hyperkalaemia treatments [created by Paul Young 17/12/07]

protecting the heart

Calcium chloride.
- Although there are no clinical studies assessing the efficacy of calcium salts in the emergency management of hyperkalaemia, there remains little doubt of their importance in emergency management even in patients with normal serum calcium.
- Both calcium salts, calcium chloride and calcium gluconate, antagonise the cardiac membrane excitability and have been widely recommended for the treatment and prophylaxis of arrhythmias due to hyperkalaemia when life threatening ECG changes (absent P waves, wide QRS, sine-wave pattern) are present or when cardiac arrest occurs.
- The decision of which calcium salt should be used, chloride or gluconate, is largely guided by practicalities such as availability and local practice. Calcium chloride contains more calcium (6.8 mmol in 10 ml) than calcium gluconate (2.2 mmol in 10 ml) and has greater bioavailability, but is more likely to cause tissue injury if extravasation occurs.

Efficacy:
- calcium chloride and calcium gluconate do not lower serum potassium.

Cautions:
- known or suspected digoxin toxicity. Rate of administration should be slower (over 30 min) in patients taking digoxin as calcium salts may contribute to toxicity.

Adverse effects:
- bradycardia, arrhythmias, tissue necrosis if extravasation occurs.

shifting of potassium into cells

(i) Insulin-glucose therapy.
- Several studies have evaluated the efficacy of insulin with glucose for the treatment of hyperkalaemia. Insulin enhances cellular uptake of potassium by stimulating the sodium-potassium (Na-K) adenosine triphosphatase (ATP) pump. This effect is independent of its effect on cellular glucose uptake.
- Administration of glucose without insulin is not recommended in non-diabetics as endogenous insulin release may be insufficient and paradoxically could increase serum potassium further.
- Efficacy: insulin reduces potassium by 0.65-1 mmol/l within 60 min of administration.
- Cautions: regular (soluble) insulin should be used.
- Adverse effects: hypoglycaemia. This may be delayed (30-60 min post-infusion) if less than 30 g glucose is given.

(ii) Sodium bicarbonate.
- Sodium bicarbonate decreases the concentration of H+ in the extracellular fluid compartment which increases intracellular Na+ via the Na+/H+ exchanger and facilitates K+ shift into cells via the Na-K-ATPase pump. However, bicarbonate does not lower serum potassium in the absence of metabolic acidosis.
- Efficacy: no study has shown an independent potassium lowering effect within 60 min but when used in combination with insulin-glucose or salbutamol, it lowered potassium by 0.47±0.31 mmol/l at 30 min.
- Cautions: calcium salts and sodium bicarbonate should not be administered simultaneously via the same route to avoid precipitation of calcium carbonate.
- Adverse effects: hypernatraemia; pulmonary oedema due to large sodium load; tetany in patients with coexistent hypocalcaemia.

(iii) Salbutamol.
- Beta agonists have been widely studied for the treatment of hyperkalaemia. Salbutamol binds to beta-2 receptors stimulating adenylase cyclase which converts ATP to cAMP. This results in stimulation of the Na-K ATP pump and intracellular potassium uptake.
- Efficacy: salbutamol lowers serum potassium by 0.87-1.4 mmol/l after iv administration and by 0.53-0.98 mmol/l after administration in the nebulised form. The response is dependent on the dose administered as greater efficacy was reported in patients receiving 20 mg versus 10 mg of nebulised salbutamol.
- It is important to note that beta-blockers may affect the response to treatment and up to 40% of patients with ESRF do not respond to salbutamol.
- Cautions: beta-agonists may exacerbate tachycardia in patients with tachyarrhythmias.
- Adverse effects: tachycardia, tremor, anxiety and flushing.

removing potassium from the body

(i) Exchange resins.
- Cation exchange resins are cross-linked polymers with negatively charged structural units which exchange calcium (calcium resonium) or sodium (sodium polystyrene sulphonate; Kayexalate) for potassium across the intestinal wall.
- Efficacy: resins do not appear to increase faecal potassium excretion above the effect of induction of diarrhoea with laxatives. Studies have reported no reduction in serum potassium at 4 h
- Cautions: slow acting, therefore unsuitable for urgent management of hyperkalaemia. Coadministration of laxative is recommended.

Adverse effects: constipation, intestinal necrosis.

(ii) Diuretics.
- The theoretical basis for the use of diuretics in the treatment of hyperkalaemia is to enhance urinary potassium excretion. However, there are no clinical trials to support their use in the treatment of hyperkalaemia.

(iii) Intravenous fluids.
- Although there is no clinical trial to support fluid replacement, it is advisable to administer 0.9% saline intravenously if there is clinical evidence of volume depletion with the aim of improving renal perfusion and enhancing urinary potassium excretion.

(iv) Dialysis.
- Dialysis is the most immediate and reliable way of removing potassium from the body.The principle mechanism of action is the diffusion of potassium across the transmembrane gradient. Haemodialysis can remove 25-40 mmol/h of potassium and is more effective than peritoneal dialysis.
- The typical decline in serum potassium is 1 mmol/l in the first 60 min, followed by 1 mmol/l over next 2 h. The efficacy of haemodialysis in lowering serum potassium can be improved by performing dialysis with a low potassium concentration in the dialysate, a high blood flow rate or a high dialysate bicarbonate concentration.

summary of medications used

Therapy	Dose	Mechanism	Onset (min)	Duration (h)
Calcium chloride	10 ml of 10% IV	Antagonise	1–3	0.5–1
Insulin/50% glucose	10 units in 25 g IV	Shift	15–30	4–6
Salbutamol	0.5 mg IV 20 mg Neb	Shift	15–30	4–6
Sodium bicarbonate	1 mmol/kg IV	Shift	15–30	Several
Calcium resonium	15–30 g PO/PR	Removes	Variable	4–6

IV: intravenous; Neb: nebulised; PO: oral; PR: per rectum; min: minute.

medical interventions in hyperkalaemic cardiac arrest

- When hyperkalaemia is suspected to be the primary precipitant of cardiac arrest, resuscitation should not be terminated until serum potassium is controlled, by any means necessary, unless there are extenuating circumstances.
- Hyperkalaemia may also arise during the resuscitation attempt as a result of metabolic changes and hypoxia but does not usually require specific intervention.
- During CPR, adrenaline (epinephrine) should be the first drug to be administered irrespective of the cause of cardiac arrest. Adrenaline is a powerful sympathomimetic amine with both alpha- and beta adrenergic activity which helps to drive potassium into cells, thereby lowering serum potassium.
- Next, calcium chloride should be administered to antagonise the toxic effects of hyperkalaemia.
- Sodium bicarbonate should be considered in the context of a metabolic acidosis.
- Insulin-glucose is thought to be ineffective during CPR, however it is unlikely to cause harm and should begin to have effect within minutes of return of spontaneous circulation.
- There is no literature available on the use of intravenous salbutamol in this scenario.
- Optimising ventilation during CPR can avoid compounding acidosis and further extracellular shift of potassium.

haemodialysis during resuscitation
- There are several reports of patients treated successfully with dialysis during CPR for cardiac arrest secondary to hyperkalaemia. In many of these reports, resuscitation combined with dialysis has been successful even after prolonged CPR (in excess of 90 min) with no neurological sequelae. The dialysis mode used was dependent on local availability and practice, but success has been reported with haemodialysis, veno-venous haemofiltration or veno-venous haemodiafiltration, and also with peritoneal dialysis.