Haemolysis in patients on haemodialysis in Northern Ireland

A number of patients have recently become unwell immediately after haemodialysis in 3 of the 6 dialysis units in Northern Ireland. Although this is normally very uncommon a total of six patients have now been affected since September 2008.

Testing showed evidence of haemolysis. It is unclear which part of the dialysis process may have caused this issue. It may cause symptoms during the dialysis process or not become apparent for up to 12 hours after the treatment.

Increased vigilance for this condition is essential and all haemodialysis patients have been given information on what to be alert to. (see attached patient letter)

One of the consequences of this form of haemolysis may be life threatening hyperkalaemia or hypoxia that requires urgent intervention.

Symptoms or Signs of Dialysis related haemolysis

Symptoms and signs include:

- **Feeling non-specifically unwell**
- **Chest or abdominal pain**
- **Nausea and vomiting**
- **Itch, flushing, shivering,**
- **A rise in blood pressure**
- **Visible change in blood in dialysis tubing**

Aetiology

At present the cause of this problem is not known. Similar cases have occurred in the past in dialysis units throughout the world and for a variety of reasons. The Belfast Health and Social Care Trust is making every effort to identify the cause together with other affected Trusts in Northern Ireland.

What to do with a case of suspected haemolysis

If a patient with chronic renal failure presents with symptoms that started within approximately 12 hours of a haemodialysis treatment, haemolysis should be considered as a possible diagnosis.

In addition to the standard assessment and initial management the following action should be taken.

- **An evaluation for suspected hyperkalaemia (as CREST guidelines) – an ECG and cardiac monitoring will be necessary**
- **Take samples of blood for**
    - **Electrolytes including potassium**
    - **CBC specifying also that a blood film is required.**
    - **LDH**
    - **Haptoglobin levels**
    - **Hemolytic index (10 ml clotted sample).**
    - **Coombs test**

Please telephone the laboratory and alert them that these samples come from a possible case of dialysis related haemolysis, and request that they telephone back the result of the haemolytic index. This numerical result recording visible red or brown discolouration of serum is rapidly obtained before any other tests are done and enables early reassurance in most cases.
If the laboratory reports evidence of haemolysis or possible haemolysis contact your local Renal Unit or Renal Registrar on – call at Belfast City Hospital 02890329241.
Continue to provide appropriate supportive treatment.

If contacted directly by patient with suspected haemolysis

- **Advice them to attend your Department for the necessary evaluation.**
- **Haemodialysis patients who contact A&E Departments raising the issue of haemolysis should be seen promptly and not postponed to the following day.**

Hyperkalaemia

The reported incidence of hyperkalaemia in hospitalised patients is between 1 and 10%. The vast majority of cases are related to patients prescribed angiotensin converting enzyme inhibitors (ACE) or angiotensin II receptor blockers (ARBs) in conjunction with spironolactone with pre-existing or new renal failure. Most other cases are related to potassium supplementation and prescription of diuretics/medicines with potassium-sparing properties.

AETIOLOGY OF HYPERKALAEMIA

Renal Causes
- **Acute or chronic renal failure**
- **Hyperkalaemic renal tubular acidosis (type IV)**
- **Mineralocorticoid deficiency (hypoaldosteronism states)**
- **Medicines that interfere with potassium excretion (amiloride, spironolactone)**
- **Medicines that interfere with the renin-angiotensin system (angiotensin converting enzyme inhibitors, angiotensin II receptor blockade, nonsteroidal anti-inflammatory agents, heparin)**

Transcellular shift (intracellular to extracellular compartment)
- **Acidosis (including diabetic ketoacidosis)**
- **Medicines (digoxin poisoning, suxamethonium, beta-**blockade)

Increase circulating potassium - Exogenous or Endogenous
- **Exogenous (potassium supplementation)**
- **Endogenous (tumour lysis syndrome, rhabdomyolysis, trauma, burns**)

Pseudohyperkalaemia
- **Prolonged tourniquet time**
- **Test tube haemolysis**
- **Marked leucocytosis and thrombocytosis (measure plasma not serum concentration in these disease states)**
- **Sample taken from a limb infused with IV fluids containing potassium**

ASSESSMENT OF THE PATIENT

Is this "true" hyperkalaemia?
A repeat serum potassium should be ordered urgently, especially if hyperkalaemia is an unexpected or isolated finding and there are no ECG signs of hyperkalaemia, to exclude pseudohyperkalaemia.

How severe is the hyperkalaemia?
Hyperkalaemia is classified as –
- **mild (K+ 5.5 - 6.0 mmol/L)**
- **moderate (K+ 6.1 - 6.9 mmol/L) or**
- **severe (K+ 7.0 mmol/L)**

or if ECG changes or symptoms (muscle weakness or flaccid paralysis palpitations, paresthesias) occurring at ANY level of serum potassium ^{3}5.5mmol/L especially if associated with hypoxia. Situations associated with a rapid rise in potassium (acute renal failure, rhabdomyolysis) and hypoxia of any cause are more strongly associated with the development of cardiac conduction disturbances.
Mild hyperkalaemia is common and often well tolerated in patients with chronic renal failure.

