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Review Article

Review of Fractures and Low Bone Mass in Children with Cerebral Palsy
腦癱兒童的骨折及低骨質量之回顧

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ABSTRACT

Children with cerebral palsy have an increased risk of fracture and low bone mass. A systematic review was carried out to identify the associated or risk factors. The role of bone mineral density measurement (particularly whole-body or distal femur) by dual-energy X-ray absorptiometry and quantitative computed tomography is examined. Current strategies to prevent or treat the bone fragility in children with cerebral palsy are summarised.

中 文 摘 要

腦癱兒童有較高骨折和低骨質量的風險，現就其相關或風險因素，進行了系統性探討， 檢測雙能X光骨密度儀及量化電腦掃描應用於量度骨質密度（全身或股骨下端）的角色，並總結了防治腦癱兒童的骨質脆弱性的現行策略。

Introduction

Cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances occurring in the developing fetal or infant brain. Its population-based prevalence has been reported as 1.2–3.6 per 1000 live births.[1] Among the physiological subtypes, spasticity is the most common (77–93%), followed by dyskinesias (2–15%) and ataxia (2–8%), isolated hypotonia (0.7–2.6%) being the least common physiological subtype.[1] Regarding the body part affected, total-body/quadriplegic-type CP and diplegic-type CP are more common than hemiplegic-type.

Cerebral palsy is one of the most common physical disabilities of childhood. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition and communication, and by behaviour problems. In population-based surveys, the frequency of impairments is substantial, 70% of individuals showing mental retardation (IQ < 70) and 31–40% having ongoing epilepsy, 21–63% visual impairment and 11–13% hearing impairment.[1] Musculoskeletal problems include spasticity or other movement disorders, muscle and joint contractures, joint deformities, hip instability, scoliosis, gait disturbance and fractures.

Fractures in children with cerebral palsy

Fractures are not uncommon in children with CP. In one series, 39% of children with quadriplegic CP gave a history of fracture.[2] The prevalence rate was 6% in 1637 patients with CP,[3] and 12% in another 763 children with CP.[4] A higher prevalence rate of 23% was reported in 88 children with quadriplegic CP.[5] The fracture incidence was estimated to be 4.8 per 100 person–years among one study of 261 children with moderate-to-severe CP.[6] Thus, the fracture incidence in children with CP is much higher than that in the general paediatric population.

The causes of fracture were not identified for 55% of individuals in one series.[3] These fractures occur with minimal trauma or are 'spontaneous' with no apparent history of injury. The diagnosis is thus delayed or even missed in those patients who cannot communicate. Even when there is clinical suspicion of a fracture, some low-energy metaphyseal fractures do not show up on plain radiography and can only be diagnosed with whole-body bone scanning.[7] Thus, bone fragility seems to be an underlying problem related to these 'spontaneous' fractures.

One retrospective review identified 35 non-ambulatory children with quadriplegic spastic CP, all of Gross Motor Functional Classification System (GMFCS) level V, who had 57 'spontaneous fractures' during the period 1993–2005 in an institution providing inpatient services to 200–250 severely mental handicapped

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children in Hong Kong.[8] Fractures caused by convulsions were excluded. As in most series, the most common site of fractures was the lower limb, almost 80% of fractures occurring around the knee and being metaphyseal fractures of the lower limb. One-third of children had recurrent fractures, and 17% of fractures occurred within 1 year after lower limb surgery.

Fractures in children with CP are associated with a higher complication rate than fractures in healthy children. In a study of 156 children with CP who sustained fractures,[3] there were 7 repeat fractures, 5 malunions, 4 cases of delayed consolidation or non-union, 4 with infection and 3 cases of pneumonia. The frequency of complications was 17% of all patients and 10.5% of all those with fractures.

