Investigations for Disorders of Calcium, Phosphate and Magnesium Homeostasis

Tutorial for Specialist Portfolio Biomedical Scientists
03/02/2014
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1. Calcium
Most abundant mineral in the human body

Function
- Structural – bone, teeth
- Neuromuscular – control of excitability, release of neurotransmitters, initiation of muscle contraction
- Signalling – intracellular 2nd messenger

It’s effect on neuromuscular activity of particular importance in symptomatology of hypo- and hyper-calcaemia

Serum Ca
Present in 3 forms:
- Bound to protein (e.g. albumin) – pH dependent
- Complexed with citrate and phosphate
- Free ions – physiologically active – Concentration of ionised Ca maintained by homeostatic mechanisms

Very important to remember:
Labs routinely measure total Ca concentration in a serum sample. This may give rise to problems in the interpretation of results because changes in serum albumin concentration may cause changes in total Ca concentration. Therefore, adjusted calcium (calculation of total calcium concentration if albumin had been normal) is used to check calcium levels.

Calculation of adjusted calcium
For [Alb]<40g/L, adjusted calcium = [Ca] + 0.02 x {40-[Alb]} mmol/L
For [Alb]>45g/L, adjusted calcium = [Ca] - 0.02 x {[Alb]-45} mmol/L

Homeostasis – The PTH – VitD endocrine system
Ca concentration in ECF maintained within narrow limits (ref range 2.20 – 2.60 mmol/L) by a control system involving 2 hormones and 3 organs:

Hormones
- Parathyroid hormone (PTH)
• Calcitriol or 1,25(OH)\textsubscript{2}VitD

These hormones also control phosphate concentration in ECF (discuss later)

**Organs**

- Kidney
- Bone
- Gut

Parathyroid glands sense Ca level and secrete PTH if Ca becomes too low.

PTH stimulates 1a hydroxylase enzyme activity in kidney and promotes production of calcitriol (1,25(OH)\textsubscript{2}VitD), the biologically active form of Vitamin D\textsubscript{3}.

Restores Ca levels in 3 different ways:

- GI Tract: Increased intestinal absorption of dietary Ca
- Bone: Increased mobilisation of Ca from bone into the circulation
- Kidney: Increased Ca reabsorption

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**- Hypocalcaemia (abnormally low calcium)**

**Clinical features**

- Neurological (tingling, tetany, mental changes)
- Muscle cramps (changes in muscle excitability)
- Cardiac signs (abnormal ECG)
- Seizures

**Clinical signs**

- Trousseau’s sign – BP cuff above systolic pressure and hand goes into spasm
- Chvostek’s sign – Tap facial nerve in front of ear and face muscles spasm

**Causes**

- Commonest cause in hospital patients = Mg deficiency
- Hypoparathyroidism (Di George syndrome, surgical removal of parathyroid glands)
- CRF (chronic renal failure) – failure to activate VitD
- Vitamin D deficiency
- Artefactual (blood collected in EDTA tube)

**Treatment**

Treat underlying cause if possible

Give VitD supplements, Mg supplements

If tetany/seizures – IV calcium gluconate (monitor Ca levels)

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**- Hypercalcaemia (abnormally high calcium)**

Calcium >3.5mmol/L requires urgent treatment!!
Clinical features  
Almost always present >3.5mmol/L, may be absent <3.0mmol/L  
- Neurological & psychiatric (lethargy, confusion, irritability, depression)  
- GI issues (anorexia, abdo pain, nausea & vomiting, constipation)  
- Renal issues (polyuria, renal stones)  
- Muscoskeletal issues (bone/joint pain, muscle weakness, cardiac arrhythmias)

Causes  
- Commonest in hospital patients = Malignancy (cancer) but generally primary hyperparathyroidism  
- Less common : Vit D intoxication (over supplementing), Familial hypocalciuric hypercalcaemia (genetic defect), Thiazide diuretics  
- Uncommon: Thyrotoxicosis (increased bone turnover and release of calcium in circulation), phaeochromocytoma, immobilisation, milk-alkali syndrome (increased calcium intake and bicarbonate – self medicating)

Treatment  
Depends on underlying cause:  
- Malignancy – treat with bisphosphonates (inhibit bone resoption) plus IV saline to restore GFR and promote diuresis  
- Primary hyperPTH – surgical removal of parathyroid adenoma followed by immediate treatment with VitD to avoid transient hypocalcaemia until parathyroids begin to operate normally

2. Phosphate (Ref range 0.8 – 1.4 mmol/L)

Function  
- Energy – ATP/ADP  
- Substrate – NADPH/NADP  
- Structure – Phospholipids  
- Buffers – H+ metabolism/homeostasis

Homeostasis  
Phosphate concentration is also regulated by PTH and calcitriol (1,25(OH)2VitD).  
- PTH promotes release from bone and decreases renal absorption  
- Calcitriol promotes release from bone, increases gut reabsorption and renal absorption

- Hypophosphataemia (abnormally low phosphate)

Clinical Features  
- Muscle weakness (can not generate ATP)  
- Seizures  
- Haemolysis, rhabdomyolysis
• Bone pain (PTH attempts to release phosphate from bone)

Causes
• VitD deficiency
• Hyperparathyroidism – increased renal loss
• GI loss
• Intracellular shift (high glucose load – glucose metabolised using ATP – phosphate drawn into cells)
• Respiratory alkalosis (activation of phosphofructokinase, phosphate is used up)

Treatment
Administration of phosphate

- Hyperphosphataemia (abnormally high phosphate)

Clinical Features
• Tetany and muscle weakness
• Renal bone disease (osteodystrophy)

Causes
• Renal failure (most common)
• Increased load (eg oral phosphate)
• Cellular release (rhabdomyolysis)
• Hormonal (eg hypoparathyroidism)
• Pseudo (artefactual – haemolysis)

Treatment
• Treat underlying cause
• Phosphate binders (calcium or aluminium salts) by mouth to reduce gut absorption

3. Magnesium (Ref range: 0.7 – 1.0 mmol/L)

Function
• ATP only active when Mg-ATP
• Phospholipid structure, membranes
• Several other structures eg RNA/DNA
• Cofactor for ~ 300 enzymes

- Hypomagnesaemia (abnormally low magnesium)

Clinical Features
Muscle weakness, tremor, delirium, positive Trousseau and Chvostek’s signs, increased chance of digoxin toxicity

**Causes**
- Renal: renal diseases (Gitelman’s syndrome), diuretics
- GI causes: reduced intake (anorexia) / reduced absorption (Coeliac disease, GI diseases)
- Redistribution (transient): insulin, refeeding syndrome, ‘hungry bone’ syndrome
- Endocrine: diabetes, hyperCa, hyperaldosteronism
- Alcoholism: (very high incidence, rule out first)

**Treatment**
- Mild deficiency: oral supplements (this may induce diarrhoea and further Mg loss)
- Severe deficiency: IV Mg infusion

- **Hypermagnesaemia (abnormally high magnesium)**

**Clinical Features**
Dependent on Mg levels – paralysis of voluntary muscles, heart block/cardiac arrest

**Causes**
- Excess oral intake (eg antacids)
- IV (during treatment for preclampsia)
- Renal failure (chronic or acute)

**Treatment**
IV calcium (short-time protection against adverse effects of hypermagnesaemia)
In renal failure: dialysis

- **Mg as therapeutic agent**

- Asthma
- Eclampsia
- Dysrrhythmias