Salbutamol
Newborn use only

2020

Alert	Use with caution; safety data in newborn infants are limited. Evidence in the treatment of respiratory disease and bronchospasm in neonates is poor.
Indication	Hyperkalaemia Bronchospasm (evidence for efficacy is lacking)
Action	Stimulates liver and muscle cyclic AMP production causing potassium flow into cells.
Drug type	Sympathomimetic. β_2-agonist.
Trade name	IV: Ventolin Injection Inhalation: APO-Salbutamol 2.5, Asmol uni-dose 2.5, Butamol 2.5, Chemmart Salbutamol 2.5, Pharmacor Salbutamol 2.5, Salbutamol Actavis 2.5, Salbutamol 2.5, Salbutamol Sandoz 2.5, Salbutamol Sterinebs 2.5, Salbutamol-GA 2.5, Salbutamol-GA 2.5, Ventolin Nebules 2.5
Presentation	IV: 500 micrograms/mL ampoule Inhalation: 1 mg/mL (2.5 mg in 2.5 mL) and 2 mg/mL (5 mg in 2.5 mL) inhalation solution ampoules.
Dose	**Intravenous:** 4–5 microgram/kg over 20 minutes. Monitor serum potassium and heart rate (tachycardia) closely. If potassium critical or continues to rise, consider repeating dose every 4 hours[9] or use of other strategy (insulin/glucose; addition of rectal cation-resin). **Inhalation**: 400 microgram via nebulisation. Repeat two-hourly as required and titrated to response [serum potassium or respiratory status] and heart rate [tachycardia].
Dose adjustment	
Maximum dose	
Total cumulative dose	
Route	IV, inhalation
Preparation	**IV:** Draw up 0.4 mL (200 microgram of salbutamol) and add 19.6 mL of water for injection to make a 10 microgram/mL solution. **FURTHER DILUTE** Draw up 1 mL/kg of the above solution (10 microgram/kg of salbutamol) and add to water for injection to make a final volume of 10mL with a final concentration of 1 microgram/kg/mL. **Inhalation:** Draw up 0.4 mL (400 micrograms of salbutamol) from the 1 mg/mL inhalation ampoule and add 1.6 mL sodium chloride 0.9% to make a final volume of 2 mL with a final concentration of 0.2mg/mL. **OR**. Draw up 0.2 mL (400 micrograms of salbutamol) from the 2 mg/mL inhalation ampoule and add 1.8 mL sodium chloride 0.9% to make a final volume of 2 mL with a final concentration of 0.2mg/mL.
Administration	IV: Over 15–20 minutes via syringe driver. Inhalation: Via nebuliser over 10 minutes and discard remainder..
Monitoring	Cardiac rate and rhythm, Serum potassium, blood glucose
Contraindications	
Precautions	Infants with tachycardia
Drug interactions	Non-selective beta-blockers may increase serum potassium. Diuretics (hydrochlorothiazide, furosemide) increase risk of hypokalaemia and ECG changes. Salbutamol decreases digoxin concentrations.
Adverse reactions	Tachycardia, tremor, hypokalaemia. There is some concern that a transient increase in serum potassium may occur in the first few minutes of treatment.[8]
Compatibility	IV fluids: Water for injection, glucose 5%, sodium chloride 0.9%, glucose 4% in sodium chloride 0.18%, lactated Ringer's injection Y-site: Not recommended. Do not mix with any other drugs. Inhalation: Sodium chloride 0.9%
Incompatibility	IV fluids: No information.

