperkalaemia. Other triggers include increase in potassium intake, cold, ethanol or stress.⁸

- Medication such as β-blockers, will block the β-adrenergic facilitation of potassium uptake by cells.

#### Decreased renal excretion

- Impaired kidney function leads to a reduction in potassium excretion, usually associated with reduced urine production (oliguric/anuric renal failure). Initially, potassium balance is maintained by increased excretion through the functioning nephrons, until the glomerular filtration rate drops to less than 15 ml/min/1.73 m².

- Reduced arterial blood volume causes a reduction in the delivery of fluid to the distal site, where potassium is excreted; reduced sodium delivery to the collection duct leads to reduced sodium reabsorption and therefore reduced potassium excretion.

- The absence of aldosterone, or resistance to its effect, causes a reduction in potassium and hydrogen excretion, with coexistent hypernatraemia and metabolic acidosis. Lack of aldosterone production can be due to primary adrenal insufficiency or adrenal enzyme deficiencies (congenital adrenal hyperplasia, aldosterone synthase deficiency). High aldosterone production but end organ resistance to its effect suggests a diagnosis of pseudohypoaldosteronism. Hyperkalaemic distal renal tubular acidosis (type IV) is caused by aldosterone resistance and can be found in association with sickle cell disease, urinary tract obstruction or severe renal reflux and infection.¹

- Several drugs will reduce the effect of aldosterone and are associated with hyperkalaemia (eg, potassium sparing diuretics). Table 2 provides an overview of these drugs.

### Table 1 Blood results at admission of a 16-year-old patient

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>↓ 133 mmol/l</td>
</tr>
<tr>
<td>Potassium</td>
<td>↑ 7.7 mmol/l</td>
</tr>
<tr>
<td>Urea</td>
<td>↑ 14.5 mmol/l</td>
</tr>
<tr>
<td>Creatinine</td>
<td>↑ 1221 μmol/l</td>
</tr>
<tr>
<td>Albumin</td>
<td>↓ 29 g/dl</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>↑ 14 mmol/l</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>↓ 7.7 g/dl</td>
</tr>
<tr>
<td>White cell count</td>
<td>↓ 7.9×10⁹/l</td>
</tr>
<tr>
<td>Platelet count</td>
<td>152×10⁹/l</td>
</tr>
</tbody>
</table>

### Table 2 Blood results at admission of a 22-month-old girl

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>↓ 124 mmol/l</td>
</tr>
<tr>
<td>Potassium</td>
<td>↑ 7.7 mmol/l</td>
</tr>
<tr>
<td>Urea</td>
<td>↑ 33 mmol/l</td>
</tr>
<tr>
<td>Creatinine</td>
<td>↑ 221 μmol/l</td>
</tr>
<tr>
<td>Albumin</td>
<td>↓ 28 g/dl</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>↓ 14 mmol/l</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>↓ 7.7 g/dl</td>
</tr>
<tr>
<td>White cell count</td>
<td>↓ 7.9×10⁹/l</td>
</tr>
<tr>
<td>Platelet count</td>
<td>152×10⁹/l</td>
</tr>
</tbody>
</table>

diuretics, ACE-inhibitors, non-steroidal anti-inflammatory drugs and cyclosporin).

SYMPTOMS

- Hyperkalaemia is often asymptomatic, but clinical signs can occur when serum potassium rises above 7 mmol/l.1–9

Symptoms and signs of the underlying disease may be present (polyuria, polydipsia, weight loss, failure to thrive in diabetes mellitus and tubular disorders, precocious puberty in congenital adrenal hyperplasia, hypotension with hypoglycaemia in Addison’s disease). Muscle weakness is usually seen only when serum potassium exceeds 8 mEq/l as a result of alterations in neuromuscular conduction. Weakness tends to ascend from the lower extremities, typically sparing muscles of respiration and those innervated by cranial nerves. Tendon reflexes are reduced. There are reported cases of acute flaccid quadriplegia secondary to hyperkalaemia which reversed on correction of serum potassium.10–11 Paresthesias, described usually as numbness and tingling in the upper and lower extremities, are uncommon symptoms of hyperkalaemia.

- Hyperkalaemia is associated with significant disturbances in cardiac conduction, causing palpitations. Potentially lethal dysrhythmias associated with hyperkalaemia include complete heart block and Mobitz type I and II second-degree atrioventricular block, ventricular tachycardia, ventricular fibrillation and asystole.1,12,13 There is a characteristic sequence of changes seen in ECG with increasing levels of serum potassium (figure 1):

  - Serum K⁺ 5.5–6.5 mmol/l – Tall, peaked T waves with narrow base.
  - Serum K⁺ 6.5–8.0 mmol/l – Peaked T waves, prolonged PR interval, decreased or disappearing P wave, widening of QRS, amplified R wave.
  - Serum K⁺ greater than 8.0 mmol/l – Changes occur due to delayed depolarisation. Absence of P wave, bundle branch blocks, progressive widening of QRS complex eventually merging with the T wave to form the sine-wave pattern. This is followed by ventricular fibrillation or asystole.