Risk factors associated with fractures in children with cerebral palsy

The severity of neurological involvement is an important factor. Children with CP who are non-ambulatory[4] and classified as GMFC level V[9] have the highest risk. Contractures and stiffness of the major joints create long lever arms also predisposed to fracture. Previous fracture is associated with increased fracture risk,[6] the fracture rate increasing more than threefold after a previous fracture.[10]

Fractures after lower limb surgery, particularly after hip osteotomy and surgery related to a hip spica cast, were observed in several studies. In a retrospective review of fractures in severely handicapped institutionalized children and young adults, 6 of 21 (29%) non-ambulatory patients had a femur fracture within 3 months of removal of a hip spica cast and operation for subluxed or dislocated hip, compared with 4 of 37 (11%) non-ambulatory patients who did not have hip surgery.[11]

In another retrospective review of 79 children with CP who underwent osteotomy for subluxation of the hip, 16 (20%) children sustained fractures, all of which were managed with cast or splint immobilization.[12] Indeed, the calculated fracture rate was 4.5 times higher after a hip spica cast than in those who not have a spica cast.[10]

Postoperative bone loss is found to be enormous even in normal children who are subject to a brief period of immobilization. In a study of preoperative and postoperative dual-energy X-ray absorptiometry (DXA) for 15 healthy children undergoing lower extremity surgery with a minimum of 4 weeks of either non-weight-bearing or cast immobilization, the average loss of BMD was 16.5% in cancellous regions, 11.5% in transitional bone and 4.8% in the cortical bone of the operated leg within 6 weeks, and the *z*-score fell by 1.0 for cancellous bone, 0.75 for transitional bone and 0.45 for cortical bone.[13] Thus, prolonged immobilization with or without surgery can predispose to fracture in children with CP.

Oro-motor difficulty is a common co-morbidity in CP. Poor lip closure, inadequate jaw control and a delay in swallowing and sucking are common oro-motor difficulties. Ryles tube feeding or gastrostomy is commonly used as the last resort in providing enteral feeding when faced with severe feeding difficulty. Indeed, Ryles tube feeding[4] and gastrostomy use[6] are associated with an increased fracture risk. However, even mild feeding difficulty can result in malnutrition. In a survey of 235 children with moderate-to-severe CP, 47% had a body weight below the fifth percentile, and one-third had an upper arm fat and muscle area below the 10th percentile.[14] Weight-for-age *z*-score was one of the important independent predictors of fracture risk in a multivariate analysis of children with CP.[15]

Low vitamin D status is common in children with CP. Using a 25-hydroxy vitamin D level of less than 20 ng/mL as a biochemical indicator of low vitamin D status, it has been found that the prevalence of low vitamin D status was 19% among children with CP living in a community, compared with less than 2% in the healthy paediatric population.[10] The prevalence is expected to be much higher in children with moderate or severe CP living in institutions. In one study, all 20 children and young adults with CP and pathological long bone fractures showed radiological and biochemical evidence of rickets or osteomalacia.[5]

Besides feeding difficulties and inadequate exposure to sunlight, the use of antiepileptic drugs (AED) also contributes to low vitamin D status. Local studies in children with CP showed that 30% of children living in a community had epilepsy[16] and 63% of children living in institutions were taking AEDs.[15] In severely mentally retarded children who had been receiving AEDs for more than 10 years, up to 75% had osteomalacia.[17] Furthermore, a significant relationship between the number of pathological long bone fractures and the use of AEDs was demonstrated in institutionalized residents with CP.[5]

In summary, severe neurological impairment (non-ambulatory status, GMFCS level V), severe joint contracture, a history of fracture, prolonged immobilization (particularly the use of a hip spica), malnutrition (Ryles tube feeding or gastrostomy, low body weight *z*-score) and use of AEDs are known to be associated with an increased fracture risk in children with CP.

Bone mineral density in children with cerebral palsy

As children have not yet reached peak bone mass, it is not appropriate to use the *t*-score. Instead, the *z*-score adjusted for age and sex should be used. When the *z*-score is less than or equal to −2.0, there is 'low bone mass for chronological age'. The diagnosis of osteoporosis in children, as defined by the International Society for Clinical Densitometry, includes a bone mineral density (BMD) *z*-score of less than −2.0 adjusted for age, gender and body size, plus a clinically significant fracture history: either (1) two upper extremity fractures, or (2) a vertebral compression fracture, or (3) a single lower limb fracture.[18] Indeed, CP is the most prevalent childhood condition associated with osteoporosis.

