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Paediatric Patients with Bone Quality Issues & How to Correct the Problem

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Overview of Bone Quality Issues

Bone strength is determined by the bone quantity, quality and their turnover. In children, the causes leading to their disturbance can be numerous. They can be due to the disorders of bone mineral homeostasis, imbalance of bone remodeling, disorders of collagen and drug related issues affecting calcium absorption.

A multidisciplinary team involving paediatricians, endocrinologists, geneticists, and orthopaedic surgeons can help to provide a comprehensive treatment for these children. It is important to assess the patients thoroughly through history taking, physical examination, laboratory tests and radiological assessment to determine the underlying cause.

Some of the causes are amenable to treatment e.g. rickets can be better controlled by proper dietary and supplements together with regular monitoring. However, some of the causes e.g. osteogenesis imperfecta cannot be fully corrected. The bone quality can instead be improved by proper education for fracture prevention, pharmacological treatment, and surgical intervention.

Osteogenesis imperfecta

Osteogenesis imperfecta (OI) is an inheritable bone fragility disease classically known to be due to type I collagen abnormality. The type I collagen abnormality results in reduced bone strength. Depending on the severity of involvement, the severely affected patients may present with repeated fractures shortly after birth, short stature, and multiple deformities in the limbs and spine. The disease is classified by Sillence into 4 types according to their clinical presentation1. With better understanding of the disease in particular the genetic mutation2, the classification of OI has expanded to 16 types over the past decade3-5.

At the moment, there is no medical treatment that can correct the underlying abnormality in OI. However, by either (1) inhibiting the action of osteoclast to reduce the rate of bone resorption or (2) increase bone production by the osteoblasts can help to improve bone formation. There is a good evidence supporting the use of bisphosphonate to improve the bone mineral density in particular the severe form. However, whether bisphosphonate can reduce fracture rate remains inconsistent6.

Bisphosphonate is the most commonly used medication in OI to improve the bone mineral density7,8. Treatment can be started as soon as the baby is given birth and continue until skeletal maturity. Regular monitoring of the clinical response and the bone mineral density are important. The commonly used bisphosphonates include pamidronate and zoledronic acid9-12. Their effect in improving the bone mineral density is fairly similar.

Scoliosis in OI

Scoliosis is common in OI and the severity increases with age. The more severe the scoliosis, the more likely it would affect the lung function13. It is estimated that about 25% of the OI patients aged between 1-5 have scoliosis. The number rises to as high as 80% in the OI patients > 12 years of age14. Not all OI patients' scoliosis progress that same. It is recognized that the more severely affected patients will have higher rate of deterioration (Type I: 1 degree per year; Type III: 6 degrees per year and Type IV: 4 degrees per year)15. The use of bisphosphonate can greatly improve the deterioration rate in Type III patients15.

Future Development

With better understanding of the pathogenesis of osteogenesis imperfecta, new treatment approaches are currently developing. These include antibodies against sclerostin and anti-TGF-b16,17. Both have good pre-clinical examination results and are currently on clinical trial.

Conclusion

Bone strength is governed by the bone quantity, quality and turn over. Any disturbance will result in reduced bone strength leading to bone fragility. Finding out the underlying cause of the bone fragility is the most important part in managing these children. Through proper diet, calcium, vitamin D supplement, and antiresportive agents e.g. bisphosphonate, the bone quality can be corrected.

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Optimization of Bone Health in Adult Patients in Preparation for Surgery

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Bone strength is critical to successful spine surgery. (10-12). Strength is a combination of bone quantity and quality. Quantity is measured by DXA and CT. Bone quality is related to collagen and mineral status, micro-architecture, and bone turnover dynamics. Laboratory analysis best defines normal and abnormal quality. Several laboratory markers can identify bone at risk.

Bone density is an area measurement of bone mass at the spine and hip. Scoliosis inserts artifacts to the analysis and spine density measurements should not be used if the curve is over 30 degrees and/or there is osteoarthritis of the facet joints. Although there is only moderate relationship of the hip and spine densities, hip provides a good approximation of bone mass. Alternatively one can use a quantitative CT of the vertebra. It measures specifically the trabecular bone and will not be influenced by osteoarthritis of curve. Osteopenic bone (T -1.0 to -2.4) and especially osteoporotic (T worse than -2.5) bone lacks good purchase of spinal instrumentation and has a high risk for adjacent level compression fracture.

Bone quality is compromised in the face of low Vitamin D (25-OHvitamin D < 30ng/ml), low calcium (<9.2) and low bone specific alkaline phosphatase (<6.) (10-12). Vitamin D has many functions including mineralization of bone and muscle function. (4). Vitamin D is best measured by determining the 25(OH)vitamin D levels. Values below 30ng/ml compromise bone formation and mineralization. Values below 45ng/ml interfere with muscle related strength and speed as well as balance. 2000 to 4000 international units of vitamin D3 will correct vitamin D levels in 2 to 4 weeks and should be part of preoperative treatment.

Calcium is needed for cell function and mineral formation (4,10 – 12). Calcium and PTH have a close relationship. When calcium is low the PTH is high and resorbs calcium from the skeleton to remedy the deficiency. When calcium is high PTH is turned off. Thus by measuring the PTH one can discern the appropriate calcium need. If the PTH is over 50 there is a calcium deficiency, if below 20 there is a surplus of calcium and in the normal state the PTH should be around 30. The usual calcium requirement is 500 to 750 mg of calcium citrate per day in divided doses. Calcium C is better absorbed and prevents kidney stones.

Alkaline phosphatase is needed to mineralize the bone. There is an entity of hypophosphatasia where the bone specific alkaline phosphatase is less than 6. It interferes with growth, leads to premature loss of teeth and results in stress fractures. If vitamin B6 is elevated then there is the possibility that the patient has the genetic defect of inadequate levels of BSAP.

Collagen is critical to bone strength. It provides tensile strength. Most fractures result from bone failing in tension. It can be suspected in individuals who present with hypermobility in their fingers, elbows, flat feet and ease of touching their feet. Vitamin