GUIDELINE

GIG CYMRU NHS WALES
Bwrdd Iechyd Prifysgol Caerdydd a'r Fro
Cardiff and Vale University Health Board

Guideline for testing and replacement of Phosphate

Note 1: Patients on renal replacement therapy have phosphate replacement as part of their replacement fluid regime and are excluded from this guideline.

Note 2: Patients on TPN may already be having iv phosphate supplementation – discuss with critical care pharmacist / consultant and nutrition team before initiating therapy.

Background / physiology of phosphate

Phosphate is an essential molecule for normal cellular and bone function. It is predominantly stored intracellulary. **Serum phosphate levels are subject to significant daily fluctuation[1] , are often an unreliable marker of whole body status and vary with many factors (e.g. Insulin level). Mild / moderately low serum levels often self-correct without specific supplementation** (especially if the patient is receiving nutrition)[2]. The normal range for plasma phosphate level is 0.8-1.45 mmol/l.

Low serum Phosphate can be caused by:

- Malnutrition or re-feeding syndrome
- redistribution of phosphate into cells (e.g. respiratory alkalosis, drug therapy (insulin, catecholamines)
- increased urinary excretion (e.g. metabolic or respiratory acidosis, hyperparathyroidism)
- decreased intestinal absorption (e.g. antacid abuse, vitamin D deficiency, chronic diarrhoea)

Symptomatic phosphate deficiency may be associated with:

- muscle weakness (general, cardiac and respiratory)
- development of critical illness myopathy

- increased susceptibility to sepsis due to white cell dysfunction.
- Deficiency can also cause cell membrane instability due to ATP depletion which can result in rhabdomyolysis, haemolytic anaemia, cerebral irritability, confusion, hallucinations, somnolence, convulsions and coma.
- There is also some evidence to suggest that low serum phosphate levels may be associated with atrial / ventricular tachyarrhymias[4].

Phosphate is mainly cleared by the kidneys and phosphate supplementation should be particularly cautious in those with renal impairment.

Testing regime

All patients admitted to the intensive therapy unit should have baseline phosphate levels measured as part of their admission blood testing panel.

Serum Phosphate testing is routinely performed thrice weekly (Monday, Wednesday,Friday) as part of the standard "ICU Profile" testing regime. A previous service development project determined that this 3x weekly regime is safe and reduces unnecessary testing and prescription costs[1] . Testing of phosphate levels on other days of the week (Tue,Thu, Sat, Sun) should only be performed when clinically indicated. In these circumstances Serum Phosphate testing can be added to the blood test requesting form. It is not necessary to call biochemistry as Critical Care is "exempt" from the minimum requesting intervals. It is usually recommended to check serum U&Es, Mg2+, Ca2+, and Albumin along with the serum phosphate as electrolyte deficiencies seldom occur in isolation.

<u>Legitimate reasons for testing Phosphate on "non-profile" days include:</u>

- Commencement of TPN
- Commencement of enteral feeding in patients who are suspected of having malnutrition (re-feeding)
- Low level of uncertain significance on previous day's blood tests.

Replacement

Patients with low serum phosphate can broadly be divided into three main groups:

Degree of deficiency	Range
Mild	0.6-0.8mmolL
Moderate	0.4-0.6mmolL
Severe	<0.4mmolL

Patients with severe hypophosphatemia (<0.4 mmol/l) should have immediate intravenous supplementation unless contraindicated:

For patients over 60Kg - 500mls of Polyfusor Sodium phosphate 50 mmol given iv over 12 hours. If body weight <60 Kg halve the dose – ie give 250mls / 12 hours.

Serum Ca2+ and k+ levels should be monitored 4 hourly by ABG during intravenous treatment due to the risk of significant hypocalcaemia and hyperkalaemia.

Daily testing of serum phosphate, U&Es, Mg2+ and calcium / albumin is indicated until phosphate levels are >0.4 mmol/l. Due to variation in phosphate distribution it can require several doses over multiple days to replenish stores. [4]

Severe hypophosphataemia is not usually treated by oral supplementation

Patients with moderate serum hypophosphatemia (0.4-0.6mmol/l) should be treated at the discretion of attending consultant depending on the patient history / symptoms and the perceived likelihood of the result being significant. Signs of muscle weakness or malnutrition increase the likelihood of the result being significant. In cases of uncertain significance it is reasonable to repeat the serum phosphate again the next day and treat then if the result is still low.

