Clinical Guideline

HYPERKALAEMIA IN CHILDREN: DIAGNOSIS AND TREATMENT

SETTING Bristol Royal Hospital for Children (BRHC)

FOR STAFF Medical, nursing and pharmacy staff

PATIENTS All inpatients at BRHC except patients with diabetic ketoacidosis

DEFINITION AND ACTION [2,3]:

Hyperkalaemia is a potentially life-threatening emergency

Note for this guideline K = potassium

ECG changes (even in mild hyperkalaemia) requires prompt and aggressive treatment

Hyperkalaemia in absence of ECG changes:

	Potassium level	Action
Normal	3.5 – 5.5 mmol/L*	N/A
Mild hyperkalaemia	5.5 – 5.9* mmol/L	Monitor
Moderate hyperkalaemia	*6.0 – 6.4 mmol/L	Consider treatment
Severe hyperkalaemia	≥ 6.5 mmol/L	Immediate treatment

*A potassium level of up to 6mmol/L can be normal in the neonatal period.

CONTENTS:

Author(s): V1: [redacted] (Paediatric Renal Reg) [redacted] (PICU Reg). V2: [redacted] (PICU pharmacist)

INTRODUCTION

- Potassium homeostasis is important for cellular and neuromuscular function, cell volume, pH, and enzyme function[1].
- Hyperkalaemia can cause life threatening cardiac conduction abnormalities and arrhythmias.
    - These are more likely at levels above 7mmol/L, but can occur at lower levels, particularly if the rise is acute.

CLINICAL FEATURES

Symptoms are rare but include[5]:

- Muscle weakness
- Palpitations / syncope associated with cardiac arrhythmia/conduction abnormality

ECG changes usually progress as follows[1,4-5]: (see Appendix 2) These changes do not always precede life-threatening arrhythmia.

- Peaked T waves
- Prolonged PR interval
- Loss of P wave
- Decreased R wave amplitude
- Widened QRS
- ST depression
- May progress to complete heart block, sine wave, asystole or VT and VF.

CAUSES

Pseudohyperkalaemia (Levels artificially high)	Haemolysed blood sample giving an inaccurate result
	Sampling error or EDTA contamination of sample (take lithium heparin first)
	Hereditary spherocytosis and familial pseudohyperkalaemia – excess potassium leak due to ex vivo blood cooling
	Significant leucocytosis or thrombocytosis
Increased potassium intake	High potassium load – e.g. oral supplements/ IV fluids/ parenteral nutrition
	Blood transfusion
Reduced potassium excretion	Acute Kidney Injury or Chronic Kidney Disease: The kidneys have a high capacity to excrete K until GFR falls <15 ml/min/1.73 m^2. At lesser degrees of kidney impairment, other factors such as drugs or dehydration may impair K secretion.
	Dehydration/ hypovolaemia
	Drugs(not exhaustive, see BNFC for further information): - Non-steroidal anti-inflammatory drugs e.g. ibuprofen/diclofenac - Potassium –sparing diuretics e.g. spironolactone/amiloride - ACE inhibitors e.g. captopril/ enalapril - Angiotensin 2 receptor blockers e.g. losartan - Calcineurin inhibitors e.g. ciclosporin, tacrolimus
	Aldosterone deficiency: - Primary hypoaldosteronism - Congenital adrenal hyperplasia
	Aldosterone resistance: - Pseudohypoaldosteronisim type 1 and 2

