Title: Management of Hyperkalaemia

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This clinical guideline has been developed to ensure appropriate evidence based standards of care throughout the Yorkshire and Humber ODN South. The appropriate use and interpretation of this guideline in providing clinical care remains the responsibility of the individual clinician. If there is any doubt discuss with a senior colleague.

A. Summary page

1. Summary flow chart for management of hyperkalaemia
2. Aim of guideline
   To provide evidence based management of hyperkalaemia in neonates

Stepwise Approach to Management of Hyperkalaemia

Assumed K^+ > 7.0 mmol/L

Assess for risk of arrhythmia *

ECG changes
Rapid rise of K+ to >7.5 mmol/L
Acidosis
Known hypocalcaemia or hypomagnesaemia
Oliguria
Acute renal failure
Cardiac disease

Confirm true K+ level with urgent venous/arterial sample

Stop all K+ retaining drugs, avoid the use of suxamethonium and consider stopping all K+ containing fluids, review nephrotoxic drugs

If significant risk of arrhythmia

10% Calcium gluconate 2ml/kg IV OR Calcium Chloride 0.5mmol/Kg

True K^+ > 7.0 mmol/L (sick baby)
OR
K^+ >7.0 mmol/L and rising on 2 sequential measurements (well premature baby)

Inform consultant oncall and monitor closely

See drug table for details of administration

Other Investigations

Urea and electrolytes – (baseline and 4 hourly)

Calcium
Magnesium
Chloride
Bicarbonate
Glucose

Treatment of Hyperkalaemia

Correct acidosis if pH < 7.23 and BE >8mmol/L or HCO_3 < 14mmol/L
Sodium bicarbonate 1- 2 mmol/kg (8.4% if poor urine output)
Repeat as required
Stop milk feeds and other exogenous sources of K^+

First Line
Glucose 20% 2.5 – 5 ml/kg/hour
AND
Insulin 0.1 - 0.6 units/kg/hour to keep blood sugar 4-7mmol/L
Start at 0.1 units/kg/hr and titrate
SEE FLOW CHART BELOW

Second Line
Salbutamol (IV) bolus 4 micrograms/kg repeated after 2 hours & consider
Calcium resonium (rectally)125 – 250mg/kg qds in term infant

Third Line
Furosemide (iv) 1mg/kg

Persisent hyperkalaemia
Salbutamol infusion 0.3– 1.0 micrograms/kg/min
CONSIDER
Dialysis or exchange transfusion

***ECG changes:** Serum K+ 6.5-8mmol/L – peaked T waves, prolonged PR interval, reduced p waves, widening QRS interval, amplified R wave
Serum K+ >8mmol/L – absent P waves, bundle branch block, widening QRS, eventual VF/asystole

1. Background:

Neonates with hyperkalaemia require close monitoring. Normal levels of serum potassium may differ depending on the gestation and condition of the infant.

Reversible hyperkalaemia in neonates was first recognised in 1959. It is defined as serum potassium above 6.5mmol/l.[1,2]
True hyperkalaemia is a medical emergency due to the effect on cardiac myocyte function which can result in cardiac arrhythmias and possible death[3]. Prompt treatment is necessary.

2. Aim:

To provide evidence based management and recommendations for defining, monitoring and treating hyperkalaemia in neonatal patients.

3. Areas outside remit if applicable:

Management requiring specialist renal input for rare inherited conditions.

4. Core Guideline

4.1 Definition of Hyperkalaemia

The normal range for potassium levels is 3.5-6.0 mmol/L. Gas samples that are normal are reassuring and results should be used.

Where a level between 6.0-6.9mmol/L is identified a repeat gas sample should be obtained. Patients should be regularly monitored to ensure the level is not increasing and consideration should be given to reducing additional sources of potassium e.g. in iv fluids/PN.

Hyperkalaemia K+ $\geq$7.0mmol/L
A raised K+ level on capillary sampling is commonly due to haemolysis; however, poor flowing venous samples may be as unreliable.

When interpreting a result, take the clinical state of the infant into consideration. If the baby is greater than 1kg, more than 1 week old, has good renal function, and is relatively well a routine sample can be repeated.

In all other cases, a more urgent sample should be sent (free flowing arterial or venous), with immediate simultaneous blood gas machine analysis to give an instant guide.
If the baby is unwell, or two capillary samples have already been sent, further samples should be free-flowing venous or arterial blood.