****Note: Patients requiring brain stem death testing require a serum phosphate level of at least 0.5 mmol/l before testing** ("Code of practice for the diagnosis and confirmation of brain stem death" – Academy of Medical Royal Colleges.) Patients who may need brain stem testing should have their serum level maintained above this threshold to prevent delays in testing. **

Moderate serum hypophosphataemia may be treated with:

- Intravenous 500mls Sodium Phosphate Polyfusor 50 mmol over 12 hours (250mls if <60Kg) – monitoring K+ & Ca2+ 4 hourly by ABG
  OR
- Oral/Nasogastric Phosphate Sandoz™ (contains 16.1mmol in each tablet) - give up to 4 tablets a day in divided doses if there is no GI pathology. Avoid giving at the same time as Calcium, magnesium or aluminium salts as these will decrease absorption. Oral phosphate administration may cause diarrhoea or abdominal cramps but does not require ABG Ca2+ monitoring. Phosphate Sandoz tablets also contain 3.1 mmol each of K+.

Patients receiving any phosphate supplementation should have daily testing of serum phosphate, U&Es, Mg2+ and calcium / albumin until phosphate levels normalize.

Patients with *mild* serum hypophosphatemia (0.6-0.8 mmol/l) do not usually require supplementation unless symptomatic. Rechecking at the next scheduled routine test is generally sufficient. Supplementation may be considered if persistently low levels are seen. The oral route may be the most appropriate route (unless contraindicated) but consideration should be given to reducing the dose - e.g. 1 tablet BD to reflect the mild deficiency and to reduce side effects.

Summary:

Phosphate <0.4mmol/l – replace with iv Polyfusor phosphate 500mls / 12 hours via CVC or PVC. (250 mls if <60Kg). Exercise care in renal failure. During infusion monitor iCa2+ / k+ 4 hourly by ABG.
Repeat serum phosphate, U&E, Mg2+, Ca2+ and Albumin after end of infusion.

Phosphate 0.4-0.6 mmol/l – if symptomatic treat as above (consider oral). Regardless of whether replacement is given repeat serum phosphate, U&E, Mg2+ Ca2+ and Albumin next day.

Phosphate 0.6-0.8 mmol/l – repeat serum levels at next routine test (2-3 days) unless symptomatic..

Patients who may require brain stem death testing should have their phosphate maintained above 0.5 mmol/l using Polyfusor Phosphate iv as required.

Notes - Administration of iv "Polyfusor" phosphate:

Each 500ml Phosphates Polyfusor® contains phosphate 50mmol, potassium 9.5mmol and sodium 81mmol. Max daily dose of iv phosphate is 50mmol (25 mmol if body weight <60Kg).

Polyfusor Phosphate may be given via CVC or PVC.

Note: Polyfusor Sodium Phosphate iv solution is a vesicant and should not be administered through pedal cannulae.

For consistency and to ensure infusion is finished before repeat testing, all iv phosphate on critical care is to be given @ 250 or 500mls (as per body weight) over 12 hours unless a critical care consultant decides otherwise and documents the reason in the notes.

Compatible infusion fluids: Sodium chloride 0.9% and 0.45%, glucose 5% and 10%.

Incompatible with: Magnesium and calcium salts. Amiodarone, caspofungin, ciprofloxacin, dobutamine, pantoprazole and Ringer's injection, lactated. In view of incompatibility with Ringer's injection and lactated, compound sodium lactate (Hartmann's solution) and Plasmalyte should be considered incompatible.

Caution: Polyfusor Phosphate has a high potassium content so care is required in Acute Kidney Injury / High K+ or with alternate K+ replacement. Can cause hypocalcaemia – care in already hypocalcaemic patients. 4 hourly ABG advised during infusion to watch for both high K+ and low Ca2+. Salt and water load may be significant in patients with CCF.

An alternative preparation may be used for patients with Hyperkalaemia - 10mL (10mmol) of sodium glycerophosphate 21.6% (2mmol Sodium and 1mmol of Phosphate per mL) can be added to 500mL of NaCl 0.9% or Glucose 5% and given over 12 hours. This should only be initiated after discussion with the critical care consultant and pharmacist. It may be more appropriate to initiate renal replacement therapy – which will also normalise phosphate and K+.

References

1. Diurnal variations in serum biochemical and haematological measurements Pocock et al, *J Clin Pathol*.1989;42(2):172–179

2. Impact of reduced frequency of phosphate testing on detected phosphate levels and phosphate prescription in Critical Care. Hepburn, Roberts, Zouwail. Critical care *Critical Care* 2014, **18**(Suppl 1):P432

3. Association between hypophosphatemia and cardiac arrhythmias in the early stages of sepsis Schwartz et al, *Eur J Internal Med* 2002 Oct;13(7):434

4. Treatment of hypophosphatemia in the intensive care unit

Geerse et al. *Critical Care* 2010,14:R147

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