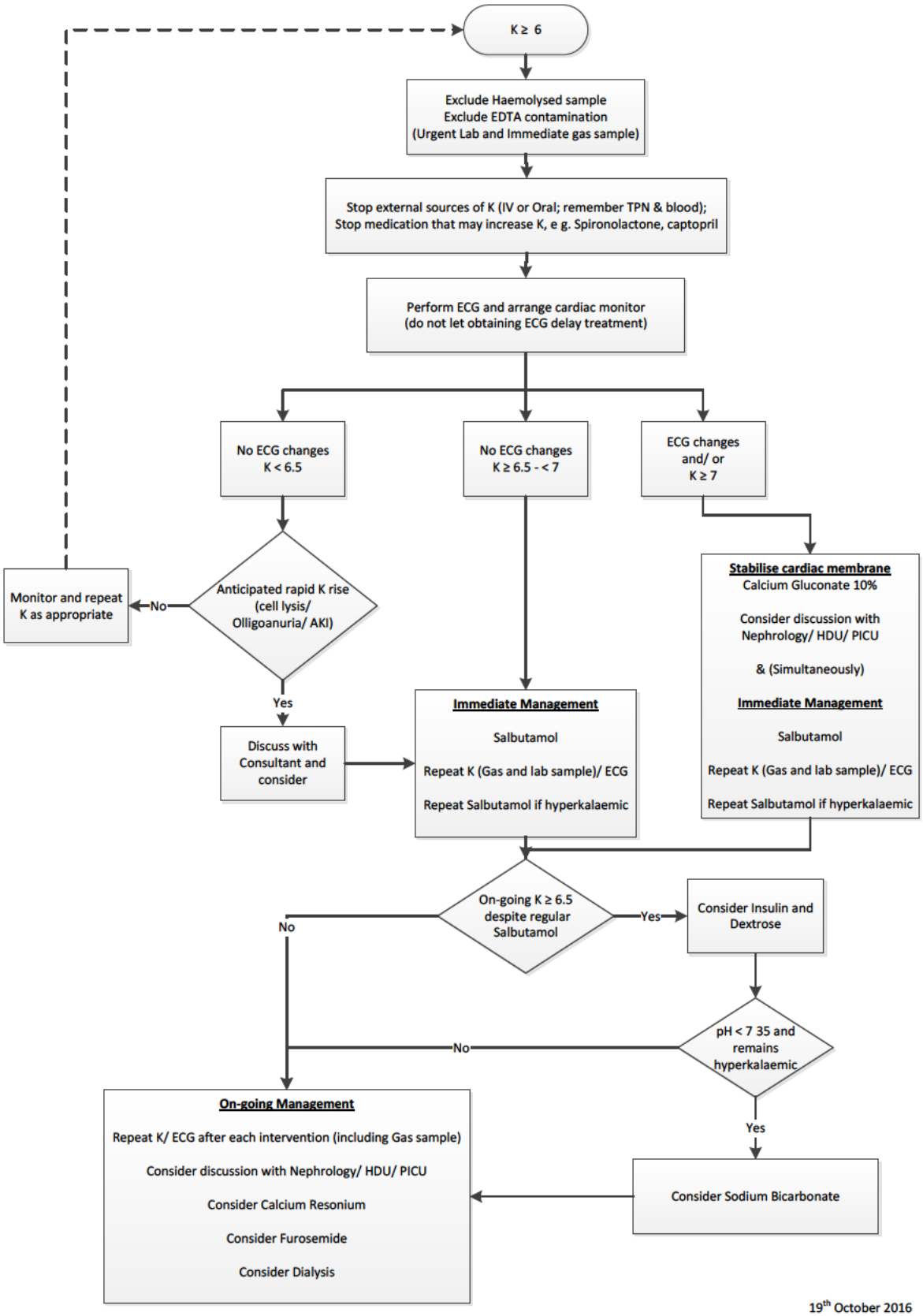
	- Secondary type 4 renal tubular acidosis may be associated with sickle cell disease, urinary tract obstruction and / or urinary tract infection
Movement of potassium from intracellular to extracellular spaces	Cell breakdown– tumour lysis/ severe haemolysis/ rhabdomyolysis/ GI bleed
	Acidosis
	Insulin deficiency
	Drugs e.g. beta blockers, suxamethonium, digoxin toxicity

MANAGEMENT (see flowchart also):

