Metabolic bone disease of prematurity

Preterm infants are at significant risk of metabolic bone disease because skeletal growth and bone mineralisation take place mostly during the latter stages of pregnancy. Metabolic bone disease of prematurity is essentially a substrate deficiency disease. Breast milk is poor in Calcium and Phosphate content and therefore treatment consists of judicious use of Calcium and Phosphorous supplements, together with sufficient vitamin D to allow efficient absorption of substrates. Vitamin D is required for the absorption of calcium and phosphorous from the intestine to enable bone mineralisation.

All babies, irrespective of type of feed, should receive 400 IU of Vitamin D (ABIDEC 0.6ml) daily until fully weaned. In line with the Department of Health recommendations, parents should be advised to continue supplementing with an appropriate multi-vitamin until the age of 5 years.

Phosphate supplementation:

Preventative treatment for High Risk Babies:

- <27 Weeks gestation
- <1000 grams
- IUGR < 2nd centile
- Very poor growth
- Preterm baby fed on EBM without BMF
- Babies on long term parenteral nutrition
- (post-surgery, post-NEC)
- Babies who are on prolonged use of demineralising drugs like steroids, loop diuretics, or methylxanthines)

Targeted treatment for abnormal biochemistry:

MBD is defined biochemically as:

- Alkaline phosphatase > 900IU/L (on 2 occasions)
- Serum phosphate < 1.8 mmol/L

Consistently rising ALP > 500 IU/L can be an early sign

Treatment:

All babies with the above risk factors and / or diagnosed to have MBD biochemically should be started on the following when tolerating 150ml/kg/day of enteral feeds:

**Sodium acid phosphate 1 mmol/kg/day**

(QDS for babies < 1500g; BD for babies >1500g)

according to the [vitamins and additives pathway](#) (click for link)

Monitoring:

Weekly or bi-weekly checks of Serum Phosphate, Calcium & ALP

- If normal results - stop treatment by 34/40 CGA; Recheck biochemistry after stopping supplements prior to discharge home
- If going home on Sodium acid phosphate – TTO for 4 weeks supply, book Phlebotomy clinic in 2 weeks
Calcium supplementation:

Aim for a Calcium level of 2.15-2.65mmol/L with a Phosphate level of 1.6-2.2 mmol/L, with Ca>P (ratio 1.7:1). If the Phosphate level is normal, but ALP remains > 900IU/L, Calcium supplements may be needed. Regular monitoring of Serum Phosphate, Calcium and Alkaline phosphatase levels should be performed, and dose adjusted based on the results.

Preparations and dose for calcium:
Cacit 500 mg effervescent tabs: 12.5mmol/25ml when made up to liquid form

Each tablet contains 1.25g calcium carbonate which when dissolved in water provides 500mg of calcium (equivalent to 12.5mmol of calcium) as calcium citrate.

Administration: Dissolve 1 tablet in 24mL water resulting in an orange flavoured solution containing 12.5mmol of Calcium in 25mL, from which the required dose can be withdrawn.

Recommended dose = 0.25mmol/kg qds

Further information:

If persistently rising ALP (>900 IU/L) despite prophylaxis -

1) Check urinary calcium and phosphate ratio:

Urinary Ca:P ratio helps to know if additional supplementation of Calcium and Phosphate is indicated.

• Ca:P ratio > 1 : Relative ↑ urinary Calcium loss, Body tries to retain Phosphate, possible Phosphate depletion, consider additional Phosphate supplements

• Ca:P ratio < 1 : Relative ↑ urinary Phosphate loss, Body tries to retain Calcium, possible calcium depletion, consider additional Calcium supplements

2) Check Serum vitamin D level:

• (25(OH)D), if < 25 nmol/L, the baby is vitamin D deficient, supplement with 3000 IU Cholecalciferol daily for 3 months. Monitor biochemistry regularly. After 3 months treatment recheck serum Vit D levels along with alkaline phosphatase, calcium and phosphate. Ensure supplementation with a daily dose of at least 400 IU vitamin D is undertaken after treatment.

• If serum levels are between 25-50 nmol/L, the baby’s vitamin D status is insufficient, provide dietary advice and ensure maintenance supplementation with a daily dose of at least 400 IU vitamin D is continued. Recheck Vit D levels in 3 months’ time.

Milk contents of vitamin D:

• 0.6 ml Abidec contains 400IU vitamin D
• 100ml NP1 – 120 IU vitamin D
• 100 ml NP2 – 68 IU vitamin D
• 1 L of unfortified EBM – less than 25 IU
• 100 ml EBM with 2% breast milk fortifier – 240 IU vitamin D
Preparations for Vitamin D:

Fultium D3 drops. 3 drops= 200 units (2740 units/ml) costs 9.52 per bottle. Information on SPC: http://www.medicines.org.uk/emc/medicine/30438;

Dose: For Vit D Deficiency: 45 drops = approximately 1 ml

3) Consider CXR to rule out fractures:

There are a number of radiological changes seen in MBD, including demineralisation or “osteopenia,” rachitic changes, and/or fractures. Consistently high ALP can indicate underlying fractures in severe MBD. Examine babies carefully to check for any bony deformities. As fractures of ribs in common in high risk preterm babies, please do a CXR and document formal report in notes.

References

- Carol L. Wagner and Frank R. Greer, Prevention of Rickets and Vitamin D Deficiency in Infants, Children and Adolescents, *Pediatrics* 2008; 122; 1142
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- Sujata Edate and Shalini Bahl, Diagnosis and Management of Vitamin D Deficiency, *ASPH Paediatric guidelines*, 2012
- Scientific Advisory committee on Nutrition, Department of Health, Vitamin D and Health, *report available online*: https://www.gov.uk/government/groups/scientific-advisory-committee-on-nutrition

Guideline
Written by Dr Szita, Neonatal Registrar & Dr V Ponnusamy, Neonatal Consultant, July 2016
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