METABOLIC BONE DISEASE

RECOGNITION AND ASSESSMENT

Definition

- Decreased mineralisation of bones due to deficient phosphate (PO_4), calcium (Ca) or vitamin D in preterm babies
- Also known as osteopenia of prematurity

Causes

- Inadequate postnatal intake or absorption to support intrauterine mineral accretion rate

Risk factors

- <32 weeks' gestation
- <1500 g birth weight
- Male gender
- Inadequate nutrition
  - suboptimal intake
  - enteral feeds with low mineral content/bioavailability [unfortified expressed breast milk (EBM), term formula]
- Phosphorus deficiency (primary nutritional reason)
- Vitamin D deficiency
- Prolonged parenteral nutrition
- Chronic use of drugs that increase mineral excretion (diuretics, dexamethasone, sodium bicarbonate)
- Lack of mechanical stimulation e.g. sedation/paralysis
- Bronchopulmonary dysplasia
- Cholestatic jaundice
- Short gut syndrome (malabsorption of vitamin D and Ca)

Symptoms and signs

- ≤6 weeks, most babies are asymptomatic and normal on examination
- Usually presents aged 6–12 weeks
- Poor weight gain or faltering growth
- Respiratory difficulties
  - failure to wean off ventilator due to excessive chest wall compliance
- Fractures with minor or no trauma; may manifest as pain on handling
- If hypocalcaemic – jitteriness
- Craniotabes (softening of skull bones)
- Low bone density on X-rays (rachitic changes, cortical thinning, periosteal elevation)

Later clinical consequences

- Marked dolicocephaly (long and narrow skull)
- Myopia of prematurity
- Reduced linear growth

INVESTIGATIONS

- Measure serum Ca, PO_4 and alkaline phosphatase (ALP) levels weekly from third week of life in high-risk babies
  - low serum PO_4 (<1.8 mmol/L) with elevated ALP (>900 IU/L) is 100% sensitive and 70% specific for diagnosing low bone mineral density. Low serum PO_4 concentrations (<1.8 mmol/L) have 96% specificity but only 50% sensitivity
  - serum Ca levels may remain normal until late in the disease
- Measure urinary Ca and PO_4. Urinary excretion of Ca >1.2 mmol/L and PO_4 >0.4 mmol/L signifies slight surplus of supply and correlates with highest bone mineral accretion rate
  - phosphaturia can occur due to aminoglycoside, indomethacin and dexamethasone therapy
  - calciuria can occur due to diuretics, dexamethasone and theophylline

- Tubular reabsorption percent (TRP) of PO_4 is also a guide to adequacy of PO_4 supplementation. TRP of >95% indicates inadequate supplementation
- TRP (%TRP) = [1 − (urine PO_4/urine creatinine) (plasma creatinine/plasma PO_4)] × 100
- Babies on unfortified human milk are relatively phosphate deficient and have:
- normal serum Ca, low serum PO_4 and high serum ALP
- very low or absent urinary PO_4 (urinary Ca excretion increases as serum PO_4 concentration decreases)
- normal serum vitamin D and parathormone levels
- Formula fed preterm babies have a low calcium absorption rate and therefore very low urinary Ca and PO_4 concentrations
- If biomarkers (ALP and PO_4) do not normalise despite appropriate Ca and PO_4 supplementation, measure serum 25(OH)D
- X-rays can demonstrate demineralised, thin bones, signs of rickets and thoracic cage and extremity fractures
- Dual-energy X-ray absorptiometry (DXA)/qualitative ultrasound (QUS)

PREVENTION

- Optimal nutritional care of preterm babies
- initiate early parenteral nutrition with optimised Ca and PO_4 content [≥12 mmol/L each of Ca and PO_4 (= 1.8 mmol/kg/day of Ca and PO_4 at 150 mL/kg/day)]
- early enteral feeds
- use of breast milk fortifier or preterm formula
- Early phosphate supplementation in high-risk babies
- Ensure appropriate handling and position using deep boundaries to promote active bone loading

TREATMENT

- Ensure adequate intake of Ca (2.5–4.0 mmol/kg/day) and PO_4 (1.9–2.9 mmol/kg/day) by using fortified breast milk or preterm formula
- Ensure daily intake of 600–800 units vitamin D per day
- If PO_4 deficient (<1.8 mmol/L): supplement PO_4 at 1–2 mmol/kg/day in divided doses
- If Ca deficient (<1.6 mmol/L): supplement Ca at 1–3 mmol/kg/day in divided doses
- do not give Ca and PO_4 at the same time as they may precipitate; give at alternate feeds
- Ca supplementation can cause intestinal obstruction and hypercalcinosis
- If no increase in PO_4 and ALP continues to rise:
- prescribe either vitamin D supplements ≤1000 units/day **or** initiate ergocalciferol/alphacalcidol therapy
  - in addition, encourage daily passive exercises and medication review to consider stopping diuretics and steroids when appropriate
- regular monitoring of urinary Ca/urinary creatinine ratio is necessary to detect hypercalciuria (urinary Ca/urinary creatinine) >0.6
- Consider other nutritional deficiencies e.g. zinc, in a baby with faltering growth with evidence of significant bone disease

MONITORING AND FOLLOW-UP

- Weekly monitoring of serum Ca, PO_4 and ALP along with urinary Ca and PO_4
- Continue treatment until biochemical indices are normal and radiographic evidence of healing, usually until term corrected gestation