Phosphate Supplementation in Neonates

Background

- Premature infants are at significant risk of reduced bone mineral content (BMC) and subsequent bone disease, variably termed metabolic bone disease of prematurity, osteopenia of prematurity or neonatal rickets.
- Clinical onset of osteopenia of prematurity is usually between 6-12 weeks postnatally.
- Reduced bone mineral content (BMC) can lead to fractures.
- Osteopenia is often implicated in myopia of prematurity, impaired respiratory function and in the longer term with poor growth in childhood.
- Several biochemical investigations e.g. calcium, alkaline phosphatase have been used to act as a marker, but these correlate poorly with bone mineralization. It can be difficult to screen for and diagnose osteopenia of prematurity.

Risk factors

- **Prematurity**
  Majority of bone mineralisation along with calcium and phosphate accretion occurs during the third trimester of pregnancy. Infants born before this have depleted stores.

- **Placenta**
  Chronic damage to placenta e.g. IUGR (Intra Uterine Growth Retardation) may alter phosphate transport.

- **Type of feed**
  40% of preterm babies fed with human breast milk showed evidence of rickets compared to 16% of those fed formula supplemented with calcium and phosphate.

- **Medications**
  Steroids, methylxanthines and diuretics increase risk of inadequate bone mineralisation.

- **Neonatal co morbidity** such as sepsis, cerebral pathology, muscular disorders may result in prolonged periods of immobility, well recognised risk factor for poor BMC.
Screening

- Babies <1.5kg
- Babies <28 weeks
- TPN >4 weeks
- Course of diuretics/steroids/methyl xanthines

When to treat

- Prevention of bone disease of prematurity should be the aim rather than treatment.
- Weekly bone profile bloods (calcium, phosphate and ALP)
- If phosphate <1.8 mmol/l and ALP >500iu/l (ALP rises in all newborns in the first 2-3 weeks of life and increases further if there is insufficient mineral supply)
- TRP (tubular reabsorption of phosphate) is an ideal screening test for phosphate and if TRP >95% then start phosphate supplements

How to treat

- Treatment is usually started on the basis of results of biochemical tests especially ALP.
- Most units use phosphate supplements as first line treatment, with Vitamin D if required.

Vitamin D

- Current recommended daily intake of Vitamin D for preterm infants is 400 IU. It is present in human milk fortifier and preterm formulae foods but can also be provided in multivitamin drops.

Phosphate

- Supplemental phosphate can be used prophylactically to prevent neonatal rickets due to phosphate deficiency in the very low birth weight infants
- The transplacental fetal uptake of calcium and phosphate is high especially in the second trimester of pregnancy and comparable intakes are hard to achieve after birth in the preterm baby. The mineral content of breast milk is particularly inadequate but ordinary milk formula is also deficient and most special preterm formulae contain additional calcium and phosphate for this reason.
- Deficient mineral intake after birth compromises subsequent bone growth. Poor bone mineralisation leads to osteopenia and pathological fractures can develop once bone growth starts to accelerate after 6-8 weeks, severe deficiency can also cause rickets with fraying and cupping of the metaphyses on X-ray. When breast milk is used
phosphate deficiency is normally a limiting factor. Low plasma phosphate levels are associated with increased hydroxylation of 25-hydroxycholecalciferol to 1.25 – dihydroxycolecalciferol, increased phosphate absorption from the gut, maximal renal retention of phosphate and hypercalciuria.

- Parenterally fed babies can develop the same problem
- Formula fed babies can sometimes develop a calcipenic type of rickets with marginal hypocalcaemia and no renal calcium spill, but secondary hyperparathyroidism with hyperphosphaturia.

**Supply**

An oral solution containing 1 mmol/ml can be obtained by dissolving a 500 mg Phosphate-Sandoz tablet in 16ml water. This solution also contains 0.2mmol/ml K and 1.3mmol/ml Na. Essentially this preparation use will depend upon serum Na and K.

**Monitoring**

- Treatment can be stopped or reduced when plasma phosphate levels exceed 1.8mmol/l, ALP < 500 and/or TRP in urine falls below 95%(in the absence of ATN)
- Ideally this supplement should be stopped once neonates reach 2kg and aim to stop at the point of discharge if possible.

**References**


Northern Neonatal Formulary (for dose and preparation)

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<tr>
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<td>Consultant Paediatrician</td>
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