In children with CP, the rate of bone mineral acquisition is diminished relative to normal; thus, the BMD and bone mineral content (BMC) are lower than age-matched normal values. With growth, BMD falls further below normal with increasing age.[10] In spite of an average of 2–5% per year increase in BMD in the distal femur, the BMD *z*-score decreases further with increasing age.[19] In a heterogeneous group of 139 children with spastic CP, BMD was on average nearly 1 standard deviation below the age-matched normal means for both the hip and the lumbar spine.[20] In another study of children with quadriplegic CP of heterogeneous GMFC level, 58% of children had a *z*-score of less than −2.0.[2]

Poor mobility status predicts a low BMD in children with CP: 97% of non-ambulatory children older than 9 years with moderate-to-severe CP had a distal femur *z*-score of less than −2.0.[10] Significantly lower *z*-scores on lumbar spine BMD were found in patients with a history of fracture.[2]

Nearly all AEDs have an adverse effect on bone mass and BMD in children. The most well known are phenytoin and phenobarbital, which are inducers of cytochrome P450 enzymes leading to the catabolism of vitamins. Treatment with phenytoin and phenobarbital can be associated with rickets. More recently established AEDs such as valproic acid, carbamazepine and oxacarbazepine have been shown to be associated with decreased BMD.[21]

Using stepwise regression analysis, severity of neurological impairment, increased feeding difficulty, use of AEDs and lower triceps skinfold measurement were identified as risk factors (in decreasing order of importance) for low BMD in the distal femur of

children with quadriplegic CP.[9] Moreover, the weight-for-age *z*-score was the best predictor of BMD *z*-score.[22]

In summary, children with CP have a low bone mass. Severity of neurological impairment (mobility status), malnutrition (body weight *z*-score, feeding difficulty, low triceps skinfold measurement), use of AEDs and previous history of fracture are associated with a low BMD in children with CP. Thus, similar factors are associated with fracture risk and low BMD in children with CP.

Correlation between bone mineral density and fracture risk in children with cerebral palsy

At least two prospective cohort studies have demonstrated an association between BMD or BMC and fracture in healthy children. The first prospective study was a 2-year follow-up of 6213 children initially aged 10 years.[23] An inverse association was observed between fracture risk and BMD, as well an 89% increased fracture risk per standard deviation decrease in size-adjusted BMC. In another prospective study of 183 children at 8 years of age, a lower BMD of the spine and total body (but not hip) at age 8 predicted a higher fracture risk for the upper limb at puberty.[24] There are a few cross-sectional studies that demonstrate the association between BMD and fractures in children with CP. In a study of lumbar spine BMD in 48 children with spastic quadriplegic CP, a significantly lower *z*-score of −2.81 was seen in children with a history of previous fracture, compared with a *z*-score of −2.11 in those without a history of fracture.[20]

The other two studies measured BMD of the distal femur. In a study of 85 non-ambulatory children, mostly with CP, a correlation was demonstrated between history of fracture and BMD of the distal femur when this was combined with body mass index (BMI).[25] The fracture risk rate was 33% or more with a BMD of 0.38 g/cm^2 or lower in the group with a BMI of less than 17 kg/m^2, and a BMD of 0.74 g/cm^2 or lower in the group with a BMI of 17 kg/m^2 or greater in non-ambulatory children.

In another study of 619 children with moderate-to-severe CP or muscular dystrophy, a strong correlation was found between fracture history and BMD *z*-score for the distal femur.[26] A total of 35–42% of those with a BMD *z*-score less than −5 had suffered a fracture, compared with 13–15% of those with a BMD *z*-score greater than −1. The risk ratio was 1.06–1.15, with a 6–15% increased risk of fracture for each 1.0 unit decrease in BMD *z*-score.