1	Cardiac protection	Protect the heart from conduction abnormalities using calcium gluconate 10%
2	Treat the underlying cause	Treat the underlying cause / decrease potassium intake / stop potassium sparing drugs
3	Drive potassium into cells	Remove potassium from extracellular space (drive potassium into cells). The following target this: a. Beta 2 agonists, e.g. salbutamol b. Insulin and glucose c. If acidotic, restoring a normal pH, e.g. using sodium bicarbonate
4	Remove potassium from the body	Remove potassium from the body, the following target this: a. Exchange resin, e.g. calcium resonium b. Diuretics, e.g. furosemide c. Renal replacement therapy (haemodialysis or continuous venovenous haemofiltration) if life threatening levels or if conservative methods fail

MANAGEMENT FLOWCHART

Hyperkalaemia Guideline



DRUG DOSING AND ADMINISTRATION

See Medusa (accessible via connect) for administration guidance of IV medication

Drug	Dose and administration		Onset of action	Notes
Calcium Gluconate 10% (0.22mmol calcium in 1ml)	**0.11mmol/kg (max 4.5mmol) IV over 5-10 minutes**[12,19] 0.11mmol/kg = 0.5ml/kg Max 4.5mmol = max 20ml *IV access:* *Central – may be give undiluted in an emergency* *Peripheral – dilute to 0.045mmol/ml with sodium chloride 0.9% or glucose 5%*		Immediate	With ECG monitoring If ECG changes persist after administration (i.e. at 10 minutes), further doses may be given (max total 3 doses) Caution in patients on digoxin, discuss with consultant[10,11] Risk of extravasation as high osmolality
Salbutamol	Nebulised	**2.5 – 5mg**[12]	20-30 mins	May be repeated after 20 mins
	IV	**4 micrograms/kg over 5 minutes**[12,19] *Dilute to a maximum concentration of 50microgram/ml with glucose 5% (preferred) or sodium chloride 0.9%*		Minimum interval between IV doses is 2 hours. No benefit of iv over nebulised salbutamol[8] Risk of extravasation due to low pH
Soluble Insulin (Actrapid) in glucose	**Under 1 month: 0.5 unit/kg/hr IV infusion for 30minutes**[12,13,17] *IV access:* *Peripheral – Dilute 0.25unit/kg in 5ml/kg 10% glucose and give over 30 minutes* *If needing to give less than 5ml/kg volume:* *Central – 0.25unit/kg in neonates in 1ml/kg 50% glucose and give over 30 minutes* **1 month and over: 0.1 unit/kg/hr (max 10 units) IV infusion for 30 minutes**[12] *IV access:* *Peripheral - Dilute 0.05unit/kg in 5ml/kg 10% glucose and give over 30 minutes* *If needing to give less than 5ml/kg volume:* *Central – Dilute 0.05unit/kg in 1ml/kg 50% glucose and give over 30 minutes*		10-20 mins	Repeat after 30 mins if needed Monitor for hypoglycaemia: Take blood glucose levels every 15 minutes from the start of the infusion for at least 6 hours.

<table>
<tr>
<td>Sodium bicarbonate

8.4%
=1mmol/mL

4.2%
=0.5mmol/mL

1.4%
=0.17mmol/mL

1.26%
polyfusor
=0.15mmol/mL</td>
<td>1mmol/kg (max 50mmol) IV over 10-15 minutes[12,19]

Check strength of available preparations:
<table>
<tr><th rowspan="2">%</th><th rowspan="2">Mmol /ml</th><th colspan="2">Maximum concentration</th></tr>
<tr><th>Central access</th><th>Peripheral access</th></tr>
<tr><td>8.4</td><td>1</td><td>0.2mmol/ml

(or give neat in an emergency/fluid restriction)</td><td>0.1mmol/ml</td></tr>
<tr><td>4.2</td><td>0.5</td><td>0.2mmol/ml (or give neat in an emergency/fluid restriction)</td><td>0.1mmol/ml</td></tr>
<tr><td>1.4</td><td>0.17</td><td>Give neat</td><td>Give neat</td></tr>
<tr><td>1.26</td><td>0.15</td><td>Give neat</td><td>Give neat</td></tr>
</table>
Suitable diluents where needed: glucose 5%, glucose 10%, sodium chloride 0.9% (avoid if renal impairment – risk of hypernatraemia)</td>
<td>15 mins</td>
<td>May be repeated after infusion (i.e. 10-15 minutes)

