Metabolic Bone Disease

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Metabolic bone disease (MBD) encompasses conditions that result from changes in the homeostasis of skeletal bone caused by defects in bone density or bone mineralisation. Osteoporosis is a defect of bone mineral density (BMD). It occurs in 57-88% of adults and 16-25% of children with chronic intestinal failure (CIF). Osteomalacia is a defect in bone mineralisation. It is much less reported but could occur in up to 75% of patients on home parenteral nutrition (HPN).

Key points

1. The common reasons for bone mineral loss are general or related to underlying disease rather than CIF/HPN.
2. A fracture risk assessment should be made, typically using the FRAX® tool, and may require a dual-energy X-ray absorptiometry (DXA) to adjust risk propensity.
3. Treatment of osteopenia/osteoporosis starts with recommendations to stop smoking, reduce alcohol, increase weight bearing exercise and have some sunlight exposure. Then ensuring adequate (adjusted according to concentrations) vitamin D (800 units or greater), calcium (700-1200mg daily) and magnesium through oral/enteral or parenteral intake. Biphosphonates may be needed if osteoporotic.
4. Causative medication, when possible, is reduced (e.g. corticosteroids, anticoagulants and proton pump inhibitors).
5. Underlying inflammatory conditions must be controlled as a priority.
6. Adequate vitamin D concentrations are ensured, and the parathyroid hormone (PTH) plasma concentration is checked.
7. All patients with CIF should have a bone density assessment using DXA initially and repeated every 3-5 years.
8. The amount of available functional intestine must be considered when choosing treatment options (e.g. oral vs. parenteral bisphosphonates).
9. Referral to a metabolic bone specialist should be recommended if the T score is decreasing despite treatment.

Explanations

1. Metabolic bone diseases (MBD) are conditions that result in changes in the homeostasis of skeletal bone. They result in firstly, pathological bone density defects, such as osteoporosis, osteopetrosis or Paget's. Secondly, they can be caused by defects of bone mineralisation, such as Ricket's, osteomalacia and renal osteodystrophy. MBD results from two main processes: Dynamic changes in serum calcium, phosphate and their controlling hormones, vitamin D or parathyroid hormone (PTH), leads to alteration in hydroxyapatite concentrations of calcium or phosphate. Alternatively, dynamic alterations occur in bone turnover or growth. Osteomalacia presents with bone or muscle pain and radiological features include Looser zones in adults and wide growth plates and frayed metaphyses is consistent with rickets in children.

   The general causes/underlying disease responsible include: older age/female, reduced physical activity, low sunlight exposure, smoking/alcohol, chronic inflammation and medication (e.g. corticosteroids, long-term anticoagulation (e.g. heparin) or proton pump inhibitors).
2. Calculation of 10-year major osteoporotic fracture risk and hip fracture risk is calculated using the FRAX® tool. This should be undertaken in post-menopausal women and men aged 50 or more who have risk factors for fracture, recent or current long-term oral glucocorticoid therapy, or a bone mineral density T-score ≤ -2.5. If the fracture risk is intermediate, a BMD measurement should be performed using a DXA and then re-estimate FRAX score. A falls assessment should also be undertaken. In pre-menopausal women and men <50yrs, the following is a non-exhaustive list of parameters that currently fall outside of the FRAX assessment and may therefore mandate a DXA assessment to determine treatment thresholds: ≥4cm height loss, kyphosis, type 2 diabetes mellitus, inflammatory conditions, hyperparathyroidism, nutritional deficiencies, and proton pump inhibitor usage.
3. Treatment is tailored to the individual and includes keeping plasma calcium at the upper limit of normal, correcting hypomagnesaemia and vitamin D deficiency. When osteoporotic or above the treatment line on the FRAX score, biphosphonates are readily used.

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4. Long term corticosteroid, proton pump inhibitor or anticoagulants (especially heparin) cause bone mineral loss. Hypophosphataemic osteomalacia can occur following administration of ferric-carboxymaltose. Whilst there may be no evidence of long-term sequelae, repeated occurrence of hypophosphataemia may result in reduction in BMD.
5. Patients may have an underlying inflammatory condition that both itself increases bone turnover and increases risk of exposure to corticosteroid medication. Chronic inflammatory conditions must be treated to reduce the inflammatory burden where possible.
6. Adequate vitamin D concentrations are ensured and the parathyroid hormone (PTH) plasma concentration is checked. As there is a loss of the diurnal parathormone rhythm with nocturnal parenteral nutrition (PN), daytime PN can be considered.
7. Osteoporosis is diagnosed by DXA scans or through assessment of plain films with general loss of bone mass or fractures in common sites. Osteopaenia is defined as a T-score -0.1 - -2.5 and osteoporosis as a T-score <-2.5. Although ESPEN recommends an annual DXA, in the UK an annual FRAX assessment is recommended, and if an intermediate/high risk of fracture if found, then a DXA should be performed. A routine DXA should be undertaken every 3-5 years.
8. Patients with CIF may have a short or dysfunctional bowel resulting in reduced absorption of calcium, phosphate and vitamin D. The oral route may not be tolerated/appropriate thus a parenteral bisphosphonates (e.g. zoledronate) or denosumab may be preferred.
9. According to the National Osteoporosis Guideline Group (NOGG), DXA frequency in UK patients should follow 3-5 years of treatment, unless a drug holiday occurs due to improved BMD, in which case it should be 1.5-3 years later.

Suggested reading:

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