Thus BMD, particularly the lateral distal femur *z*-score, is useful as it shows a good correlation with fracture risk. Unlike the situation in the elderly population with osteoporosis, the use of fracture risk reduction as the standard for success of an intervention may not be feasible in children with CP. In an editorial overview of the effects of pharmacological agents on bone in childhood, it was estimated that a formidable cohort size of 3422 children with severe disabilities would have to be recruited if one were using fracture prevention as the standard for therapeutic success.[27] Such a large cohort size was calculated using a 5% annual fracture rate, a 40% treatment efficacy (similar to that of bisphosphonates in the reduction of fragility fractures in post-menopausal women), a 20% effect of control therapy and 20% attrition. As bone fragility is a major contributory factor in fracture in children with CP, and low BMD shares similar risk factors, it is logical to think that BMD might be used as a surrogate outcome parameter to evaluate and monitor therapy for bone health or fracture reduction in children with CP.

Assessment of bone mineral density in children with cerebral palsy

BMD may be measured by DXA or quantitative computed tomography (QCT). DXA is currently the method of choice for the diagnosis and monitoring of BMD over time as it has good precision and low irradiation exposure. The typical scanning time for cooperative children is about 1 minute per scan for the lumbar spine or distal femur and 5–7 minutes for a whole-body scan. A normative database of BMD in children is available.

QCT involves more than 10 times the amount of irradiation that is used in DXA. QCT is not widely available in hospitals and has a limited paediatric normative database of BMD in children. However, there are a number of limitations to the use of DXA studies for BMD.

In a DXA scan, the areal BMD (g/cm^2) is derived by dividing the BMD (g) within a defined anatomical region by the projected area of bone (cm^2). The measured areal BMD (a two-dimensional measurement of the three-dimensional bone) is thus influenced by body size. For example, a study found that 19% of participants had a low spine BMD with a *z*-score less than −2.0 on DXA, compared with only 6% of participants when volumetric BMD measurement from QCT was used.[28]

A low BMD in a child may reflect the smaller body size or a lower bone density, and longitudinal changes in BMD can reflect changes in bone density, bone size or both. Thus, the use of DXA BMD requires adjustments for body size, pubertal status and skeletal maturity. Such adjustment may be difficult in children with CP as they are known to have a large variation in age of attainting puberty, with a high prevalence of both delayed and advanced skeletal maturity. In children with moderate-to-severe CP, 10% had a delayed and 7% had an advanced skeletal age (relative to chronological age) of more than 2 years.[29]

The measurement of total-body BMD/BMC or total-body-less-head (TBLH) BMD/BMC (to eliminate the influence of the skull on the result of whole-body DXA) has been attempted to lessen artefacts related to bone size.[30] Another approach is the use of bone mineral apparent density, an estimated vertebral volumetric BMD using paired posteroanterior and lateral scans to determine whether a low bone mass is due to small bone size or low BMD.[31] Thus, the influence of bone size on BMD in DXA may be minimized by the use of TBLH BMD or bone mineral apparent density.

Total-body BMD and spinal BMD were found to be more accurate and reproducible than total-hip BMD, particularly in younger children.[32] Spine and TBLH BMC and areal BMD, adjusted for absolute height or height age, or compared with paediatric reference data that provide age-, gender- and height-specific *z*-scores, was recommended for children by the International Society for Clinical Densitometry.[18]

Proper positioning in DXA can be difficult for children with CP. Many children with quadriplegic CP have severe deformity or multiple joint contractures, for example scoliosis, pelvic obliquity, windswept deformity of the hips or flexion contracture of the knees. In a simulated altered body posture resulting from only knee contracture in children, the mean errors could be up to 4–6% for BMD measurement.[33] Further interference from artefacts from previous surgery, such as hip varus derotation osteotomy, abnormally healed fractures or the presence of a metallic implant in the hip or spine may make scanning of the lumbar spine and hips difficult, if not impossible, in children with CP. In one study of 119 children, 20% (24/119) of children had an orthopaedic implant that made whole-body scanning unusable, and in 17% (20/119) of the children the only scan that could be obtained was a distal lateral femur scan.[34]