Avoid if low calcium – risk severe hypocalcaemia, seizures / tetany – calcium gluconate is probably a better option

Do not administer sodium bicarbonate and calcium salts via same line— risk of precipitation</td>
</tr>
<tr>
<td>Furosemide</td>
<td>1mg/kg IV bolus (max 40mg).

Maximum rate 0.5mg/kg/minute or 4mg/minute[12,19]

IV administration: can be given neat via peripheral or central access but dilute with sodium chloride 0.9% to suitable volume to aid slow administration if needed (Ideally give via central access as risk of extravasation due to high pH)</td>
<td>1 – 2 hours</td>
<td>Replace fluid losses as appropriate.

Effect dependent upon good renal function.

Risk of ototoxicity with rapid administration.</td>
</tr>
<tr>
<td>Calcium Resonium
(also called Resonium A or sodium polystyrene sulfonate)</td>
<td>Oral/NG: 500mg - 1g/kg/day given in 3 divided doses (max 60g daily)[12]
Oral/NG administration:
Mix with water to give (not squash/juice)

Rectal: 500mg - 1g/kg/day given in 3 divided doses (max 30g daily)[12]
Rectal administration:
Dilute to 200mg/ml with water or 10% glucose. Irrigate colon 8-12 hrs post dose to ensure removal of resin</td>
<td>>4hrs</td>
<td>Avoid in preterm neonates and any children with or at risk from obstructive bowel or reduced gut motility.

Use laxative (eg lactulose) to avoid colonic impaction

Stop if plasma potassium concentration falls below 5 mmol/L[12]</td>
</tr>
</table>

Table A

REFERENCES	1. Masilamani K, van der Voort J, Management of acute hyperkalaemia in neonates and children. Arch Dis Childhood 2012; 97: 376-380 2. Lott, C., Truhlar, A., Alfonzo, A. et al. European Resuscitation Council Guidelines 2021: Cardiac arrest in special circumstances. Resuscitation 161 (2021) pp.152-219 3. Renal Association Clinical Practice Guidelines July 2020 – Treatment of Acute Hyperkalaemia in Adults. Available at: HYPERKALAEMIA GUIDELINE 2019 (ukkidney.org) [Accessed 22/12/21] 4. Daly et al, Hypokalaemia and hyperkalaemia in Infants and Children: Pathophysiology and treatment. Journal of pediatric health care 2013; 27(6): 468-496 5. Rees L, Brogan P, Bockenhauer D, Webb N. Paediatric Nephrology 2nd ED. Oxford University Press 2012 6. Somers MJ. Causes, diagnosis and evaluation of hyperkalaemia. In UpToDate, Matoo TK (Ed), last updates Nov 2015, current through Oct 2016 7. Somers MJ, Management of hyperkalaemia in children: www.uptodate.com, last updated Nov 2015, current through Oct 2016 8. Mahoney BA, Smith WA, LO DS et al. Emergency interventions for hyperkalaemia. Cochrane Database Syst Rev 2005;(2):CD003235 9. Ahee P, Crowe AV. The management of hyperkalaemia in the emergency department. J Accid Emerg Med 2000;17:188-191 10. Davey M. Letter, Calcium for hyperkalaemia in digoxin toxicity. Emergency Med J 2002;19:183 11. Levine M. The effects of intravenous calcium in patients with digoxin toxicity. J Emerg Med. 2011 Jan;40(1):41-6 12. Paediatric Formulary Committee. *BNF for Children* (online) – Fluids and Electrolytes. London: BMJ Group, Pharmaceutical Press, and RCPCH Publications <http://www.medicinescomplete.com> [Accessed on 16/12/21] 13. Neonatal Formulary 7th Edition. Wiley 2014. 14. Brookbank D, Lanstaff C. Hyperkalaemia Guideline. Nottingham Children's Hospital Guideline. 2014 March 15. Skellet S. et al 2021. Paediatric advanced life support Guidelines. Resuscitation Council UK. Available at: https://www.resus.org.uk/library/2021-resuscitation-guidelines/paediatric-advanced-life-support-guidelines [Accessed 23/12/21] 16. Guyton & Hall, Textbook of Medical Physiology ninth edition. WB Saunders Company 1996 17. Guys and St Thomas Paediatric Formulary– available via mobile app only [Accessed 22/12/21]. 18. NHS Improvement, 2018. Patient Safety Alert – Resources to support safe and timely management of hyperkalaemia (high level of potassium in the blood). Available at: https://www.england.nhs.uk/publication/patient-safety-alert-safe-and-timely-management-of-hyperkalaemia/ [Accessed 13/12/21] 19. Medusa, 2021. Paediatric monographs: Calcium Gluconate monograph v.7 / Salbutamol monograph v.7 / Sodium Bicarbonate Monograph v4 / Insulin Soluble v5 / Furosemide v9. Accessed via intranet 13/12/21
RELATED DOCUMENTS AND PAGES	Adult hyperkalaemia guideline: [redacted] Tumour Lysis Syndrome Investigation and Management:

	http://nww.avon.nhs.uk/dms/download.aspx?did=9006
AUTHORISING BODY	Paediatric renal governance
SAFETY	Patient safety alert 2018 – safe and timely management of hyperkalaemia
QUERIES AND CONTACT	For urgent clinical queries regarding the treatment of hyperkalaemia in a certain patient, contact PICU or the renal team.

Appendix 1 – Evidence and rationale behind guideline recommendations

Role of potassium:

Potassium is predominantly intracellular (98%); potassium homeostasis is important for cellular and neuromuscular function, cell volume, pH, and enzyme function[1]. Concentration in the extracellular fluid is tightly regulated, between 3.5 – 5.5 mmol/L[4].

Thresholds for treatment:

There is some debate around what level of potassium should trigger treatment in the absence of related ECG changes or arrhythmias. Rate of rise in potassium is important in deciding this. There is agreement that K > 7 mmol/L should be treated. The UK Renal Association and European Resuscitation Council suggest K≥ 6.5 mmol/L should also constitute severe hyperkalaemia and be treated[2,3] Cochrane database review acknowledged K≥ 6.5 mmol/L as treatment level, although included studies with treatment at K>6mmol/L[8], with several adult papers suggesting treatment if K>6 mmol/L[4,9]. We recommend treatment of K≥ 6.5 mmol/L, with K 6 – 6.4mmol/L acknowledged as moderate hyperkalaemia and treatment considered, e.g. if rapid rate of rise anticipated.

Some sources suggest that cardiac membrane stabilisation using calcium gluconate should only be considered if K>7mmol/L and/or significant ECG changes are present[7]. The Renal Association suggest calcium gluconate should only be used if ECG changes are present irrespective of K level[3]. We recommend calcium gluconate if K≥7 mmol/L or ECG changes present.

We recommend nebulised salbutamol therapy as immediate management of hyperkalaemia in view of the ease and familiarity of use and evidence of efficacy in treatment of hyperkalaemia. There is no evidence of difference between nebulised and IV salbutamol on reduction of potassium level[8]. There is evidence to support the use of insulin and glucose to shift K into cells, but regular blood sugar monitoring must be undertaken to avoid potentially serious side effects[8]. The combination of insulin and glucose with salbutamol is more effective than either treatment alone[3,7,8]. There is no clear evidence that sodium bicarbonate is beneficial in hyperkalaemia so it is not recommended as monotherapy in hyperkalaemia[3,7,8].

In patients taking digoxin presenting with ECG changes and hyperkalaemia, digoxin toxicity should be considered, and treatment discussed with the consultant[10,11].