The Yorkshire and Humber Neonatal Operational Delivery Network

Title: Management of Hyperkalaemia

Author: Reviewed by Dr Anjana Adonchiyalage (June 2020), updated 2012 by Dr. Ranganna, original 2003

Date written: January 2018, Updated August 2020

Review date: August 2023

This clinical guideline has been developed to ensure appropriate evidence-based standards of care throughout the Yorkshire and Humber ODN. 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

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

If significant risk of arrhythmia

10% Calcium gluconate 0.5 ml/kg IV OR Calcium Chloride 0.125mmol/Kg
(Repeat after 5min if ECG changes persists)

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

***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

Treatment of Hyperkalaemia

Stop milk feeds and other exogenous sources of K^+

First Line
Salbutamol (IV) bolus 4 micrograms/kg (can repeat after 2 hours)
OR
Nebulised Salbutamol 2.5-5mg (can repeat as needed)
OR
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
(Consider combining Salbutamol (IV or Nebulised) with IV Insulin + Glucose in severe or resistant cases)
Consider correction of acidosis if pH < 7.2 and BE <-10mmol/L or HCO_3 < 16mmol/L
Sodium bicarbonate 1- 2 mmol/kg (8.4% if poor urine output)
(Do not give Sodium bicarbonate if Corrected Ca<2 or Ionised Ca<1, Correct low Ca before correcting Acidosis)

Second Line
Furosemide (iv) 1mg/kg

Persisent hyperkalaemia
Salbutamol infusion 0.3– 1 micrograms/kg/min
CONSIDER
Regular Furosemide +/- Calcium resonium or Dialysis or exchange transfusion

Refer to the table on page 6 and appendices for more details on medication doses & administration

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) 0.5 ml/kg (0.11 mmol/kg) (Alternative higher dose 2ml/kg (0.46mmol/kg))
or
calcium chloride 0.125mmol/kg [5,6] (Alternative higher dose 0.5mmol/kg)

Onset is within 5 minutes. Can repeat dose after 5 minutes if ECG changes persists.

Check concentrations available on ward when calculating dose and give ideally via central line (in an emergency can give peripherally with caution). Do not administer calcium simultaneously with sodium bicarbonate or with parenteral nutrition through the same venous access, use a separate access.

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.

4.5. 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.

4.6. 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.

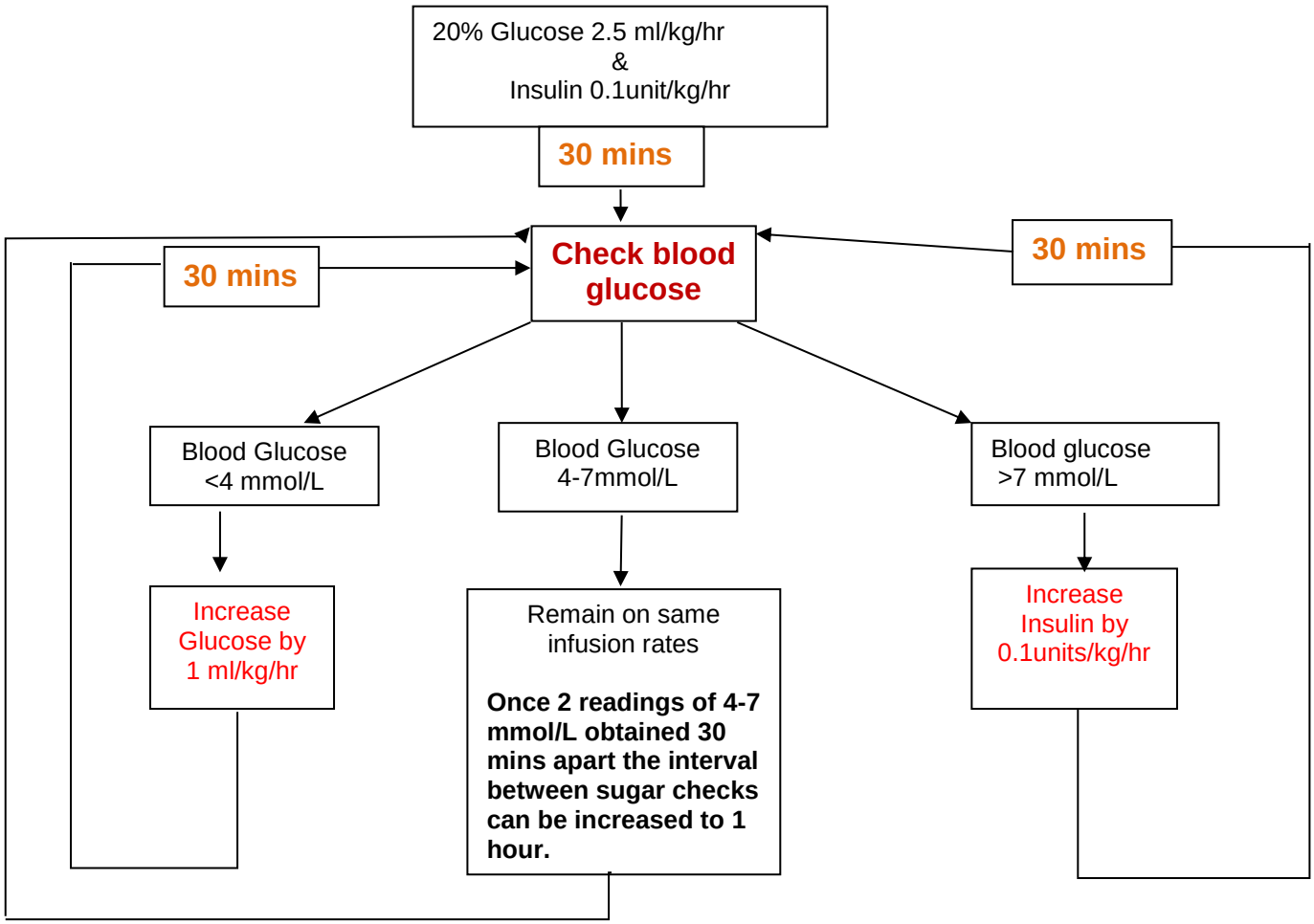
Drug Treatment of Hyperkalaemia (see additional information in Appendix 1 and 2)

