Management of Significant Hypophosphataemia in Neonates

NHS University Hospitals of Leicester NHS Trust

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1. Introduction and Who Guideline applies to

This guideline is aimed at all Health care professionals involved in the care of infants within the Neonatal Service.

Key Points

- Oral/enteral is the preferred route to correct hypophosphataemia
- Hypophosphataemia in neonates is often asymptomatic. Be aware of high risk infants
- Assess renal function and other electrolyte abnormalities prior to correcting

Background

The definition of severe hypophosphataemia in neonates varies depending on which assay is used. Those most at risk are extreme preterms, IUGR and extremely unwell neonates. These infants are at risk because maximal mineral accretion occurs at 32-36 weeks in utero.

With placental insufficiency there is reduced active transport of minerals in utero. Infants at high risk also include those on diuretics, steroids, with low magnesium and potassium (as renal phosphate excretion is affected), with vitamin D deficiency, or on insulin or oral calcium.

Hypophosphataemia in early life often corrects itself with parenteral nutrition (PN) or enteral feeds and rarely needs additional phosphate infusions. There is a possibility of using bespoke PN particularly in extreme preterm infants with persistent electrolyte derangements. Intravenous infusions of phosphate can potentiate/cause acidosis and therefore gases should be monitored closely and phosphate infusions slowed or stopped if significant changes in pH become apparent. High doses of phosphate may increase serum phosphate transiently before redistribution into intracellular components or bone leading to a paradoxical drop in measured serum phosphate.

2. Guideline Standards and Procedures

In babies receiving enteral feeds it is preferable to correct phosphate with oral supplements but caution is required as low serum phosphate may actually be a reflection of calcium deficiency in developing metabolic bone disease (please see Metabolic Bone Disease of Prematurity - Prevention and Treatment UHL Neonatal Guideline)

Consider intravenous replacement if the serum phosphate is <1mmol/L (please see Appendix 1) and ensure that other electrolyte imbalances are concurrently monitored and corrected. Where the phosphate is 1.0 - 1.5mmol/L, this should be monitored daily to look for trends and where a baby is on PN discussed with the pharmacist to ensure optimal phosphate is being given. A phosphate level of <0.3mmol/L is life threatening and needs emergency treatment (see section 8).
Consider intravenous correction if:

- Severe hypophosphataemia <1mmol/L
  AND
- PN phosphate already maximised
  AND
- Enteral/oral route not available

Bespoke PN is available and will need discussion with pharmacy and the consultant
The maximum amount of phosphate in bespoke PN is between 2.7-3 mmol/kg/day due to stability of the solution. A discussion with pharmacists will allow evaluation of options using the bespoke ordering programme on a case by case basis.

2.1 Deciding to replace phosphate with an infusion:

1. **Prior to starting an infusion it is vital to check U+E, Bone, magnesium, blood gas**
   If there is low magnesium or potassium these should be corrected first prior to correcting phosphate.

2. **Calculate current delivery of electrolytes**
   Calculate how much phosphate is in infusions currently (NB the current infusion rate of the PN may be lower than the current prescribed rate). This can be seen in Table 1 as a quick guide. Phosphate in the PN comes from both the aqueous and the lipid phase. The table includes a rate of 1mL/kg/day to allow calculations based on low rates of PN delivery. Bag 1 has no electrolytes and so is not shown.

Table 1: Amount (in mmol/kg/day) of sodium, potassium and phosphate depending on run rates of stock bag 2 or 3 aqueous PN and lipid

Aqueous PN (ie stock bag)							
mLs/kg/day							
	1	50	60	75	80	90	100
Bag 2							
Sodium	0.04	2	2.4	3	3.2	3.6	4
Potassium	0.02	1	1.2	1.5	1.6	1.8	2
Phosphate	0.02	1	1.2	1.5	1.6	1.8	2
Bag 3							
Sodium	0.08	4	4.8	6	6.4	7.2	8
Potassium	0.02	1	1.2	1.5	1.6	1.8	2
Phosphate	0.02	1	1.2	1.5	1.6	1.8	2

Lipid PN								
mLs/kg/day								
	2.5	5	7.5	10	12.5	15	17.5	20
NNU Lipid +vits syringe OR NNU SMOF Lipid + vits syringe OR Intralipid 20%								
Sodium	0	0	0	0	0	0	0	0
Potassium	0	0	0	0	0	0	0	0
Phosphate	0.037	0.075	0.112	0.15	0.187	0.225	0.262	0.3

For example if a patient is receiving 50mL/kg/day aqueous phase bag 2 and 5mL/kg/day of lipid, they would be receiving a total of 1.075 mmol/kg/day phosphate.

