

## HYPERKALAEMIA

### Supporting information

#### **What is the evidence for the use of salbutamol, and is it superior to insulin as a treatment for hyperkalaemia? Has nebulised salbutamol been evaluated?**

A 2019 RCT compared the effectiveness of salbutamol nebulization with glucose-insulin infusion for the treatment of non-oliguric hyperkalemia in premature infants (Saw, 2019). The serum potassium levels were reduced after treatment in both groups. No significant changes in heart rate or blood pressure were observed in either group. The fluctuation in glucose levels was gentler in the salbutamol-treated group than in the glucose-insulin infusion group. The authors concluded that salbutamol nebulization is as effective as glucose-insulin infusion and can avoid potential side effects such as vigorous blood glucose fluctuations.

Saw HP, Chiu CD Chiu YP et al. Nebulized salbutamol diminish the blood glucose fluctuation in the treatment of non-oliguric hyperkalemia of premature infants. *J Chin Med Assoc.* 2019;82:55-9

#### **Evidence Level: II**

#### **Is rectal calcium resonium a safe treatment in neonates?**

Intestinal perforation has been reported in infants treated with exchange resin enemas (Grammatikopoulos, 2003; Bennett, 1996), although these may have been spontaneous rather than as a result of the treatment.

Nausea and vomiting are common side effects of oral administration, but changing to the rectal route is "less effective" (Helfrich, 2001).

A recent Cochrane review (Vemgal 2012) identified only two randomised trials of resins in the treatment of hyperkalaemia in neonates (Malone 1991 cited Vemgal 2012; Hu, 1999). In the larger, Hu (1999) study, 40 VLBW infants were randomised to receive either glucose/insulin infusion (n=20) or kayexalate resin enema (n=20). Duration of hyperkalaemia was significantly shorter (26.4 +/- 14.9 vs 38.6 +/-13.3 hours) in the insulin group.

An appropriately-sized randomised trial is necessary to evaluate the risks and benefits of this treatment in premature infants (Grammatikopoulos, 2003). Vemgal (2012) continued to call for larger, high quality studies of interventions for patients with hyperkalaemia, but from the three trials it reviewed (which included the Hu study), noted that "it appears that the combination of insulin and glucose is preferred over treatment with rectal cation-resin"

Bennett LN, Myers TF, Lambert GH. Cecal perforation associated with sodium polystyrene sulfonate-sorbitol enemas in a 650 gram infant with hyperkalemia. *Am J Perinatol* 1996;13:167-70

Grammatikopoulos T, Greenough A, Pallidis C, et al. Benefits and risks of calcium resonium therapy in hyperkalaemic preterm infants. *Acta Paediatr* 2003;92:118-27

Helfrich E, de Vries TW, van Roon EN. Salbutamol for hyperkalaemia in children. *Acta Paediatr* 2001;90:1213-6

Hu PS, Su BH, Peng CT, et al. Glucose and insulin infusion versus kayexalate for the early treatment of non-oliguric hyperkalaemia in very-low-birth-weight infants. *Acta Paediatr Taiwan* 1999;40:314-8

Vemgal P, Ohlsson A. Interventions for non-oliguric hyperkalaemia in preterm neonates. *Cochrane Database of Systematic Reviews* 2012, Issue 5. Art. No.: CD005257

<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005257.pub3/full>

#### **Evidence Level: II (For no evidence of benefit of resins over glucose/insulin)**

#### **Evidence Level: V (For case report evidence of harm from resins)**

#### **Do some VLBW infants without renal failure suffer from hyperkalaemia?**

Both renal and non-renal causes of neonatal hyperkalaemia have been suggested (Singh, 2002), and the cause of the condition is generally held to be multi-factorial (Ditzenberger, 1999). One study of 48 infants (Fukuda, 1989) implicated metabolic acidosis and catabolic state, but another, in 33 infants (Stefano, 1993), found no difference in muscle protein catabolism between 12 infants with hyperkalaemia and 21 without.

In a study of 18 VLBW infants (Gruskay, 1988) no differences in renal glomerular function were noted in 8 who developed hyperkalaemia and 10 who did not.

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Inability to regulate potassium balance, as a result of immature distal tubule function, may result in hyperkalaemia in the absence of renal failure (Mildenberger, 2002; Lorenz, 1997; Matsuo, 1995; Sato, 1995).

Ditzenberger GR, Collins SD, Binder N. Continuous insulin intravenous infusion therapy for VLBW infants. *J Perinat Neonat Nurs* 1999;13:70-82

Fukuda Y, Kojima T, Ono, A, et al. Factors causing hyperkalemia in premature infants. *Am J Perinatol* 1989;6:76-9

Gruskay J, Costarino AT, Polin RA, et al. Nonoliguric hyperkalemia in the premature infant weighing less than 1000 grams. *J Pediatr* 1988;113:381-6

Lorenz JM, Kleinmann LI, Markarian K. Potassium metabolism in extremely low birth weight infants in the first week of life. *J Pediatr* 1997;131:81-6

Matsuo Y, Hasegawa K, Doi Y, et al. Erythrocyte sodium-potassium transport in hyperkalaemic and normokalaemic infants. *Eur J Pediatr* 1995;154:571-6

Mildenberger E, Versmold HT. Pathogenesis and therapy of non-oliguric hyperkalaemia of the premature infant. *Eur J Pediatr* 2002;161:415-22

Sato K, Kondo T, Iwao H, et al. Internal potassium shift in premature infants: cause of nonoliguric hyperkalemia. *J Pediatr* 1995;126:109-13

Singh BS, Sadiq HF, Noguchi A, et al. Efficacy of albuterol inhalation in treatment of hyperkalemia in premature neonates. *J Pediatr* 2002;141:16-20

Stefano JL, Norman ME. Nitrogen balance in extremely low birth weight infants with nonoliguric hyperkalemia. *J Pediatr* 1993;123:632-5

#### **Evidence Level: IV**

##### **What level of hyperkalaemia should prompt treatment?**

The criteria on which to treat hyperkalaemia have ranged from 6.8 to 7.5 mmol/L, but 6.5 mmol/L may be a better level at which to begin treatment, as rhythm disturbances are to be expected above 7.0 mmol/L (Grammatikopoulos, 2003). If treatment is not initiated until symptoms appear (or the serum level exceeds 7.0 mmol/L), the potential for success is reduced (Ditzenberger, 1999). Mortality rates may be as high as 80% once arrhythmias have appeared (Singh, 2002).

Ditzenberger GR, Collins SD, Binder N. Continuous insulin intravenous infusion therapy for VLBW infants. *J Perinat Neonat Nurs* 1999;13:70-82

Grammatikopoulos T, Greenough A, Pallidis C, et al. Benefits and risks of calcium resonium therapy in hyperkalaemic preterm infants. *Acta Paediatr* 2003;92:118-27

Singh BS, Sadiq HF, Noguchi A, et al. Efficacy of albuterol inhalation in treatment of hyperkalemia in premature neonates. *J Pediatr* 2002;141:16-20

#### **Evidence Level: V**

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