Hypophosphataemia – NOT Refeeding Syndrome
Full Clinical Guideline

Reference No: CG-CLIN/1164/23

The management of hypophosphataemia depends on whether the patient has refeeding syndrome or not. **Patients with refeeding syndrome require much higher levels of phosphate to maintain normal levels. In addition, patients with refeeding syndrome require treatment in addition to correction of hypophosphataemia – see refeeding syndrome guideline - see CG-T/2013/03**

*Consider risk of refeeding syndrome in the following and use **Refeeding Syndrome Guideline:***

- poor dietary intake pre-admission
- compromised nutrition due to prolonged diarrhoea/vomiting
- nil by mouth for prolonged period
- anorexia nervosa
- high alcohol intake
- oncology patient on chemotherapy
- T1DM

These guidelines apply to adult patients but do **NOT** apply in:

- **Patients on ICU and SDU** - see specific guidelines for these areas
- **Patients with eGFR < 30ml/min/1. 73m^2 or on renal replacement therapy** discuss with nephrologist as these patients will have reduced phosphate clearance

In patients with hypophosphatemia, an underlying cause should be identified and treated where possible, which is usually apparent from the patient's history. Other potential causes could include (but list not exhaustive):

- Acute respiratory alkalosis
- Inhibition of phosphate absorption (e.g. antacids, phosphate binders)
- Steatorrhoea or chronic diarrhoea
- Vitamin D deficiency (if calcium is low, measure vitamin D levels)
- Primary and secondary hyperparathydroidism (if calcium is high measure PTH)
- Other drug adverse events e.g. acetazolamide, tenofovir, IV iron, chemotherapeutic agents

Phosphate ranges

Normal	0.8 – 1.50mmol/l
Mild hypophosphataemia	0.65-0.79mmol/l
Moderate hypophosphataemia	0.32 – 0.64mmol/l
Severe hypophosphataemia	< 0.32mmol/l (or patient symptomatic)

If the cause of hypophosphatemia is not apparent from the history and initial laboratory testing, measurement of urinary phosphate excretion can be helpful to distinguish between gastrointestinal and renal phosphate losses.The **normal kidney response** to phosphate depletion is to increase phosphate reabsorption, leading to virtual abolition of phosphate excretion in the urine.

Treatment
For patients with refeeding syndrome please refer to Refeeding guideline on Koha

Hypophosphataemia (NOT REFEEDING)

Any underlying cause (see above) should be identified and treated where possible, which is usually apparent from the patient's history. **Treat the cause where possible and then repeat serum phosphate levels**. Transient hypophosphatemia (due to redistribution of phosphate) usually resolves within 6-12 hours as long as the underlying cause is corrected. **In addition to treatment of the underlying cause, some patients will require phosphate supplementation.**

Mild hypophosphatemia

No treatment required

Moderate hypophosphataemia (use oral treatment whenever possible)

- ***Asymptomatic or symptomatic and serum phosphate >0.48 to 0.64mmol/L***

Sodium acid phosphate effervescent tablets 1936mg providing 16.1mmol of phosphate per tablet (=**Phosphate Sandoz**, other brands may be in use): 1-2 tablets three times a day

Note: tablets also contain 20.4mmol sodium and 3.1mmol of potassium per tablet. Oral phosphate should not be given at the same time as calcium, magnesium or aluminium compounds as these will bind phosphate and prevent its absorption.

Recheck serum phosphate every 24 hours of oral replacement. Reassess using same approach to either stop (once serum level >0.64mmol/L or continue further doses.

If oral route unavailable, replace using IV phosphate as per *table 1* below.

- **Symptomatic and serum phosphate 0.32 to 0.48mmol/L**

Replace with IV phosphate as per *table 1* below. Switch to oral phosphate, if available, once the serum phosphate reaches 0.48mmol/L or if route unavailable, adjust dosing according to serum phosphate as per *table 1* below.