	Drug	**Mechanism of Action**
Prevention Of Arrhythmias	**Calcium Gluconate 10% (iv) 0.5ml/kg (0.11 mmol/kg)** slow injection over 5-10 minutes (Alternative higher dose 2ml/kg (0.46mmol/kg)) Or **Calcium Chloride 0.125 mmol/kg** iv infusion over 15 minutes (Alternative higher dose 0.5mmol/kg) **NB: Check concentrations available on ward when calculating dose. Ideally give via central venous route. Give via separate intravenous line from sodium bicarbonate and parenteral nutrition, if needs administering them simultaneously.**	**To stabilise myocardium. Used if K+ >7.5 or ECG is abnormal** **Onset of action within 5 minutes. Can repeat dose after 5 minutes if ECG changes persists (Caution in repeating doses if used higher dose)**

1st Line	**Salbutamol bolus** (IV) 4 micrograms/kg bolus over 5 - 10 minutes - may be repeated after 2 hours[2] **OR** **Nebulised Salbutamol 2.5 – 5 mg[6] (Alternative lower dose in Australasian guidelines is 400micrograms/kg)** can repeat as needed. (If readily available, consider in patients with no IV access, while establishing IV access or while preparation of IV medications) **OR** **Glucose** (Dextrose) 20% 2.5 - 5 ml/kg/hour (equivalent to glucose 0.5 - 1 g/kg/hr) via central line OR Glucose 10% 5-10ml/kg/hr peripherally if no central access available. It may be appropriate to include the Glucose within the maintenance fluids if being given peripherally or if there are concerns regarding fluid balance/overload. Consider higher concentration (Up to Glucose 30%)[7] in fluid restricted patients with central venous access. **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 (Can use your own unit insulin regimen if available and preferred) **NB: Glucose 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)**	Both Salbutamol and Insulin + Glucose reduce plasma K^+ by redistribution to intracellular space Onset of action: Salbutamol within 5 minutes Insulin + Glucose within 15 minutes Evidence suggest equal efficacy of Salbutamol and Insulin + Glucose in lowering of plasma K+ and Combining Salbutamol (IV or Nebulised) with IV Insulin + Glucose is more effective than monotherapy and should be considered in more severe and resistant cases [8,12,13,14] Recommend to consider patient factors (Renal function/ Fluid restriction/ availability & type of vascular access / type of airway support) and Unit factors (Availability of medications/ devices/ trained staff) in selection of 1st line medication.
2nd 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** 0.3 – 1 microgram/kg/min (watch for fluid overload in renal failure) To be given after second salbutamol bolus **+/-** Regular Furosemide **CONSIDER**	

