Local Guideline

Metabolic Bone Disease in Neonates

Sites where Local Guideline and Procedure applies	Neonatal Intensive Care Unit (NICU) JHCH
This Local Guideline and Procedure applies to:	
1. Adults	No
2. Children up to 16 years	No
3. Neonates – less than 29 days	Yes
Target audience	All clinicians caring for infants in NICU
Description	Provides guidance to neonatal clinicians for the screening and treatment of Metabolic Bone Disease (MBD) in infants

Go to Guideline

Keywords	NICU, SCU, JHCH, neonate, newborn, metabolic bone disease, rickets, osteopenia, MBD
Document registration number	JHCH_NICU_16.02
Replaces existing document?	No

Related Legislation, Australian Standard, NSW Ministry of Health Policy Directive or Guideline, National Safety and Quality Health Service Standard (NSQHSS) and/or other, HNE Health Document, Professional Guideline, Code of Practice or Ethics:

- NSW Health Policy Directive PD 2017_013 Infection Control and prevention Policy
- HNELHD Policy Compliance Procedure PD2013_043:PCP 31 Medication Safety in HNE Health
- HNELHD Policy Compliance Procedure PD2013_043:PCP 47 Medications in Paediatrics

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Note: Over time links in this document may cease working. Where this occurs please source the document in the PPG Directory at: http://ppg.hne.health.nsw.gov.au/

PURPOSE AND RISKS

This local clinical procedure has been developed to provide instruction to the health clinician and to ensure the prevention of Rickets in preterm infants. Rickets in preterm infants is almost always attributable to decreased total absorbed calcium and phosphorus.

The risks are:

- *At risk infants could develop Rickets*
- *Inadequate nutritional requirements for at risk infants*
- *Inappropriate screening for Rickets*

The risks are minimised by:

- *Clinicians having knowledge of infants at risk of Metabolic Bone Disease (MBD) and appropriate screening occurs*
- *Clinicians seeking assistance if any area of Metabolic Bone Disease is outside their scope of practice*
- *Following the instructions set out in this clinical guideline*

Any unplanned event resulting in, or with the potential for injury, damage or other loss to infants/staff/family as a result of this procedure must be reported through the Incident Information management system and managed in accordance with the NSW Health Policy Directive PD2019_034: Incident Management Policy. This would include unintended injury that results in disability, death or prolonged hospital stay.

*It is mandatory for staff to follow relevant: "Five moments of hand hygiene", infection control, moving safely/safe manual handling, documentation practices and to use HAIDET for patient/carer communication: **H**and hygiene **A**cknowledge, **I**ntroduce, **D**uration, **E**xplanation, **T**hank you or closing comment.*

Risk Category*:* *Clinical Care & Patient Safety*

CLINICAL PROCEDURE SAFETY LEVEL

Every clinician involved in the procedure is responsible for ensuring the processes for clinical procedure safety are followed. The following level applies to this procedure (click on the link for more information):

Level 1 procedure

CONTENT

METABOLIC BONE DISEASE SUMMARY

- Metabolic Bone Disease of prematurity is the under-mineralisation of the preterm infant's skeleton arising from inadequate calcium and phosphate mineral, both prenatally and postnatally
- Severe Metabolic Bone Disease of prematurity can result in fragility fractures
- Providing at-risk infants with adequate calcium and phosphate through breast milk fortification or specific preterm formulae helps prevent metabolic bone disease of prematurity
- Screening (ALP, Ca, P) should start at 4 weeks postnatal age and be repeated every 14 days until ALP decreasing and full enteral feeds achieved
- Stop screening after peak ALP is reached and a decrease is seen and the infant has achieved full feeds of human milk with a mineral-containing fortifier or formula designed for preterm infants

GUIDELINE

While not requiring mandatory compliance, staff must have sound reasons for not implementing standards or practices set out within guidelines issued by HNE Health, or for measuring consistent variance in practice.

Introduction

Infants born premature are at risk of Metabolic Bone Disease (MBD). Identification of risk factors, careful screening and appropriate treatment is critical.

Background

Top

Preterm infants are at significant risk of poor mineralisation due to 80% of bone mineral content being actively acquired during the 3rd trimester. The average daily accretion during this time is 90-120mg/kg/day of calcium and 50-75mg/kg/day of phosphorus. Infants born prematurely (<32 weeks) therefore miss out on this period of mineral accretion and are at risk of inadequate dietary intake of minerals (see Figure 1).