When hyperkalaemia is identified, and suspected to be true: Stop all potassium retaining drugs, avoid the use of suxamethonium and stop all exogenous sources of potassium early.

Unwell babies
Where acute renal failure is known or possible, a single true K+ > 7.0mmol/L should be monitored closely. Repeat a venous sample after 2-3 hours.

Well babies
Premature infants in particular, may develop hyperkalaemia without significant renal impairment (non-oliguric hyperkalaemia of prematurity). This requires monitoring but may not need treatment. Repeat sample after 4 hours. Two sequential measurements of K+ $\geq$ 7.0mmol/L, and rising, require treatment.

4.2. Cardiac Arrhythmias
Arrythmias are unlikely unless K+ > 7.5 mmol/L with ECG changes best confirmed on formal ECG. Early changes include peaked T waves, prolonged PR interval and widened QRS and are due to decreased conduction velocity. Continued rises in K+ levels may lead to ventricular tachycardia or sinus bradycardia and in severe cases ventricular fibrillation and asystole.[3,4]

4.3. Emergency Treatment if risk of arrhythmia
To control cardiac excitability give:
calcium gluconate 10% (IV) 2 ml/kg (0.46 mmol/kg)
or
calcium chloride 0.5mmol/kg [5,6,7]

Onset is within 5 minutes. Check concentrations available on ward when calculating dose and give via separate intravenous line from sodium bicarbonate and parenteral nutrition.

Hyperkalaemia inactivates sodium channels and increases membrane excitability by reducing the membrane resting potential. Calcium antagonises the effects of hyperkalaemia on the cardiac myocyte. returning the resting potential to near normal. It is cardio-protective but does not reduce potassium serum levels.

Aim to keep the ionised calcium levels (on the blood gas) > 1.0.

4.4 Causes of Hyperkalaemia
The cause must be considered and in general, appropriate management will reduce the potassium level. Hyperkalaemia can result from:
1. Increased K+ intake
2. Decreased K+ excretion

3. Shift of K+ from the intracellular to extracellular space in the immature erythrocyte. (Non-oliguric hyperkalaemia of prematurity without significant renal impairment)[8].

Other causes of neonatal hyperkalaemia are relatively rare and may be seen in the following conditions:

- Oliguric acute renal failure due to potassium retention.
- Shock with tissue damage causing potassium leakage from the intracellular space - some potassium will be redistributed to the intracellular space if acidosis is corrected (see below).
- Unexplained in the acute phase of respiratory distress syndrome - incidence may be reduced if mother receives antenatal steroids. [9]
- Hypoaldosteronism and hypoadrenalism (with hyponatraemia) - rare.
- Drug induced due to potassium retention (spironolactone, potassium supplements) or release from cells (suxamethonium).
- Accidental overdose in intravenous fluids. If this is considered retain IV fluids once stopped for analysis in pharmacy.

2.5. Investigations

When commencing treatment for hyperkalaemia the following may aid identification of the cause and set a baseline for treatment:

- Urea and electrolytes - repeat 4 hourly until serum potassium has stabilised
- Calcium, magnesium, chloride, bicarbonate, glucose and urine analysis.

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2.6. Other aspects of Management