	Y-site: Pantoprazole. Inhalation: No information
Stability	IV: Ampoules should be used immediately after opening. Any unused solution should be discarded. Diluted solution stable for 24 hours below 25°C. Inhalation: Ampoules should be used immediately after opening. Any unused solution should be discarded.
Storage	IV ampoule: Store at room temperature below 30°C. Protect from light. Inhalation ampoule: Store at room temperature below 25°C. Protect from light.
Excipients	
Special comments	Cross-check the correct strength of salbutamol intravenous and inhalation ampoules.
Evidence	**Efficacy and safety** **Treatment of hyperkalaemia:** A systematic review identified one study (Singh et al., 2002) of 19 infants which compared inhaled salbutamol [albuterol] versus placebo for non-oliguric hyperkalaemia (serum K^+ 5–7.5 mmol/L) in premature newborns.[1] Inhaled salbutamol 400 microgram, repeated 2-hourly as required, reduced serum K^+ from baseline at 4 hours (mean difference 0.69 mmol/L) and 8 hours (mean difference 0.59 mmol/L).[1] All-cause mortality was not reduced and cardiac arrhythmia did not occur in either study group. There was no significant difference in severe IVH, tremor, hyperglycaemia or pulmonary haemorrhage.[1] A number of case reports and case series have been published documenting the efficacy of salbutamol by infusion for treatment of hyperkalaemia in the newborn. Greenhough et al reported the use of IV salbutamol 4 microgram/kg over 20 minutes in 10 consecutive neonates with hyperkalaemia.[2] The potassium fell in 7 of the 10 infants (range 0.7–1.8 mmol/L) but continued to rise in 3 infants, all of whom had a persistent metabolic acidosis.[2] Murdoch et al reported on the use of IV salbutamol 4 microgram/kg over 20 minutes in 13 children (ages 0.01–16.7 years) with hyperkalaemia.[3] The mean reduction in plasma potassium concentration was 1.48 mmol/L at 40 minutes and 1.64 mmol/L at 120 minutes.[3] Kemper et al reported on the use of IV salbutamol at 5 microgram/kg over 20 minutes in 15 children (ages 0.1–16 years) with hyperkalaemia.[4] The mean reduction in plasma potassium concentration was 0.87 mmol/L at 30 minutes and 1.69 mmol/L at 120 minutes. Transient tachycardia was detected in three patients.[4] Recommendation: Salbutamol (either inhaled or intravenously administered) may be used in the treatment of hyperkalaemia in the neonate. Salbutamol may be useful in settings where hypoglycaemia limits the use of insulin. Salbutamol may have additive effects when used with insulin and glucose. Salbutamol appears to be generally safe with limited risk of tachycardia. (LOE II – III, GOR B). **Treatment of respiratory disease:** Systematic review of 3 trials including 140 infants comparing salbutamol versus placebo in near term or term infants less than three days of age with transient tachypnoea of the newborn found a reduction in the duration of oxygen therapy (MD -43.10 hours, 95% CI -81.60 to -4.60), but no difference in the need for CPAP, mechanical ventilation or duration of hospital stay and tachypnoea. At present there is insufficient evidence to determine the efficacy and safety of salbutamol in the management of transient tachypnoea of the newborn.[5] Systematic review[6] found a single study that reported prophylaxis of preterm infants at risk of chronic lung disease with salbutamol led to no difference in mortality (RR 1.08, 95% CI 0.50 to 2.31) or CLD (RR 1.03, 95% CI 0.78 to 1.37). There is no evidence for the use of salbutamol for prevention of chronic lung disease.[6] Recommendation: There is insufficient evidence to recommend use of nebulised salbutamol in newborn infants with respiratory disease. (LOE I GOR C)

	Pharmacokinetics Reports describing the pharmacokinetics of intravenous salbutamol in neonates and children are limited. Kirpalani et al studied the pharmacokinetics of a single dose of intravenous salbutamol in six preterm infants (GA 24 to 28 weeks), postnatal age 54 to 105 days, with bronchopulmonary dysplasia.[7] The elimination half-life of salbutamol was 118 minutes (range 69 to 162 minutes), volume of distribution was 1291 mL/kg (range 246 to 2997) and clearance 7.5 mL/kg/min (range 2.46 to 20.1).[7] The authors noted that the elimination half-life in their neonates was slightly shorter than that of healthy adults.[7]
Practice points	
References	1. Singh B, Sadiq H, Noguchi A and Keenan W. (2002). Efficacy of albuterol inhalation in treatment of hyperkalemia in premature neonates. *The Journal of Pediatrics*, 141(1), pp.16-20. 2. Greenough A, Emery E, Brooker R and Gamsu H (1992). Salbutamol infusion to treat neonatal hyperkalaemia. *Journal of Perinatal Medicine*, 20(6), pp.437-441. 3. Murdoch I, Dos Anjos R and Haycock G. (1991). Treatment of hyperkalaemia with intravenous salbutamol. *Archives of Disease in Childhood*, 66(4), pp.527-528. 4. Kemper M, Harps E, Hellwege H and Müller-Wiefel D. (1996). Effective treatment of acute hyperkalaemia in childhood by short-term infusion of salbutamol. *European Journal of Pediatrics*, 155(6), pp.495-497. 5. Moresco L, Bruschettini M, Cohen A, Gaiero A, Calevo MG. Salbutamol for transient tachypnea of the newborn. Cochrane Database Syst Rev. 2016. 6. Ng G, da Silva O, Ohlsson A. Bronchodilators for the prevention and treatment of chronic lung disease in preterm infants. Cochrane Database Syst Rev. 2016. 7. Kirpalani H, Doren G, Schmidt B, Tan Y, Santos R, Soldin S. (1990). Respiratory response and pharmacokinetics of intravenous salbutamol in infants with bronchopulmonary dysplasia. *Critical Care Medicine*, 18(12), pp. 1374-1377. 8. Mandelberg A, Krupnik Z, Houri S, Smetana S, Gilad E, Matas Z, Priel IE. Salbutamol metered-dose inhaler with spacer for hyperkalemia: how fast? How safe?. CHEST Journal. 1999 Mar 1;115(3):617-22. 9. Yaseen H, Khalaf M, Dana A, Yaseen N, Darwich M. Salbutamol versus cation-exchange resin (kayexalate) for the treatment of nonoliguric hyperkalemia in preterm infants. American journal of perinatology. 2008 Feb;25(03):193-7.

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