Lateral distal femur scanning has been developed specifically for children with CP as it is the common site of fractures at least in children with CP. Around 36–80% of fractures in children with CP occur around the knee,[3,8] and this is a more readily usable region in CP. The scanning region in the distal femur includes three areas: the metaphysis (mostly trabecular bone), the diaphysis (mostly cortical bone) and the diaphyseal-metaphyseal junction (the transitional

site between the metaphyseal trabecular bone and the diaphyseal cortical bone). It compensates to a certain extent for the inability of DXA to distinguish trabecular bone from cortical bone. In addition, a normative reference of 256 healthy children aged 3–18 was published in 2002 and later revised after the database of 821 healthy children aged 5–18 was updated in 2009.[35] BMD of the distal femur (mean *z*-score −3.5) was much lower than that of the lumbar spine (mean *z*-score −2.0), and the correlation in BMD between these two areas was poor in children with quadriplegic CP.[9]

Although not readily available, QCT can overcome some of the limitations of DXA. DXA does not distinguish between cortical and trabecular bone, which differ in their rate of bone turnover and bone accrual pattern during growth. Trabecular bone in particular is often more rapidly affected by disease or therapy, and a separate analysis of trabecular bone BMD can be advantageous when studying the response to therapeutic interventions.

Peripheral QCT (pQCT) can provide an independent assessment of trabecular and cortical bone in the appendicular skeleton. The trabecular site is evaluated at an ultradistal area at a relative or fixed location from the end of the growth plate, and the cortical site is evaluated along the shaft of the length of tibia or forearm. BMC, volumetric BMD and the areas of the trabecular and cortical compartments can be calculated at both sites.

The effect of growth on bone size in prepubertal children is obviated by the use of volumetric BMD in QCT. Besides BMD, bone fragility in children is also influenced by bone size, bone geometry and bone strength, which are areas in which DXA is deficient. Bone strength is better delineated by QCT as the technique is able to estimated cortical width and the endosteal and periosteal circumference of the bone. The polar strength strain index can be calculated by considering the geometric properties (bone cross-sectional area, cortical thickness and cortical area) and material properties (volumetric BMD and cortical BMC) of the bone.

The pQCT holds all the advantages of QCT but with less irradiation and a shorter scanning time. In addition, normative data for the young population have become available in recent years.[36] However, a single-scan pQCT may reduce the reproducibility. In a study examining pQCT data for the proximal tibia in 35 children with CP, a large variability in bone morphology and trabecular bone density values along the length of the metaphysis was demonstrated, indicating the difficulty of obtaining reproducible pQCT measures from a single scan in the appendicular skeleton of children.[37]

Prevention of bone fragility and fractures in children with cerebral palsy

Obviously, prevention of bone fragility and fractures is the best strategy in order to avoid pain and suffering, muscle wasting and disuse osteoporosis, increased disability, complications from fractures and missed school time in children with CP. All known risk factors should be minimized.

Physical activity and standing weight-bearing should be encouraged. Any stiffness of the major joints and extended periods of immobilization should be avoided. Stable internal fixation of any osteotomy, particularly of the hip, will minimize the postoperative duration of cast immobilization. Lower limb joint deformities, particularly foot and ankle deformities not amenable to bracing, may make standing or physical activities painful and not well tolerated. Orthopaedic operations to correct lower limb joint deformities in order to provide plantigrade feet and straight knees will allow standing weight-bearing and physical exercise in children with severe CP.

It is clear that the absence of weight-bearing loading and muscle forces leads to bone fragility and fracture risk, so it is logical to introduce standing weight-bearing and physical exercise for children with CP to improve their bone health. After an 8-month weight-bearing physical activity intervention in 18 children with CP, an increase in BMC and volumetric BMD was observed in the femoral neck and proximal femur in the intervention group compared with control subjects.[38]

In a randomized clinical trial of 26 non-ambulatory children with severe CP, the treatment group who underwent a 50% increase in regular standing were compared over a 9-month period with a group with no increase in standing. There was an improvement in lumbar spine BMD of 6% but no change in BMD in the proximal tibia, as estimated by QCT, in the treatment group. The authors concluded that longer periods of standing for non-ambulatory children with CP may reduce the risk of vertebral fractures but are unlikely to reduce the risk of lower limb fractures.[39]