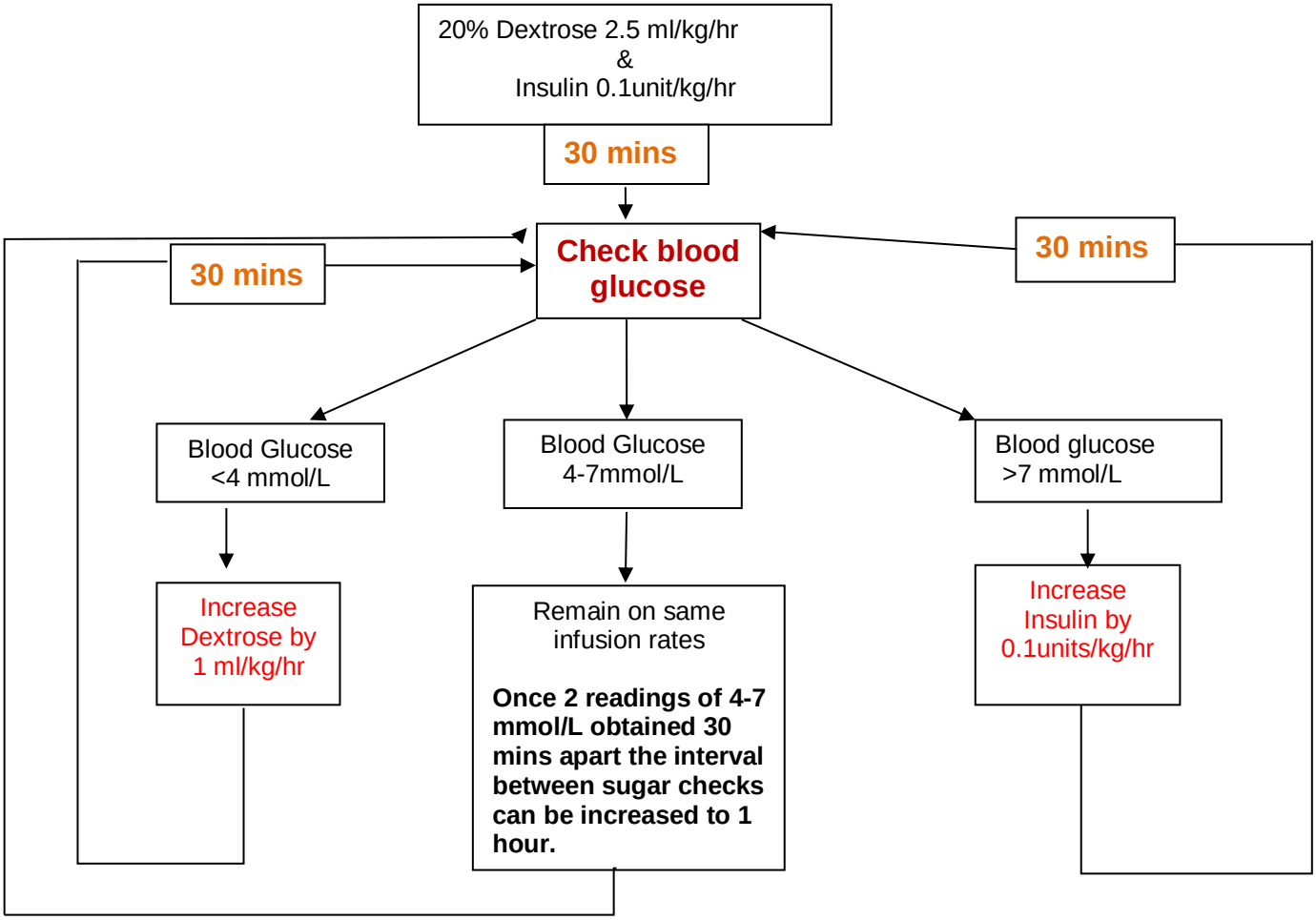
- Recheck serum potassium levels after each intervention or at least every 4-6 hours until normal levels are stabilised.
- Watch for fluid overload in the presence of renal failure and adjust fluid intake accordingly.
- Monitor blood glucose hourly if treating with glucose and insulin.

Drug Treatment of Hyperkalaemia (see additional information in Appendix 1)

Prevention	Drug	Mechanism of Action
Of Arrhythmias	**Calcium Gluconate 10%** (iv) 2ml/kg (0.46 mmol/kg) slow injection over 2-10 minutes Or **Calcium Chloride 0.5 mmol/kg** iv infusion over 15 minutes **NB: Check concentrations available on ward when calculating dose. Give via separate intravenous line from sodium bicarbonate and parenteral nutrition.**	**Onset of action within 5 minutes** **To stabilise myocardium. Used if K+ >7.5 or T wave abnormalities**
Acidosis pH <7.23 and BE > -8 mmol/L	**Sodium bicarbonate** (IV) 1 - 2 mmol/kg (2-4 ml/kg 4.2% solution or 1-2 ml/kg 8.4% solution) over 20-30 minutes. Monitor for hypernatraemia and fluid overload	Onset of action 1 hour Reduction of plasma K^+ by redistribution to intracellular space[3]
1st Line	**Glucose** (Dextrose) 20% 2.5 - 5 ml/kg/hour (equivalent to glucose 0.5 - 1 g/kg/hr) via central line OR Dextrose 10% 5-10ml/kg/hr peripherally if no central access available. It may be appropriate to include the dextrose within the maintenance fluids if being given peripherally or if there are concerns regarding fluid balance/overload. **AND** **Insulin** 0.1 - 0.6 units/kg/hour increasing to keep blood sugar 4-7 mmol/L Start at 0.1 units/kg/hour **NB: Dextrose infusions and insulin infusions should always be run through the same intravenous line (central or peripheral) to ensure both infusions stop if the IV line blocks or leaks.** **Close monitoring is required (see flow chart below)** There is evidence to suggest that a combination of salbutamol and dextrose/insulin may be more effective than either alone and this should be considered in hyperkalaemia resistant to monotherapy.[8,12,13,14]	Onset of action within 15 minutes Reduction of plasma K^+ by redistribution to intracellular space Reduction of plasma K^+ by redistribution to intracellular space