Severe (< 0.32mmol/l) or oral route not available

Replace with intravenous phosphate as per *table 1* below

Table 1. Dosing and infusion time of IV phosphate polyfusor infusion*

Serum phosphate (mmol/L)	**Dose in mmol (and volume to be administered of 10mmol/ml polyfusor)**			**Suggested infusion time**
	40-60kg	**61-80kg**	**>81kg**	
<0.32 symptomatic or asymptomatic	25mmol (250mL)	35mmol (350mL)	50mmol (500mL)	6 hours
0.32 to 0.48 and symptomatic	20mmol (200mL)	25mmol (250mL)	30 mmol (300mL)	4 hours
0.33-0.6 but oral route unavailable	10mmol (100mL)	15mmol (150mL)	20mmol (200mL)	4 hours

*Please note: If a Phosphates Polyfusor is not available in the hospital, alternative phosphate formulations are available - discuss with pharmacy

Switch to oral phosphate, if route available, once the serum phosphate reaches 0.48mmol/L.

ADMINISTRATION OF INTRAVENOUS PHOSPHATE

A phosphate polyfusor containing 50mmol in 500ml may be used to administer the dose if a volumetric pump is used, which has been set to only infuse the calculated dose. The remaining solution should be discarded. A 500ml polyfusor also contains 9.5mmol potassium and 81mmol sodium.

Phosphate is also compatible with 5% glucose, but concomitant administration with calcium should be avoided as an insoluble complex may form. For further information on infusion, including other dilutions and compatibilities, see Medusa (the injectable medicines guide on the Trust intranet - Click link in Pharmacy intranet page on NET

Monitoring

Recheck phosphate levels at the end of each infusion before another dose is given. IV therapy can lead to transient hyperphosphatemia, socheck other U+Es for hyperkalaemia, hypernatraemia and hypocalcaemia, as well as renal function and any signs and symptoms of arrhythmias. Also monitor the patient for clinical signs of hypocalcaemia, which can be caused by a large increase in plasma phosphate. Other side effects include metastatic calcification, volume excess and metabolic acidosis.

Phosphate replacement can be stopped once serum phosphate is 0.64mmol/L unless there is an indication for chronic therapy.

Further Information

Physiology of phosphate

Phosphate is predominantly an intracellular ion with only 1% of total body phosphate found in the plasma, therefore it is difficult to predict the extent of any deficit based on plasma levels. Phosphorous is absorbed from the small intestine under the influence of vitamin D, and is renally excreted.

Clinical conditions in which hypophosphataemia may be seen

There are three major mechanisms by which hypophosphataemia may occur;

1. Reduced absorption

- Starvation/severe dietary restriction (refer to refeeding guidelines):

In starvation and recovery from malnutrition, plasma phosphorous levels are maintained by transfer of intracellular phosphate. However, if these patients are then given a carbohydrate (glucose) load, this causes shift of phosphorous intracellularly for use in glucose metabolism and profound hypophosphataemia may result. This “refeeding syndrome” may be seen for example when feeding is started in patients with anorexia nervosa, chronic alcoholism or those who have received prolonged IV fluids only e.g. following a stroke.

- Alcoholism and alcohol withdrawal
- Overuse of antacids which bind phosphate
- TPN with insufficient added phosphorous
- Impaired intake, absorption or activation of vitamin D
- Prolonged diarrhoea and vomiting

2. Internal redistribution

- DKA and HHS (formerly known as HONK)
- Respiratory alkalosis
- Rapid cell proliferation e.g. hungry bone syndrome, acute leukaemia
- Metabolic acidosis
- Glucocorticoid/mineralocorticoid treatment