In a study of 31 children with CP of level I–IV GMFCS, low-magnitude, high-frequency vibration (30 Hz, 0.3 gravity) for 10 minutes per day for 6 months resulted in a greater increase in cortical bone area and moments of inertia during the vibration period compared with the control standing period.[40] Another study of 20 children with CP treated by side-alternating whole-body vibration for 9 minutes per school day did not detect a positive treatment effect on bone, as assessed by areal BMD.[41] A recent systematic review and meta-analysis concluded a significant but small improvement in hip areal BMD in postmenopausal women and in tibial and spine volumetric BMD in children/adolescents treated with this technique.[42] As a noninvasive and non-pharmacological intervention, low-magnitude, high-frequency vibration therapy warrants further investigation in children with CP.

A multidisciplinary feeding team approach with participation of a child neurologist, speech therapist, occupational therapist and

Table 1
Risk factors for fracture or low bone mass and measures for their prevention and/or treatment

Risk factors for fracture or low bone mass	Preventive or treatment measures
Non-ambulation or GMFSC level V[2,4,9]	Standing weight-bearing [38,39]
	Low-magnitude, high-frequency vibration[40,42]
Immobilization:	Avoid immobilization
Previous fracture[6,10]	Stable internal fixation for hip osteotomy to minimize hip spica casting
Hip spica cast after hip osteotomy[10–12]	
Poor nutrition:	Multidisciplinary feeding team approach[43]
Poor feeding from oro-motor difficulty[4,6,9]	Early use of Ryles tube, surgical correction of gastro-esophageal reflux or gastrostomy
Weight-for-age *z*-score[15,22]	
Low triceps skinfold measurement[9]	
Abnormal vitamin D metabolism:	Ensure adequate vitamin D intake
Low vitamin D status[5]	Vitamin D treatment for rickets or osteomalacia[5]
Use of AEDs[5,9,17,21]	Use of AEDs with the lowest impact on bone metabolism[44]
	Vitamin D and calcium supplementation in children receiving AEDs[45]

AED = antiepileptic drugs; GMFCS = Gross Motor Functional Classification System.

Table 2
Advantages and disadvantages of DUAL-energy X-ray absorptiometry (DXA) and quantitative computed tomography (QCT) in the monitoring of bone mineral density (BMD)

	DXA	QCT
BMD	Areal	Volumetric
Influence of growth effect on body size	Yes; needs adjustment (total-body/total-body-less-head BMD or bone mineral apparent density)	No
Bone geometry assessment	No	Yes (bone cross-sectional area, cortical thickness and cortical area)
Independent assessment of trabecular and cortical bone	No	Yes
Availability	Widely available	Not widely available
Scanning time	Fast	Long (less in pQCT)
Irradiation exposure	Low	High (less in pQCT)

pQCT = peripheral quantitative computed tomography.

dietitian is ideal during assessment and planning for the management of feeding problems. A beneficial outcome was demonstrated from oro-motor training in a local study with short-term follow-up.[43] Video-fluoroscopic studies of swallowing are helpful to identify a need for Ryles tube feeding or surgical correction of gastro-esophageal reflux or gastrostomy.

Adequate vitamin D and calcium intake should be assured. A period of 10–15 minutes of exposure to the sun three times a week provides most of the vitamin D needed. Another convenient source of vitamin D is vitamin D-fortified milk and food.

The use of AEDs should be minimized and the AED with the least impact on bone health should be used. Studies suggested a differential impact of AEDs on vitamin D metabolism and BMD. Phenytoin, phenobarbital and primidone are most consistently associated with a negative impact on bone; carbamazepine and valproate may also result in bone abnormalities, but data are mixed; and lamotrigine may have limited (if any) effect.[44]

Vitamin D and calcium supplementation should be considered in children with CP who have an insufficient dietary intake and are on chronic AED therapy. A large but non-significant increase in lumbar spine BMD was observed after vitamin D supplementation in 13 children with CP and epilepsy who were living in residential care, compared with a decreased BMD in the seven children who did not receive supplements.[45]