	For Term Neonates: Calcium Resonium (rectally): 125 - 250 mg/kg 3-4 times per day - exclude if any risk of GI tract pathology[8,10,11] (Suspend powder in 5ml of water or 10% Glucose per 1 g calcium resonium given. Irrigate the colon 6 - 12 hours after with a gentle saline lavage) **NB** Ineffective and dangerous in preterm infants for treatment of non-oliguric hyperkalaemia.[12] **Dialysis or exchange transfusion** - discuss with Consultant Neonatologist and Paediatric Nephrologists. There is limited evidence to support exchange transfusion.	Removal of K^+ by cation exchange
Acidosis **pH <7.2 and BE < - 10 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 Do not give Sodium bicarbonate if Corrected Ca<2 or Ionised Ca<1. Sodium bicarbonate will further reduce plasma Ca and destabilise myocardium.	Onset of action 1 hour Reduction of plasma K^+ by redistribution to intracellular space[3]

Flow chart for Administration of Glucose and Insulin



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

It may be appropriate to include the Glucose within the maintenance fluids if being given peripherally (due to larger volume) or if there are concerns regarding fluid balance/overload.

If there are difficulties in maintaining blood glucose levels with increasing rates of Glucose 20% consideration should be given to increasing the Glucose concentration further (Can go up to 30%. Concentrations >12.5% should only be administered via central route). Discuss with consultant.

Can use your own unit Insulin/Glucose regimen if available and preferred.

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.

1. Mildenberger E. & Versmold HT. 2002. Pathogenesis and therapy of non-oliguric hyperkalaemia of the premature infant. European Journal of Pediatrics 161: 415–422)
2. Vemgal P et al. Cochrane database of systematic reviews 2009. Interventions for non-oliguric hyperkalaemia in preterm neonates (review)
3. Masilamani K & Van der Voort J. 2012. The Management of acute Hyperkalaemia in neonates and children. Archives of Disease in Childhood 97 376-380
4. Usher R. 1959. The Respiratory Distress Syndrome of Prematurity. Changes in Potassium in the Serum and the Electrocardiogram and Effects of Therapy. Pediatrics 24 562
5. Neonatal Formulary 5th Edition 2008. BMJ Books. www.neonatalformulary.com
6. Children's BNF 2019-2020. BMJ Publishing Group. Royal Pharmaceutical Society of Great Britain and RCPCH Publications.
7. Guidance for prescribing and administration of Parenteral Nutrition on Paediatric Intensive Care. http://www.leedsformulary.nhs.uk .Accessed on May 2020
8. Mahony BA. Cochrane database of systematic reviews 2005 Apr. Emergency interventions for Hyperkalaemia
9. Uga N. Pediatr Int. Dec 2003;45(6):656-60. Antenatal steroid treatment prevents severe hyperkalaemia in very low birth weight infants.
10. Haycocl GB. Management of acute and chronic renal failure in the newborn. Seminars in neonatology Aug 03; 8:325 – 334.
11. Grammatikopoulosa T. Acta Pediatr 2003;92(1):118-20. Benefits and risks of calcium resonium therapy in hyperkalaemic preterm infants.
12. O'Hare F & Molloy E. 2008. What is the best treatment for hyperkalaemia in the preterm infant? BestBets- Best Evidence Topics as accessed on trip database Sept 2016 http://www.bestbets.org/bets/bet.php?id=01571
13. Hu PS, Su BH, Peng CT & Tsai CH. 1999. Glucose and insulin infusion versus kayexalate for the early treatment of non-oliguric hyperkalemia in very-low-birth-weight infants. Acta Paediatrics Taiwan 40 314–318
14. Malone TA.1991. Glucose and insulin versus cation-exchange resin for the treatment of hyperkalemia in very low birth weight infants. Journal of Pediatrics 118 121–123
15. British National Formulary for Children. NICE 2016
16. Guy's and St Thomas's paediatric formulary 2012
17. Management of hyperkalaemia in children. EMEESY Children's Kidney Network guidelines. https://www.emeesykidney.nhs.uk/ Accessed on January 2020.
18. NW Newborn drug protocol – salbutamol administration. http://www.adhb.govt.nz/newborn/DrugProtocols/SalbutamolAdministration.htm Accessed on May 2020