The cardiac toxicity is enhanced by hypocalcaemia, hypopon- traemia, metabolic acidosis and an acute rather than chronic rise in potassium.

DIAGNOSIS AND INVESTIGATIONS

A complete history should include details on diet (potassium rich food includes fruits, potatoes, beans and grains) and dietary supplements (reduced sodium salts contain 66% potassium chloride, ‘low salt’ packaged food often contains potassium), medication, episodic weakness, failure to thrive, polydipsia and polyuria.

An ECG is mandatory but may be normal in significant hyperkalaemia and should not be used to guide management. Laboratory investigations include tests for renal failure, metabolic acidosis, diabetes mellitus, tissue or cell breakdown and (pseudo) hypoaldosteronism (table 3).

ACUTE MANAGEMENT

Hyperkalaemia is a medical emergency. Treatment is recommended when ECG changes are present or when serum potassium levels are greater than 6.0–6.5 mEq/l, regardless of the ECG.12 The first step is to identify and remove sources of oral or parenteral potassium intake or medication that increase potassium concentration. Cardiac monitoring and frequent 12-lead ECG if abnormalities are present is mandatory.

The three approaches to treatment are described below.

Antagonising the membrane effect of potassium to stabilise the myocardium

Calcium infusion

Hyperkalaemia causes a decrease in membrane resting potential by inactivation of sodium channels and increasing membrane excitability. Calcium antagonises this effect within 1–5 min, returning the resting membrane potential to nearer normal values. Although it does not alter serum potassium levels, it increases the threshold resting membrane potential at which excitation occurs.1,9,13 The effects only last for 30–60 min, and so more definitive methods to lower serum potassium are required.

Dose

By slow intravenous injection over 5–10 min: 0.11 mmol/kg (0.5 ml/kg of calcium gluconate 10%). Dose may be repeated after 5 min if ECG changes persist.14

Driving extracellular potassium into the cell

Glucose and insulin infusion

Insulin lowers the serum potassium by driving the potassium intracellularly in exchange for sodium. This is mediated via the sodium potassium ATPase pump.1,13 A glucose infusion will enhance endogenous insulin production, so an insulin infusion will only need to be started when blood glucose is over 10 mmol/l.13

Figure 1 Changes in ECG with increasing hyperkalaemia. Serum K⁺ values are mmol/l.

Table 3 Investigation and diagnosis in acute hyperkalaemia

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Differential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full blood count</td>
<td>Haemolysis, HUS, sepsis, pseudohyperkalaemia</td>
</tr>
<tr>
<td>Urea, creatinine and parathyroid hormone, urine protein</td>
<td>Acute/chronic renal failure</td>
</tr>
<tr>
<td>Bicarbonate, urine pH</td>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td>Blood glucose/glycosylated haemoglobin/urine ketones</td>
<td>Diabetic ketoacidosis</td>
</tr>
<tr>
<td>LDH, uric acid, phosphate, alanine aminotransferase, urine dipstick for blood and haemoglobin</td>
<td>Tissue breakdown secondary to haemolysis, rhabdomyolysis or tumour lysis syndrome</td>
</tr>
<tr>
<td>Creatine kinase</td>
<td>Rhabdomyolysis</td>
</tr>
<tr>
<td>Renin, angiotensin and aldosterone</td>
<td>(Pseudo) hypoaldosteronism</td>
</tr>
<tr>
<td>Cortisol, 11-β hydroxylase, 21-hydroxylase, 17 OH progesterone</td>
<td>Congenital adrenal hyperplasia</td>
</tr>
</tbody>
</table>

HUS, haemolytic uraemic syndrome; LDH, lactic dehydrogenase.
Dose
Intravenous solution of insulin (0.1–0.6 units/kg/h in neonates, 0.05–0.2 units/kg/h for children over 1 month) with glucose infusion of 0.5–1 g/kg/h (5–10 ml/kg/h of glucose 10%). This regimen lowers the potassium by 0.5–1.5 mEq/l. The effect begins within 15 min and can last for hours. Blood sugars must be carefully monitored to avoid both hypoglycaemia and hyperglycaemia (which leads to an increase in osmolality exacerbating hyperkalaemia).