3. **Decide on dose to be used**
   Dose: Start by replacing 0.5 to 0.6mmol/kg phosphate infused over 12 hours. Up to 1.2 mmol/kg can be replaced in a 24 hour period in addition to the phosphate delivered in PN but this must be in discussion with the consultant. For higher rates of replacement see section 8.

4. **Decide on appropriate formulation to be used**
   Phosphate can be corrected with either a phosphate polyfusor, sodium glycerophosphate 21.6% or potassium acid phosphate 13.6%. Table 2 shows how much phosphate and other electrolytes the preparations contain.

Table 2: Electrolyte composition of each phosphate preparation in **mmol/mL**

	Phosphate	**Sodium**	**Potassium**
Sodium glycerophosphate 21.6%	1	2	0
Potassium acid phosphate 13.6%	1	0	1
Phosphate polyfusor	0.1	0.162	0.019

Unless there is hypernatraemia (Na >145mmol/L), it is safest to correct low phosphate with either sodium glycerophosphate 21.6% or phosphate polyfusor as potassium acid phosphate 13.6% contains as much potassium as phosphate. Be aware of combined intravenous sodium or potassium in fluids/infusions/PN. Table 1 can be used to work out the electrolytes in PN depending on the rate it is running at.
If there are other infusions running use the calculation below to work out the other electrolytes being delivered by these fluids/infusions.

To work out the electrolytes in an infusion:
Rate infusion running at (mL/h) = **A**
Prescribed rate (mL/h) = **B**
Prescribed electrolyte in infusion = **C** mmol/kg/day
Electrolyte actually received = **A/B x C** mmol/kg/day

5. **Monitoring**

   Prior to starting an infusion - check U+E, Bone, magnesium, gas (acid-base balance), ECG and BP.
   ECG and blood pressure monitoring to continue during phosphate infusion.
   If correcting severe hypophosphataemia with bespoke PN only: phosphate should be monitored daily with calcium and ALP.
   If baby is receiving standard phosphate in pre-prepared PN, and there are no concerns of serum phosphate abnormality twice weekly assessment is adequate
   With IV serum phosphate infusions: Monitor gas, U+E, Alkaline phosphatase, calcium and phosphate 6 hours into an infusion and 8 – 12 hourly after that. Monitor fluid balance. Stop the infusion if the baby becomes acidotic. Care must be taken to recognise the starting point of the acid base balance when dealing with babies with a compensated respiratory acidosis. The base excess may not reach negative values but may still reflect a big swing towards acidosis.

6. Prescribing Guidance

a. Prescribing guidance when using phosphate polyfusor

- Phosphate polyfusor contains 50mmol of phosphate in 500mL (0.1mmol/mL).
- Does not need diluting.
- Should not be infused down the same lumen as PN, magnesium or calcium.
- Can be administered intravenously peripherally or centrally at 0.05mmol/kg/hour (=0.5mL/kg/hour) for 10 hours so that infant receives 0.5mmol/kg. This will also infuse 0.81mmol/kg sodium and 0.09mmol/kg potassium.

For example: An infant weighing 1.8kg
Rate = 0.5mL/kg/h = 1.8 x 0.5 = 0.9mL/h for 10 hours
Total volume = 9mL

b. Prescribing guidance when using sodium glycerophosphate 21.6%

- Sodium glycerophosphate contains 1mmol/mL phosphate.
- Central administration is preferred
- Further dilution is needed if given peripherally – please refer to NNU sodium glycerophosphate IV monograph for details
- Should not be infused down the same lumen as PN, magnesium or calcium.
- Infusions are run for 24 hours and will supplement 1.2mmol/kg/day (and give 2.4mmol/kg/day extra sodium)