Is urgent treatment required?
Urgent treatment is required if the serum potassium is >7 mmol/L OR hyperkalaemia is accompanied by ECGhanges or above symptoms - even in the presence of mild hyperkalaemia (K+ 5.5 - 6.0 mmol/L).

Haemodialysis
If despite the above measures the potassium remains greater than 7mmol/L or if pathological ECG changes/symptoms persist, the renal team should be contacted to arrange urgent dialysis if appropriate.

Emergency management of hyperkalaemia in adults

Incidence between 1 and 10% in hospitalised patients. Majority of cases are related to pre-existing or new Renal Failure, potassium supplementation or diuretics/medicines with potassium - sparing properties. Classified as mild (serum potassium 5.5 - 6.0 mmol/L), moderate (serum potassium 6.1 - 6.9 mmol/L), severe (serum potassium ≥7.0 mmol/L) Consult senior colleagues in clinical team

REVISED 23 JULY 2008

COMMON CAUSES OF HYPERKALAEMIA IN ADULTS

RENAL CAUSES

- Acute or Chronic Renal Failure*
- Medicines inhibiting R-A-A system (ACE inhibitors, ARBs, NSAIDs, heparin)*
- Medicine induced inhibition of potassium excretion (eg amiloride, spironolactone)*
- Hyperkalaemic RTA (Type IV)*

TRANSCELLULAR SHIFT OF POTASSIUM

- Acidosis (including Diabetic Ketoacidosis)*
- Medicines (digoxin poisoning, suxamethonium)

INCREASED CIRCULATING POTASSIUM

- Exogenous serum potassium (potassium supplements in medicines)
- Endogenous (burns, trauma, rhabdomyolysis)

* = MOST COMMON CAUSES

STEP 1: COMPREHENSIVE HISTORY AND EXAMINATION to determine and treat reversible causes of hyperkalaemia: ALWAYS TREAT THE UNDERLYING CAUSE.

- Non-specific symptoms include fatigue, weakness, paresthesias, palpitations (may be absent even with severe hyperkalaemia).
- Focus on past history of renal problems and medication usage: **Stop potassium containing fluids/foods and medicines inhibiting potassium excretion.**
- Exclude urinary tract obstruction (examine for bladder distension/prostatic hyperplasia). Catheterise if appropriate.

STEP 2: QUESTIONS AND INITIAL INVESTIGATIONS

Q: Is hyperkalaemia really present?:
Pseudohyperkalaemia (e.g. haemolysed sample). Repeat **serum potassium** urgently but do not delay treatment if **renal failure** or if **hyperkalaemic ECG changes.**

Q: Is Emergency Treatment needed?:
Yes if ECG changes present (Peaked T waves, PR prolongation, decreased or absent P waves, QRS widening, AV block, sine wave QRST)
A normal ECG does not obviate the need for therapy - the ECG can be normal in severe hyperkalaemia.
Yes if severe hyperkalaemia. Acute changes in serum potassium are more likely to cause cardiac arrhythmias.

A 12-lead ECG with cardiac monitoring, **repeated** assessment of **glucose** (BM, testing) urea and electrolytes is mandatory. Creatinine kinase/blood gas analysis (if indicated).

STEP 3: MANAGEMENT Use Hyperkalaemia Kit

1. Protect the cardiac membrane:

Administer 10ml calcium gluconate 10% solution IV over 2 minutes.
Effects noted 1 to 3 minutes and last approximately 30-60 minutes. Caution if patient taking digoxin.

2. Shift potassium into cells:

(a) Insulin
Withdraw 10 units of Actrapid® insulin using an INSULIN syringe.

Always obtain a check of volume from a senior nurse before proceeding.
Add to 50ml glucose 50% and administer by slow IV injection over 5 minutes. Effects observed in 15 minutes and last 4-6 hours.
Monitoring – blood glucose should be measured 30 minutes after insulin/glucose administration and then hourly up to 6 hours after completion of administration. Check urea and electrolytes 30 minutes after each administration of insulin/glucose.

(b) Beta 2 Adrenergic Therapy
Administer 10mg nebulised salbutamol.
Effect observed 15-30 minutes. May not always reduce **serum potassium** and not used as a single agent. Synergistic **serum potassium** lowering effect when used with insulin/glucose above.

Calcium gluconate, Insulin and Beta-2 agonists buy time and can be repeated multiple times while definitive measures are pursued.

3. Stop potassium intake:

Stop potassium supplements and potassium containing drugs. Avoid potassium rich fluids or foodstuffs in diet.

4. Remove potassium from the body:

(a) Use dialysis
Required only in exceptional circumstances where severe hyperkalaemia persists despite appropriate management. Ask senior colleague to consult with renal team.

(b) Use the gut
Calcium polystyrene sulphonate (Calcium Resonium®) orally. Limited efficacy and delayed action (BNF for details)

GAIN
GUIDELINES AND AUDIT IMPLEMENTATION NETWORK