19. Neonatal Medication protocol – Kings Edward Memorial Hospital. https://www.wnhs.health.wa.gov.au/ Accessed on May 2020
20. Babylog VN800/ VN600 – Draeger. https://www.draeger.com/Library/Content/9055638_04_IfU_Babylog_VN800_600_SW1_n_en.pdf Accessed on July 2020

7. Appendices

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

Appendix 2: Guide for Salbutamol nebulisation (This is a suggestion to consider, Can follow own individual unit guide if available and preferred)

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

Drug	Stock on NICU	Dilution	Administration
Calcium Gluconate	Solution for injection 10%, 225 micromol/ml	Used undiluted in emergency (Central) For peripheral administration dilute X 5 volumes with Glucose 5% or Sodium chloride 0.9%.	Infuse over 5- 10 minutes (Preferred via central route, needs cautions to avoid extravasation)
Calcium Chloride	Solution for injection 10% (0.7mmol Ca in 1ml) 14.7% (1mmol Ca in 1ml)	Dilute with Sodium chloride 0.9%	Infuse over 15 minutes (Only via central route, needs cautions to avoid extravasation)
Salbutamol IV	Solution for injection 500 microgram/ml	Dilute with Water for Injection, 0.9% Sodium chloride, Glucose 5% 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*.
Salbutamol Nebulisation	Please refer to appendix 2 below		
Insulin	Humulin S (Soluble insulin) 100 units/ml Actrapid (Soluble insulin) 100 units/ml	Add 10 units of Humulin S/ Actrapid 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
		This is a suggestion to consider only. Can follow individual unit's Insulin administration guide if available and preferred.	
Glucose (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/kg/hr via a central line. Run dextrose solution and insulin on the same IV line.
Furosemide	Furosemide solution for injection 10mg/ml	Dilute with Sodium chloride 0.9%	Infuse over 5-10 minutes

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. Ideally be given centrally, if given peripherally (≤4.2%) needs extra cautions (Should not administer simultaneously with Calcium or Parenteral nutrition through the same line)
Calcium resonium	Calcium resonium powder for Oral/Rectal Suspension	Mix each 1g of resin with 5 ml of water or 10% glucose (Familiarise with the local hospital products. Contact your pharmacist)	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

Appendix 2: Guide for Salbutamol nebulisation (This is a suggestion to consider, Can follow own individual unit guide if available and preferred)

In neonates preferred route of administration of Salbutamol is intravenous. But nebulisation route can be useful in certain circumstances as hyperkalaemia is a medical emergency.

Consider nebulised salbutamol for: patients with no IV access or limited IV access, fluid restricted patients.

Drug preparation: Salbutamol nebuliser liquid 2.5mg/2.5ml or 5mg/2.5ml

Dose: 2.5 – 5 mg (BNFC recommended dose) (the alternative lower dose recommended in Australasian guidelines is 400 micrograms/Kg/dose[18,19])

Dilution: Dilute with 0.9% Sodium Chloride solution

Administration (for patients on minimal or no respiratory support):

- Use standard nebulisation device with correct size mask.
- Needs cautions to keep nebuliser liquid chamber upright to avoid spilling of liquid (may need to elevate head end of patient).
- Needs gas flow of 4-6 L/min to generate aerosols. In preterm neonates use air instead of Oxygen to avoid hyperoxia.

Administration (for intubated and ventilated patients)[20]:
Consider the intravenous route of administration of Salbutamol as the first option. If Salbutamol nebulisation is chosen, **strongly recommend to familiarise and adhere with the user guide of your own unit ventilator specific nebulisation technique.** Hyperkalaemia is an emergency the staff should be trained enough to assemble equipment and start nebulisation very quickly if this method of administration is chosen. Following steps are only a general guide and may vary depending on the type of ventilator.

- Patient should be on the pressure controlled ventilation mode (Change mode if on the volume controlled mode).
- Most ventilators have nebulisation option on advanced settings under Procedures/Manoeuvres option.
- May need to remove the Neonatal flow sensor from the ventilator circuit and switch off flow sensor option before starting nebulisation.
- Nebulisation device is needed to connect to either inspiratory limb of gas circuit or between ‘Y’ connector and ET tube depending on the ventilator.

- Familiarise with additional equipment needed and make sure those equipment and medication are readily available.

- Additional devices used in nebulisation can increase respiratory dead space and resistance of gas flow. Therefore, needs close monitoring of patents during nebulisation.

Frequency of administration: Repeat as required (BNFC) (Australasian guidelines recommend repeat 2 hourly, maximum 12 doses[18,19])