For central line administration
Volume of diluent to be prescribed = 40mL 10% glucose
Add 10mL = 10mmol of sodium glycerophosphate 21.6% to give a 0.2mmol/mL solution
Infuse at a rate of 0.25mL/kg/h to give 1.2mmol/kg/day

For example: An infant weighing 1.8kg
Rate = 0.25mL/kg/h = 0.45mL/h

c. Prescribing guidance when using potassium acid phosphate 13.6% if baby is hypernatraemic (Na>145mmol/L)

- Potassium acid phosphate 13.6% contains 1mmol/mL of phosphate.
- Central administration is preferred
- Should not be infused down the same lumen as PN, magnesium or calcium.
- For central administration dilute 1 in 10 with glucose 5%, glucose 10% or sodium chloride 0.9%.
- Further dilution is needed if given peripherally – please refer to NNU potassium acid phosphate IV monograph for details
- Volume of diluent to be prescribed = (mmol required) x 9

Resulting strength = 0.1mmol/mL

For example: An infant weighing 1.8kg
Dose of phosphate = 1.8kg x 0.5mmol/kg = 0.9mmol (≡ 0.9mL of potassium acid phosphate 13.6%)
Volume of diluent to be prescribed = 0.9mL x 9 = 8.1mL
Total volume to run over 12 hours = 9mL ÷ 12 = 0.75mL/hour
Please see the NNU IV monograph for further details.

7. **Total Potassium delivery**

Combined potassium-containing infusions/PN should not exceed 0.5mmol/kg/hour of potassium
Check this by adding up how much potassium is in each infusion.

For example:
PN 2 mmol/kg/day (2 ÷ 24 = 0.08mmol/kg/hour)
Potassium acid phosphate infusion 0.5mmol/kg over 12 hours (0.5 ÷ 12 = 0.04mmol/kg/hour)
Total = 0.12mmol/kg/hour potassium

8. **Preparation and Compatibilities:**
   Please see the NNU IV monographs for phosphate polyfusor, sodium glycerophosphate 21.6% and potassium acid phosphate 13.6%.

9. **Running higher rates of phosphate infusions**
   - A serum phosphate level of <0.3mmol/L is a life threatening emergency. It is possible to run a phosphate infusion at a higher rate on the NNU in ITU. Rates of up to 0.5mmol/kg/hour can be administered CENTRALLY ONLY.
   - When infused at emergency rates of up to 0.5mmol/kg/hour, ECG monitoring should be continuous, and the infusion should be stopped after no longer than 4 hours.
   - 2 hours into the infusion send a lab sample for phosphate and a gas (sodium, potassium, calcium, acid-base) with a consultant decision whether to continue for the full 4 hours pending the result.
   - At 4 hours re-check bloods immediately. Consultant to review phosphate status as soon as the new level is available and assess ongoing need for phosphate replacement and appropriate route and rates.

   When potassium acid phosphate is used for emergency phosphate correction no other potassium containing infusion (ie PN/fluids) should be administered.

3. Education and Training

None

4. Monitoring Compliance

None

5. Supporting References

None

6. Key Words

Parenteral nutrition, Phosphate, Phosphate polyfusor, Potassium acid phosphate, Sodium glycerophosphate

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
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Details of Changes made during review:

Date	Issue Number	Reviewed By	Description Of Changes (If Any)
April 2024	**1**	**Neonatal guidelines group** **Neonatal Governance** **UHL Women's Quality & Safety Board**	New document

Appendix 1: Summary table to studies using cut-offs for definition of hypophosphataemia and severe hypophosphataemia (in mmol/L)

Study	Hypophosphataemia	Severe Phosphataemia
Chaudhary, 2020	< 1.29	<0.8
Cormack, 2021	<1.39	<0.9
Al-Wassia, 2019	<1.45	
Bustos Lozano, 2019	<1.29	<0.65
Sung, 2019	<1.61	<0.81
Pajak, 2018	<1.42	<1
Brener Dik, 2019	<1.29	
Igrashi, 2017		< 1.13
Mulla, 2017	<1.50	< 1
Boubred, 2015	<1.6	<0.9
Brener Dik, 2015	<1.29	<0.65
Senterre, 2015	<1.60	< 1
Bonsante, 2013		< 1
Moltu, 2013	<1.39	<0.9
Ross, 2013	<1.29	<0.81
Ichikawa, 2012		<0.81