Human milk has insufficient calcium and phosphorous for normal bone accretion. Preterm infants fed unfortified human breast milk have progressive decreases in serum phosphorous and increases in serum calcium and alkaline phosphatase (ALP) compared to infants fed formula. Advances in the nutritional care of preterm infants such as the initiation of early intravenous nutrition, early enteral feeds, breast milk fortification and preterm formula have been associated with a decrease in the incidence of MBD.

MBD in many infants is a self-resolving process, however it may be associated with clinical conditions such as fractures, marked Dolichocephaly and reduced linear growth. The long term consequences of MBD later in life are unclear.

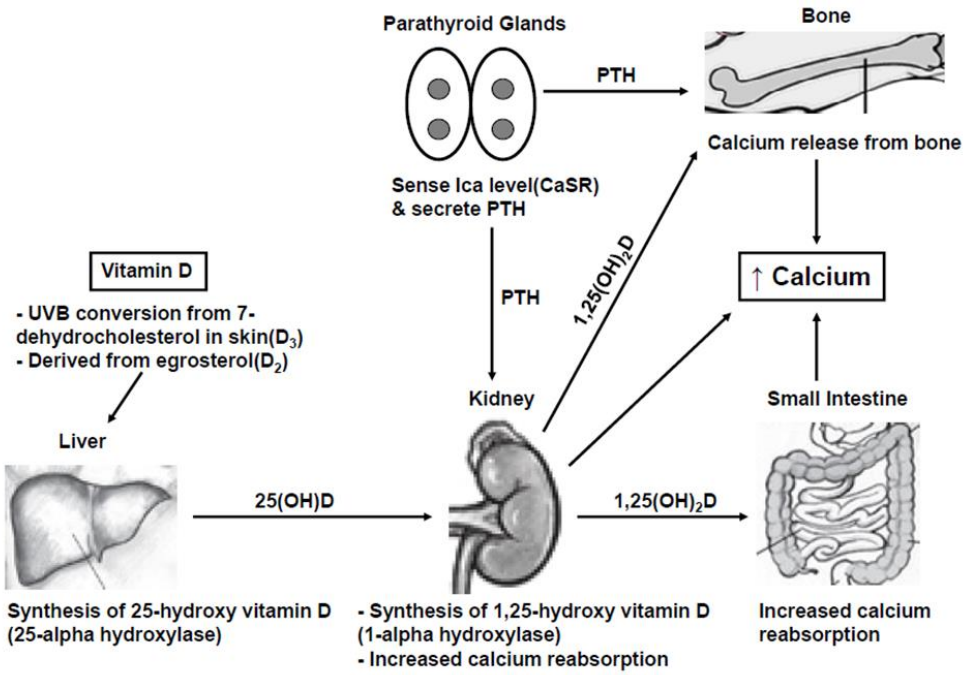

Figure 1: *Regulation of Calcium Homeostasis (Image from Backström et al 2000)*

Consequences of MBD

Top

- Fracture rate is estimated at 17-34% (usually in long bones)
- Rib fractures are present in 7% of infants <1000 grams with MBD
- Long term (adult) outcomes not fully established

Risk Factors for MBD

Top

- Infants <32 weeks
- Birth weight <1500 grams
- Long term parenteral nutrition (> 4 weeks)
- Postnatal steroid use (steroid course > 3 days)
- Loop diuretics use (> 7 days, not thiazides)
- History of necrotising enterocolitis

Screening for MBD

Top

Screening should occur when identified risk factors are present. Screening should start at 4 weeks postnatal age and be repeated every 14 days.

Tests should include:

- Serum ALP
- Serum Phosphate
- Serum Calcium

Stop screening after peak ALP is reached and a decrease is seen and the infant has achieved full feeds of human milk with a mineral-containing fortifier or formula designed for preterm infants

Treatment of MBD

Top

ALP is not useful on its own as a guide to starting treatment. Phosphate levels are important for linear growth and if levels are low in conjunction with a raised ALP, there is a risk of metabolic bone disease.

Commence Treatment with Phosphate if:

- ALP > 900 IU/L with a phosphate level <1.8 mmol/L. This is reported to be 100% sensitive and 71% specific for low bone mineral density in preterm infants
- If Phosphate <1.4 mmol/L, regardless of the ALP, start oral Phosphorus. Normal phosphate serum concentrations optimise mineralisation and linear growth regardless of the ALP level

Pentavite to commence on day 14 as per unit policy which will provide 400 IU Vitamin D (to optimise plasma 1,25-dihydroxyvitamin D levels) which will optimise mineralisation substrate availability. This is the widely recommended dose (given limited data) for Very Low Birth Weight (VLBW) infants when > 1500gms and when the infant is tolerating full enteral nutrition. Vitamin D levels are not routinely measured.