2nd Line	**Salbutamol bolus** (IV) 4 micrograms/kg bolus over 5 - 10 minutes - may be repeated after 2 hours[2] **AND CONSIDER IN TERM INFANTS** **Calcium resonium** (rectally) 125 - 250 mg/kg qds - exclude if any risk of GI tract pathology[8,10,11] (Irrigate the colon between doses and after 12 hours with a gentle saline lavage) **NB** Ineffective and dangerous in preterm infants for treatment of non-oliguric hyperkalaemia.[12]	Removal of K^+ by cation exchange
3rd Line	**Furosemide (iv)** 1 mg/kg slow injection over 5-10 minutes.	Increased renal excretion of K+ ion by reduced re-absorption in Loop of Henle[3]. Less effective if renal impairment present.
Persistent hyperkalaemia	**Salbutamol infusion** 0.5 – 1 microgram/kg/min (watch for fluid overload in renal failure) To be given after second salbutamol bolus **CONSIDER** **Dialysis or exchange transfusion** - discuss with Consultant Neonatologist and Paediatric Nephrologists. There is limited evidence to support exchange transfusion.	Reduction in total K^+

Flow chart for Administration of Dextrose and Insulin



NB. If Blood glucose < 2, stop insulin until glucose delivery increased and blood glucose above 4 mmol/L

5. Audit criteria:

Management following the guideline with levels done at appropriate time.

6. References

The guideline has been adapted from the Hull & East Yorkshire, Leeds Teaching Hospital and Jessop Wing hyperkalaemia guidelines. Thank you to all those who have contributed.

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Appendix 1 Unit specific example: Drugs for the management of hyperkalaemia in the neonate

Drug	Stock on NICU	Dilution	Administration
Sodium bicarbonate	Solution for injection 8.4%, 10 ml amps.	8.4% sodium bicarbonate solution can be used neat if given slowly and *via central line only.* It is preferably diluted to 4.2% with 5 or 10% Dextrose, or 0.9% Sodium chloride (not in renal patients).	Infusion over 20-30 minutes.
Calcium Gluconate	Solution for injection 10%, 225 micromol/ml	Used undiluted in emergency	Infuse over 5- 10 minutes
Salbutamol	Solution for injection 500 microgram/ml	Dilute with Water for Injection, 0.9% Sodium chloride, Dextrose/sodium chloride or Dextrose solution. 1. Take 1 ml of the 500 micrograms/ml solution and dilute **to** a total volume of 25 mls → this gives a 20 microgram/ml solution 2. Take 1 ml of this 20 microgram/ml solution and dilute **to** a total volume of 5 mls → this gives a 4 microgram/ml solution (= final solution)	For salbutamol bolus: 4 microgram/kg = 1 ml/kg of final solution; give over 5-10 minutes For salbutamol infusion the 4 microgram/ml can be used as well. In fluid restricted patients higher concentrations (e.g. 20 microgram/ml) can be used. If necessary, neat solution can be given, *via central line only*.
Calcium resonium	15 gram powder in tub + bottle methylcellulose	Dissolve contents of one tub (15 gram) calcium resonium in 25 mls of methylcellulose; then make up **to** total of 50 mls with water → this gives a solution of 300 mg per ml.	For rectal use only The dose should be retained as long as possible, up to 12 hours The colon should be irrigated with 1-2 mls of 0.9% sodium chloride before a new dose is inserted or 12 hours after
Insulin	Humulin S (soluble insulin) 100 units/ml	Add 10 units of Humulin S to 50 mls of 5% dextrose → 0.2 unit per ml	Using this solution 0.1-0.6 unit/kg/hour corresponds with 0.5 - 3 ml/kg/hour
Dextrose 20% (may be available as stock solution)	Dextrose 50% Dextrose 10%	Remove 125 mls from bag of 10% dextrose. Add 125 mls of dextrose 50% to make an overall concentration of 20% dextrose	Run this solution at 2.5 – 5 mls/hr via a central line. Run dextrose solution and insulin on the same IV line.
Furosemide			Infuse over 5-10 minutes