3. Increased urinary loss

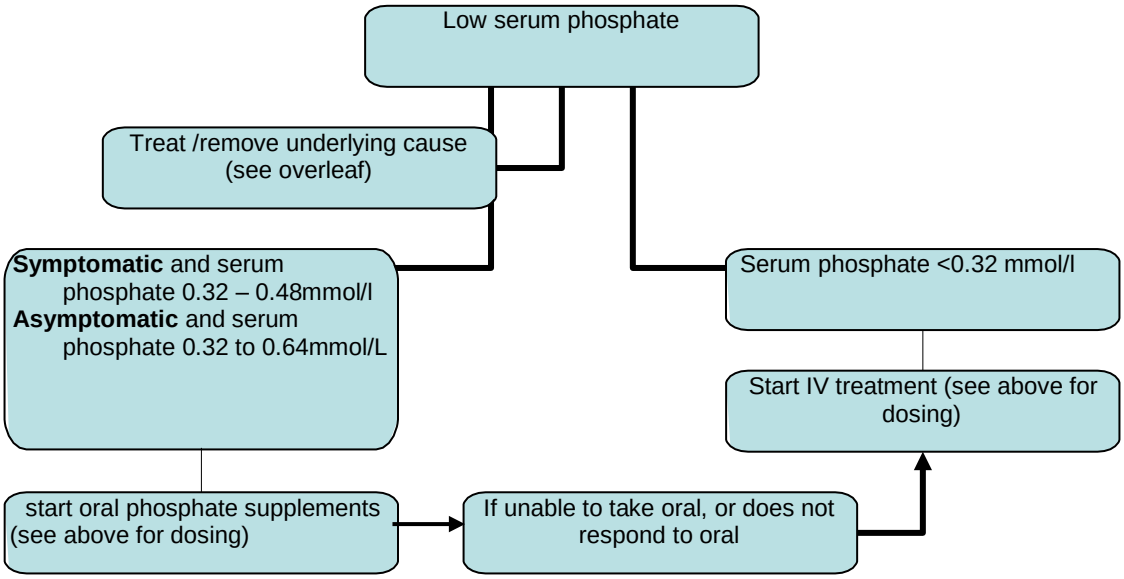
- Hyperparathyroidism (PTH inhibits tubular reabsorption of phosphate)
- Renal losses due to diuretics
- Early acute renal failure (due to loss of reabsorptive capacity)

Symptoms of hypophosphataemia

As serum phosphate levels do not accurately reflect total body phosphorous stores, the degree of hypophosphataemia does not always correlate with the presence of symptoms. Symptoms are also dependent on cause and duration of the hypophosphataemia and are most likely to occur in patients with severe and/or chronic hypophosphataemia. Symptoms of hypophosphatemia rarely occur unless the serum phosphate is less than 0.64mmol/L. Depletion of ATP, which is the energy source for most cellular functions, leads to a wide range of symptoms. In addition, tissue hypoxia occurs. The following signs and symptoms may be apparent:

- Respiratory insufficiency due to muscle weakness.
- Failure of weaning from ventilator
- Muscle weakness, myalgia and bone pain, rhabdomyolysis
- Decreased myocardial contractility and arrhythmias
- Neurological manifestations e.g. seizure, neuropathy, neuropsychiatric disturbances.
- Haematological disturbance e.g. haemolysis, platelet dysfunction

Summary of treatment of hypophosphataemia (Not refeeding syndrome)



References

Dickerson RN (2001) Guidelines for the intravenous management of hypophosphataemia, hypomagnesemia, hypokalaemia and hypocalcaemia Hospital Pharmacy 2001:36 (11); 1201-1208

Taylor BE et al. Treatment of hypophosphataemia using a protocol based on patient weight and serum phosphate level in a surgical intensive care unit. Journal of the American College of Surgeons 2004: 198(2); 198-204. Cited in UKMi QA 371.1

Geerse D et al (2010) Treatment of hypophosphataemia in the intensive care unit:a review. Critical Care 2010;14:\R147 http://ccforum.com/content/14/4/R147

Gaabeek A (2005)Hypophosphatemia: An update on its etiology and treatment. American Journal of Medicine 2005

UKMi QA 371.1 (September 2012). How is acute hypophosphataemia treated in adults? UK Medicines Information Network, Leeds Medicines Information Centre. Accessed via http://www.evidence.nhs.uk on 24/10/2014

UpToDate (Wolters Kluwer). Hypophosphatemia: Evaluation and treatment. Available online at www.uptodate.com. Last updated 14/12/2023 using literature review 11/2023. Accessed 21/12/2023

Documentation Controls

Development of Guidelines:	Clinical Pharmacist, Suraj Pankhania
Consultation with:	Clinical Pharmacy Team, Dr. Stephen Hearing Gastroenterology Consultant
Updated (Dec 2023) by:	Rebecca Greenham Pharmacist 21/12/2023
Approved by:	Drugs and Therapeutics Committee Dec 2020 Medical Division 13/5/21, 29/12/2023 CDCS division 29/12/2023
Review Date:	December 2026
Key Contact:	Clinical Pharmacy Team