Determination of vitamin D status is desirable in children with CP who sustain fractures. A study showed that all 20 institutionalized children and young adults with quadriplegic CP and a history of long-bone fractures had radiological and biochemical evidence of rickets or osteomalacia, and vitamin D treatment resulted in marked clinical improvement with no recurrence of fracture during the treatment period.[5]

Growth hormone may also be deficient in children with CP. A recent large-scale study of 46 children with CP aged between 3 and 11 years showed that 70% of these children lacked normal growth hormone secretion.[46] Bone growth is largely dependent on growth hormone before puberty, and thus growth hormone deficiency can have a large impact on bone growth and bone health. In a randomized controlled trial of growth hormone therapy in 10 children with CP, the therapy group showed a statistically significant improvement in height-for-age *z*-scores and spinal BMD *z*-scores compared with the control group.[47]

Treatment of bone fragility in children with cerebral palsy

With the increasing accessibility of DXA, the introduction of the web-based Fracture Risk Assessment Tool to calculate the absolute fracture risk, and the availability of effective drug treatment for osteoporosis, significant progress has been made in the prevention of fragility fractures in the elderly. Bisphosphonates are often the first-line treatment to prevent fragility fractures in post-menopausal women.

The initial experience of bisphosphonates in CP is promising, but the experience is limited to small series. Only one study has reported the use of oral risedronate, while other studies focused on the use of intravenous pamidronate. In a randomized placebo-controlled study of six pairs of non-ambulatory children with CP, intravenous pamidronate at 3-monthly intervals for 1 year produced an increase of 89% in BMD in the metaphyseal region of the distal femur, and an improvement in *z*-score from −4.0 to −1.8 over the 18-month study period.[48]

In a study of 18 children with quadriplegic CP with a prior fracture treated by intravenous pamidronate, the gain in BMD of the spine was 47%, and that of the lateral distal femur was 65.7%, and these children did not sustain more fractures.[49]

Another study of nine children with spastic quadriplegic CP demonstrated an average increase in spinal *z*-score from −4.0 to −2.8, and in distal femur *z*-score from −3.6 to −2.7 after 1 year of treatment. Although most but not all gains in BMD were lost over the first 2 years after treatment, no patient sustained another fracture over an average 3-year follow up.[50]

Similarly, in another study, the mean increase in BMD was 1.9 for spinal *z*-score and 1.6 for femoral neck *z*-score in 23 non-ambulatory children with CP.[51] On the whole, there was an increased BMD in children with CP, with a range of increase in *z*-score of 1.2–1.9 for the spine, 1.6 for the femoral neck, and 1.1–2.2 for the distal femur after 1 year of treatment with intravenous pamidronate.[48,50,51] In two of the above studies, the treated children did not sustain a fracture during the follow-up period.[49,50]

In a study focusing on the incidence of fracture before and after 1 year of treatment with pamidronate for 25 children with quadriplegic CP level GMFCS IV or V, the fracture rate significantly decreased from 30.6% per year to 13.0% per year.[52] In these studies, no adverse effects of treatment were noted.

Conclusion

Non-ambulatory children with CP have an increased risk of fractures. The risk factors of fracture or low bone mass and the corresponding preventive measures are summarised in Table 1.[4–6,9,10–12,15,17,21,22,38–40,42–45] Weight-bearing activities cannot be overemphasized. Optimization of nutrition and intake of calcium and vitamin D, together with physical activity, should be enforced. Bisphosphonates should be considered in children with CP and a history of fracture and low bone mass. Growth hormone replacement is useful in children with growth hormone deficiency, which is common in children with CP. In addition, low-magnitude, high-frequency vibration warrants further investigation.

Currently, BMD (total-body or of the distal femur), BMI or body weight *z*-score may be used to predict fracture risk. BMD may be used as a surrogate outcome parameter to monitor bone health or to test the efficacy of fracture prevention or treatment in children

with CP. The advantages and disadvantages of DXA and QCT in the measurement of BMD are summarised in Table 2.

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