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Adults with spastic cerebral palsy have lower bone mass than those with dyskinetic cerebral palsy

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ABSTRACT

Adults with cerebral palsy (CP) are known to have low bone mass with an increased risk of fragility fracture. CP is classified into two major types: spastic (pyramidal) and dyskinetic (extrapyramidal). Spastic CP is the most common and is characterized by muscle hypertonicity and impaired neuromuscular control. By contrast, dyskinetic CP is characterized by mixed muscle tone with involuntary movements. The aim of this study was to elucidate the relationship between bone metabolism and subtype of CP. Fifty-eight adults with CP (aged 18 to 49 years, mean age 33.2 years; 32 men, 26 women) were included in this cross-sectional analysis. Lumbar spine and femoral bone mineral density (BMD) *Z*-scores were measured. Bone markers, including C-telopeptide of type I collagen (CTx) and osteocalcin (OCN), were also analyzed. Among these participants, 30 had spastic CP and 28 had dyskinetic CP. The *Z*-scores of lumbar spine BMD did not differ between the two types. However, the *Z*-scores of femur trochanteric BMD were significantly lower in participants with spastic CP than in those with dyskinetic CP (-1.6 ± 1.2 vs. -0.9 ± 1.1, $p < 0.05$). Seventy-four percent of participants with either type of CP had abnormally elevated CTx, while about 90% of participants showed normal OCN levels. When participants were subclassified into nonambulatory and ambulatory groups, the nonambulatory group had significantly lower BMD in the femur, including the trochanteric and total regions, whether they were spastic or dyskinetic ($p < 0.05$). Because the type of CP affects bone mass, nonambulatory spastic CP participants showed the lowest total hip region BMD among the four groups. These results reveal that reduced weight bearing and immobility related to CP cause a negative bone balance because of increased bone resorption, which leads to a lower bone mass. In addition, hypertonicity of the affected limbs in participants with spastic CP resulted in lower bone mass than in those with dyskinetic CP. Type of CP and degree of ambulatory function in adults with CP should be regarded as important factors affecting bone metabolism.

Introduction

Cerebral palsy (CP) has been described as a group of permanent disorders in the development of movement and posture that result in the limitation of activity and are attributed to nonprogressive disturbances that occurred in the growing fetal or infant brain. The motor disorders of CP are frequently associated with disturbances of sensation, perception, cognition, communication, and behavior caused by epilepsy or by secondary musculoskeletal problems [1].

CP is usually classified into two major types: spastic (pyramidal) and dyskinetic (extrapyramidal). Spastic CP is the most common type and is characterized by increased muscle tone and pathological reflexes: either increased reflexes, known as hyperreflexia, or pyramidal signs [2]. Increased muscle tone in spasticity features an increased velocity-dependent resistance. By contrast, dyskinetic CP is characterized by mixed muscle tone with involuntary, uncontrolled, repetitive, and occasionally stereotyped movements. Primitive reflex patterns predominate and muscle tone varies [2].

Because of their developmental problems, people with CP face a number of medical complications during their growing years: gastrointestinal reflux, aspiration syndromes, respiratory infections, seizures, and contractures. In addition, they are prone to suffer common age-related conditions such as atherosclerosis, muscle wasting, osteoarthritis, bone loss, and low-trauma fractures [3].

There have been several studies on low bone mass in children and young adults with CP [4–7]. In these reports, children with moderate to severe functional disabilities of CP showed low bone mass in the lumbar spine and hip [5,7]. Several factors influence their lower bone

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mineral density (BMD), such as poor nutrition, anticonvulsant medications, and decreased weight bearing or bone loading because of functional disabilities [8]. Previous studies have shown that people with CP or muscular dystrophy [4] or with stroke [9] have low BMD because of immobilization and disuse of the affected sites. These studies proposed that the decreased mechanical force of muscles in the affected sites might decrease anabolic influences on bone metabolism.

Moreover, as there are two types of CP, which result in different muscle tonicity and movements, it bears consideration that while immobilization usually results in bone loss, moderate loading by motion might exert positive effects on bone. In other words, the dynamic and hyperkinetic muscle movements featured in dyskinetic CP might be beneficial for bone density compared with the limited movements derived from muscle spasm and hypertonicity of spastic CP. Although many studies have previously reported low BMD in children with CP, data about low bone mass in adults with CP are limited, and there are no reports on differences in bone metabolism between CP subtypes combined with concurrent classification of ambulatory function.

We hypothesized that adults with CP, who show different muscle tones and movements, would have lower BMD than normal populations, and sought to confirm this hypothesis. We divided people with CP by their CP subtype and their ambulatory abilities (nonambulatory vs. ambulatory). Participants with the spastic type of CP had lower BMD compared with those with the dyskinetic type. In addition, the nonambulatory subgroups had lower bone mass, specifically in the hip region.

Materials and methods

Participants

This study was a retrospective cross-sectional investigation of adults with CP. Fifty-eight participants, aged 18 to 49 years, who were diagnosed with CP, were recruited into this study. There were 32 men and 26 women. Their types of CP were defined by characteristic movement patterns and muscle tone. Baseline characteristics including age, height, weight, and body mass index (BMI) were measured.

