4. Bone Complications

Principles

- To prevent the bone disorders associated with thalassemia.
- To provide effective monitoring and treatment for patients with evidence of bone disease.

Recommendation

- All Thalassemia centres should have a pediatric and an adult endocrinologist with expertise in management of thalassemia bone complication.
- All children with thalassemia should have routine monitoring of height, weight, growth velocity and assessment of setting to standing height at each visit.
- All children needs close monitoring for bony complications resulting from under transfusion and iron chelation toxicity.
- Transfusion therapy needs to be started early in childhood to prevent bone marrow expansion resulting in irreversible bony deformities.
- All bony changes needs to be managed with adequate transfusion or monitoring of iron chelation dose depending on the underlying etiology.
- All adult thalassemia patient s should be encouraged to quit smoking to improve bony health.
- Vitamin D level needs to be optimized in all patients with Thalassemia.
- Routine monitoring of zinc and other trace elements is advisable with possible replacement if deficient.
- All patient should be encouraged to participate in regular weight-bearing low impact sport activity.
- All patients should have routine monitoring of bony health by a DEXA scan.
- If low bone density is detected, all patients needs to be referred to an endocrinologist for managment.

Background

Bone disorders are common and multifactorial in patients with thalassemia and may be related to inadequate transfusion, iron overload, adverse effects of chelation with Deferoxamine or Deferiprone, nephrolithiasis, and other endocrine disorders.[100,101] These factors contribute to the development of low bone mineral density (BMD), which is seen in >50% of adult patients, and is more common at the spine than hip. The pathophysiology of low bone density differs between thalassemia major (high bone turnover) and intermedia (low bone turnover). Bone pain and fracture has been reported in up to 1/3rd of patients[356]. Low BMD has also been associated with cardiac iron overload. Bone disorders may additionally present as skeletal deformities, growth retardation, arthropathies, disc degeneration, fractures, or back pain.

Interventions

- Every specialist centre should have access to an endocrinologist with knowledge of managing thalassemia associated bone disease.
- All children should have routine monitoring of height, weight, and growth velocity at each visit and these should be plotted on ethnic- appropriate standardised growth charts.
- All patients should be closely monitored for bone changes and deformities associated with under-transfusion and chelator-related toxicity.[382]
- Transfusion therapy should be started early in children to prevent the bone changes and deformities associated with bone marrow expansion.[378, 379,380,381]
- Bone expansion should be managed by adjustment of transfusion regimen to further suppress endogenous erythropoiesis.[379, 381-383]
- Adequate chelation therapy should be maintained in patients on a chronic transfusion program since iron overload is

associated with abnormalities of the synovium and articular cartilage.[389]

- Use of Deferoxamine under the age of 6 years and at high doses (> 50 mg/kg/day) should be avoided to limit its effect on bones (dysplastic changes in the spine and long bones, and growth retardation) [382,383]
- All patients prescribed Deferiprone should be assessed clinically for arthralgias and arthropathy
- Deferiprone arthropathy may be managed with dose reduction or cessation and NSAIDs
- Bone mineral density of the hip and spine should be measured using dual energy x-ray absorptiometry (DEXA) and commence at 12 years of age.[357, 384-388]
- Neither the WHO Fracture Risk Assessment tool or Canadian Association of Radiologists and Osteoporosis Canada tool are validated in young Thalassemia patients.[358]
- Quantitative ultrasound or CT should not be used as an alternative to DEXA scan in assessment of thalassemia related bone densit.[359, 360]
- Frequency of repeat DEXA scan should be determined on a per patient basis in consultation with an endocrinologist.
- Patients reporting new or worsening back pain should be screened with x-ray for vertebral fractures.[361]
- Low BMD for age should be managed with 1200mg elemental calcium and 1000IU – 2000IU vitamin D, preferably from dietary sources, regular exercise to improve core stability and resistance training as well as weight bearing exercise, limitation of caffeine intake, and cessation of smoking.[362]
- Serum 25-hydroxyvitamin D should be measured after three to four months of adequate supplementation and should not be repeated if an optimal level (≥ 75 nmol/L) is achieved.
- Patients with low bone density despite optimisation of lifestyle and dietary factors should be referred to a specialist for consideration of drug therapy.
- Care should be taken to treat men and women equally when considering bone health.[363]
- Whole body vibration therapy may have a beneficial impact on bone density content, though adherence to therapy reduced over time.[364]
- Neridronate[365, 366] Pamidronate[367-370], Zolendronic Acid[371-374] and Alendronate[369,375] has been shown to improve BMD in thalassemia major patients and benefit may persist after stopping the drug.[388,390,391]
- Patients with thalassemia intermedia may respond less well to bisphosphonates.[376]
- Bisphosphonates should be avoided in women of child bearing potential due to possible effects on future fetal bone health.
- Hypogonadism contributes to short stature and low BMD.[384]
- Patients with hypogonadism should be referred to an endocrinologist and consideration given for hormone replacement therapy (HRT). However, HRT is not as effective in Thalassemia as in premature ovarian failure at normalising spinal DEXA score.
- All other endocrine abnormalities should also be sought for and corrected since they are contributory factors.