

hypophosphataemia [created by Paul Young 17/12/07]

general

- the body of an average 70kg adult contains 712g of phosphorus (28000mmol)
- 85% is stored in bone as hydroxyapatite crystals; 14% is found in soft tissues and 1% is found in the blood
- phosphate is the most abundant intracellular anion with an intracellular concentration of 100mmol/L which is 100 fold greater than levels found in the plasma

definitions

- the normal plasma level of phosphate is 0.8-1.3mmol/L
- moderate hypophosphataemia is defined as 0.32mmol/L to 0.65mmol/L
- severe hypophosphataemia is defined as <0.32mmol/L
- phosphorus depletion describes a situation of total body depletion. This may exist with normal plasma phosphate levels such as in malnutrition and DKA

homeostasis

- normal dietary intake of phosphorus is 800g-1000g
- the homeostasis of phosphate is under the control of parathyroid hormone, vitamin D & calcitonin and depends in the intestine, kidneys and bone
- bone metabolism is linked to calcium homeostasis. In the setting of hypocalcaemia, increased parathyroid hormone levels cause phosphate and calcium to be released from bone
- intestinal absorption of phosphate occurs in the small bowel, mainly the jejunum. Vitamin D which is produced by the kidneys in increased amounts when serum phosphate levels are low increases the intestinal absorption of both calcium and phosphate
- phosphate is excreted from the kidneys, but most of the excreted phosphate load undergoes resorption in the proximal tubule. Parathyroid hormone increase phosphate excretion by inhibiting reabsorption of phosphate

physiological functions of phosphate

1. it is the source of high energy phosphate bonds in ATP
2. it is a component of nucleic acids, phospholipids and enzymatic cofactors
3. it is a component of cGMP and cAMP which are important intracellular messengers
4. it is a component of 2,3 DPG which is important in oxygen delivery to tissues
5. it is an essential regulator of enzymes of the glycolytic pathway
6. it acts as a buffer in maintenance of plasma pH
7. it has a role in the immune system and the coagulation system

causes

1. inadequate intake or absorption
 - malnutrition
 - phosphate binding antacids
 - vitamin D deficiency
 - chronic diarrhoea
 - malabsorption syndromes
2. redistribution into cells
 - refeeding syndrome (chronic malnutrition leads to protein catabolism with total body phosphate depletion despite normal serum phosphate. Introduction of carbohydrates leads to an anabolic state which unmasks total body phosphate depletion and leads to precipitous drop in serum phosphate)
 - insulin administration in DKA leads to correction of acidosis and unmasking of existing total body phosphate deficit due to urinary loss by osmotic diuresis
 - alkalosis causes shift into cells
3. renal losses
 - diuretic therapy (acetazolamide produces greatest loss of phosphate while frusemide has minimal effect; mannitol produces minimal phosphate loss but interferes with the assay of serum phosphate producing falsely low levels)
 - osmotic diuresis
 - hyperparathyroidism
 - proximal renal tubular dysfunction (Fanconi's syndrome)
4. extreme catabolic states
 - burns, trauma and sepsis

effects

- respiratory effects
 - acute respiratory failure
 - ventilator dependence
 - decreases 2,3 DPG causing leftward shift of the oxygen dissociation curve
- musculoskeletal effects
 - muscle weakness
 - rhabdomyolysis
 - bone demineralisation
- haematological effects
 - haemolysis
 - disorders of leukocyte phagocytosis or chemotaxis
- neurological
 - altered mental state
 - gait disturbance
 - paraesthesias
- cardiovascular
 - reversible dilated cardiomyopathy
 - decreased inotropy

treatment

- specific approaches:
- KH₂PO₄ contains 10mmol phosphate and 10mmol K per 10ml ampoule
 - NaKH₂PO₄ contains 13.4mmol phosphate, 21.4mmol Na, 2.6mmol K in a 20ml ampoule
 - if phosphate 0.65 to 0.89 oral phosphate is most appropriate
 - if phosphate is 0.4-0.65 then 3 ampoules in 100ml normal saline over 3 hours
 - if phosphate <0.4 then 4 ampoules in 100ml normal saline over 4 hours

general

- high dose iv phosphate therapy is not without complications and hyperphosphataemia, hypocalcaemia, hypotension, tetany and ECG abnormalities may all occur
- iv phosphate therapy should be administered with extreme caution in patients with renal failure; iv phosphate therapy should also be avoided in patients with hypercalcaemia as it may cause metastatic calcification
- it is important to be aware of the potassium content of intravenous phosphate preparations