Based on the gross motor function classification system (GMFCS) [10], functional independence measure (FIM) [11], and modified Barthel index (MBI) [12], the participants were subdivided into nonambulatory and ambulatory groups based on their ambulatory abilities. Two participants in the spastic CP group were excluded from the subgroup analysis because they underwent orthopedic surgery within 12 months of beginning the study, which made it difficult to measure their functional capacities. The study protocol was approved by Institutional Review Board of Yonsei University Health System (IRB, No. 4-2012-0751).

Biochemical analysis and BMD

Routine chemistry measurements, including calcium and phosphate, were performed using standard automated techniques. Blood samples were collected in the morning after an overnight fast. Bone turnover markers were measured using the following methods: osteocalcin (OCN) (by enzyme-linked immunosorbent assay (ELISA); CIS Bio International, Gif-sur-Yvette, France; intraassay coefficient of variation (CV) < 2.0%, interassay CV < 5.0%); C-telopeptide of type I collagen (CTx) (by ELISA with Osteomark; Ostex International, Seattle, WA, USA; intraassay CV < 5.8%, interassay CV < 5.9%); intact parathyroid hormone (by IRMA; Biosource, Nivelles, Belgium; intraassay CV < 2.7%, interassay CV < 3.5%); and 25-hydroxyvitamin D (25(OH)D) (by D3-RIA-CT; Biosource; intraassay CV < 11.0%, interassay CV < 12.5%).

BMD in the lumbar spine (L1–L4), femur neck, femur trochanter, and total hip was measured in all participants by dual-energy X-ray absorptiometry (Delphi A, version 12.6; Hologic, Waltham, MA, USA).

Assessment of ambulatory function

Functional outcomes and ambulatory function were measured using various methods. Manual muscle test (MMT) grading at the hip region was performed to measure muscular strength. As mentioned above, GMFCS, FIM, and MBI were applied to determine the functional capacities of participants with CP, and were used to define their ambulatory function.

The GMFCS is a standardized system to classify gross motor function, specifically developed for adults with CP [10]. The GMFCS is divided into five levels: level I, walking without limitation; level II, walking with limitations; level III, walking using a handheld mobility device; level IV, self-mobile with limitations; and level V, being transported in a manual wheelchair. The FIM is composed of 18 items on a seven-level scale with scores from 18 (total assistance) to 126 (complete independence), that assess basic activities of daily living in areas of self-care, sphincter control, transfer, locomotion, communication, and social cognition [11,13]. The MBI is composed of 10 items such as feeding, bathing, grooming, dressing, bladder and bowel control, toileting, transfer, mobility, and stair climbing with scores from 0 (totally dependent) to 100 (independent) [12,13].

The participants were subdivided into two groups by their ambulatory abilities. The nonambulatory group consisted of participants who depend on assistance during movement or who use a wheelchair (GMFCS IV–V). By contrast, the ambulatory group consisted of participants who are ambulatory without need of help. The person may use gait aids, or supervision may be needed for safety (GMFCS I–III).

Statistical analysis

All analyses were performed using SPSS statistical software (version 18.0; SPSS, Chicago, IL, USA). We performed the Shapiro–Wilk test to identify whether or not data were normally distributed. Continuous variables with a normal distribution are expressed as means ± SD unless otherwise indicated. A p value < 0.05 was considered significant. Differences between the two types of CP were compared using Student's t test.

Because we subdivided participants with each type of CP into subgroups according to their ambulatory ability as determined by the GMFCS, continuous variables were compared using Student's t test in each group. Multiple regression analysis was used to identify the interaction effect between subtypes of CP and the participants' ambulatory abilities. We used total hip BMD as the outcome measure, and age, sex, and BMI were included as covariates. In this model, dummy variables (reference category dyskinetic ambulatory group) were used to create an interaction term.

Results

Baseline characteristics of CP participants

Fifty-eight adults with CP (32 men and 26 women; mean age, 33.2 ± 9.3 years) were included in this study. Participants were divided into two groups according to whether they had spastic or dyskinetic CP, which are the major types of CP; there were 30 adults with spastic CP and 28 with dyskinetic CP. The baseline clinical, laboratory, and rehabilitative parameters in these two groups are shown in Table 1. The mean age of the spastic group was younger than that of the dyskinetic group (29.6 ± 9.2 vs 37.0 ± 7.8 years, $p < 0.05$). Metabolic parameters, serum calcium, phosphorus, and bone turnover markers, and rehabilitative parameters, showed no significant differences between the groups. However, vitamin D level was significantly higher in the spastic group (13.1 ± 5.3 vs. 9.3 ± 4.3 ng/mL in the spastic vs. the dyskinetic group, $p < 0.05$).

No differences were observed between the spastic and dyskinetic groups with respect to lumbar spine or femoral neck BMD Z-scores (lumbar spine, −1.1 ± 1.2 vs. −0.5 ± 1.2; femoral neck, −0.9 ± 1.2 vs. −0.5 ± 1.1, respectively, p = NS). However, femur trochanteric