Serum calcium values tend to remain normal (compensation) until late in the course. Phosphate supplementation can sometime unmask a calcium deficiency and infants may need calcium supplementation. If the serum calcium is low, then measurement of vitamin D (25-OH) and Parathyroid Hormone (PTH) in mother and infant should be considered. A high serum calcium indicates over-treatment.

If supplementing, remember calcium and phosphate must not be given at the same time due to possible precipitation and high urinary calcium increasing the risk of nephrocalcinosis, therefore, monitoring with urinary calcium may be required. For dosage review Neomed calcium guideline.

If ALP > 500 IU/L with normal phosphate, continue to monitor levels fortnightly. Typically, the ALP will peak at 400 to 800 IU/L and then decrease in VLBW infants who do not develop rickets. Clinical experience indicates that if the infant has ALP values in this range, has achieved full feeds of human milk with a mineral-containing fortifier or formula designed for preterm infants there is minimal risk of developing rickets and screening can be stopped.
Continue supplements until the bone profile has normalised (ALP <500 IU/L and phosphate > 1.5mmol/L) and ideally stop phosphate supplements prior to discharge.

Ongoing Screening

Top

- Repeat Screening should occur every 14 days as an inpatient
- Monthly after discharge from the neonatal unit
- 4 weeks after treatment has stopped

If Ongoing Bone Profile Abnormalities:

- Consider calculating urinary Tubular Reabsorption of Phosphate (TRP). If TRP >95%, this suggests that phosphate supplementation is still insufficient and increasing or adding phosphate supplementation is appropriate

TRP % = (1 - (Urine phosphate/Urinary Creatinine) x (Plasma Creatinine/Plasma phosphate)) x 100

All units must be in mmol/L, therefore divide serum Creatinine (µmol/L) by 1000

- Measure plasma Vitamin D (25-OH) and PTH and consult the endocrine team. If Vitamin D is low (< 50nmol/L) consider increasing Vitamin D supplementation by doubling Pentavite (800 IU) until reviewed by the endocrine team. Advice on Calcium supplementation may be needed in the setting of elevated PTH

Management of Infants Diagnosed with Radiological Rickets

Top

Infant's need special management when there is radiological evidence of Rickets. This may include:

- Careful handling
- 5 to 6 weekly radiology rechecks
- Maximizing nutritional intake with the continuation of fortification or supplementation
- LFT/GGT and Vitamin D Levels (in consultation with Endocrine team)
- Monitoring 4 weeks post resolution of radiological findings

IMPLEMENTATION PLAN

The clinical guideline will be:

- Circulated to Head of Department and Managers in NICU
- Circulated to the clinicians via the Children Young People and Families Network and the Women's Health and Maternity Network (where applicable)
- Made available on the intranet (PPG) and HNEKids website
- Presented at facility/unit meetings and tabled for staff to action

MONITORING AND AUDITING PLAN

- The person or leadership team approving the clinical guideline is responsible for ensuring timely and effective review of the guideline.
- Evaluation will require a review of the most current evidence as well as consideration of the experience of Neonatal staff at JHCH in the implementation of the clinical guideline.
- Data derived from monitoring and evaluation should inform the review of the clinical guideline either as required or scheduled.
- Implementation, education support and monitoring compliance be completed by local Clinical Educators and Unit Managers.
- Amendments to the guideline will be ratified by the Clinical Director and Manager of Newborn Services prior to final sign off by the JHCH.

CONSULTATION WITH KEY STAKEHOLDERS

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APPENDICES

1. Glossary & Abbreviations

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FEEDBACK

Any feedback on this document should be sent to the Contact Officer listed on the front page.

APPENDIX 1

GLOSSARY & ABBREVIATIONS

Acronym or Term	Definition
ALP	Alkaline Phosphatase
Ca	Calcium
CYPFS	Children, Young People and Families Service
GGT	gamma glutamyl transferase
HNELHD	Hunter New England Local Health District
IU	International Units
JHCH	John Hunter Children's Hospital
kg	Kilogram
L	Litre
LFT	Liver Function Test
MBD	Metabolic Bone Disease
mg	Milligram
mmol	Millimole
NICU	Neonatal Intensive Care Unit
nmol	Nanomole
P	Phosphate
PTH	Parathyroid Hormone
SCU	Special Care Unit
TRP	Tubular Reabsorption of Phosphate
VLBW	Very Low Birth Weight