Sodium bicarbonate infusion
Metabolic acidosis causes hydrogen ions to move intracellularly to maintain the intravascular pH as close to normal as possible, leading to an extracellular move of potassium to maintain electroneutrality. This movement is reversed when acidosis is corrected. Even when blood pH is near normal, because of respiratory compensation, bicarbonate normalisation will reduce serum K+ concentration.

Dose
Intravenous sodium bicarbonate 1 mmol/kg over 10–15 min or alternatively a half correction of the base excess (BE): 0.3 × weight × BE. The onset of action is within 1 h and the effects last for up to 2 h. Potential complications include hypernatraemia, volume overload and tetany in patients with CKD and coexistent hypocalcaemia (metabolic acidosis causes a shift of H+ ions into the bone, with calcium moving into the blood stream; this reverses when acidosis is corrected).

β-2 Adrenergic agonists
β-2 Adrenergic agonists act by driving the potassium intracellularly by increasing sodium potassium ATPase activity. Salbutamol is the most commonly used drug in this group, either nebulised or by intravenous infusions. Salbutamol can produce a reduction in potassium of 0.5–1 mmol/l after nebulisation and 0.9–1.5 mmol/l after intravenous administration, with the maximum effect achieved sooner.

Dose
Nebulised salbutamol: 2.5 mg (under 25 kg) or 5 mg (over 25 kg). Intravenous salbutamol: 4 µg/kg given as an intravenous bolus over 5 min. Doses maybe repeated as often as necessary every 6–8 h. Tachycardia is the main side effect.

Removing excess potassium from the body
Diuretics
Loop diuretics prevent reabsorption of sodium and potassium in the loop of Henle and directly increase urinary potassium excretion. The increase in sodium delivery to the cortical collecting duct will increase sodium reabsorption, leading to increased potassium excretion. Their value in patients with chronic renal failure is limited due to the poor response to diuretics, but this treatment is useful when hyperkalaemia is due to hypoadosteronism or congestive heart failure.

Dose
Furosemide 1 mg/kg intravenously over 5 min. When failure is present doses in excess of 1 mg/kg may be needed. Avoid rapid intravenous administration.

Cation exchange resins
Calcium resonium (calcium polystyrene sulfonate) given orally or rectally acts by binding potassium in the gut in exchange for calcium. Each gram of resin can potentially bind up to 0.5–1 mmol of potassium. Its onset of action is slower than other modalities, its effects being seen after 1–2 h. It is unpalatable and can cause electrolyte abnormalities, especially in neonates, where it must be used with great caution. Contraindications include obstructive bowel disease and neonates with reduced gut motility, because of the risk of intestinal necrosis.

Dose
Oral: 1 month–18 years: 125–250 mg/kg (max 15 g) 3–4 times daily.
Rectal: neonate–18 years: 125–250 mg/kg, repeated as necessary every 6–8 h. Colonic irrigation to remove resin after 6–12 h. Dilute 1 g resin with 5–10 ml methylcellulose or water.

Peritoneal dialysis, haemodialysis or continuous veno-venous haemofiltration
Renal replacement therapy is used when conservative methods fail. Haemodialysis (or continuous veno-venous haemofiltration in haemodynamically unstable patients) is more effective compared to peritoneal dialysis and is the preferred method when hyperkalaemia is the result of cell breakdown. A reduction in serum potassium level is seen immediately and the action is sustained as long as dialysis continues.

CHRONIC MANAGEMENT
Most patients with persistent hyperkalaemia have CKD. Hyperkalaemia is present in 14% of patients with CKD on peritoneal dialysis. A low potassium diet might be appropriate, with explanation and supervision of a multi-disciplinary team, including a renal dietician.

Alkali treatment is used to normalise bicarbonate and may help reduce the potassium. Exchange resins can be used to delay dialysis, but haemo- or peritoneal dialysis is the definitive treatment for hyperkalaemia when conservative methods fail.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Commissioned; externally peer reviewed.

REFERENCES
Review


The management of acute hyperkalaemia in neonates and children

Kavitha Masilamani and Judith van der Voort

Arch Dis Child 2012 97: 376-380 originally published online September 13, 2011
doi: 10.1136/archdischild-2011-300623

Updated information and services can be found at:
http://adc.bmj.com/content/97/4/376.full.html

These include:

References
This article cites 17 articles, 3 of which can be accessed free at:
http://adc.bmj.com/content/97/4/376.full.html#ref-list-1

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections
- Arrhythmias (39 articles)
- Metabolic disorders (435 articles)
- Rheumatology (277 articles)
- Drugs: cardiovascular system (252 articles)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/