Evaluation of bone mineral density in children with cerebral palsy*

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In the present study, bone mineral density of 40 children with cerebral palsy (study group) and the effects of various risk factors on bone mineralization in these children were investigated by comparing with 40 age-matched healthy children (control group). Weight, height, skinfold thickness, body-mass index measurements, and serum levels of calcium, phosphorus, alkaline phosphatase and 25 OH vitamin D were not significantly different between the study and control groups ($p>0.05$). The mean bone mineral density value of the study group measured by dual-energy X-ray absorptiometry method at L_2-L_4 levels of lumbar vertebrae was significantly lower than that of the control group ($p<0.05$). When the patients in the study group were assessed with respect to ambulation status, pattern of involvement, calcium and energy intakes, and whether or not they had taken and/or were taking a regular physical therapy program, there was a significant difference only between the hemiplegic and tetraplegic patients ($p<0.05$), while there were no significant differences among the patients who were ambulant versus non-ambulant, who had sufficient versus insufficient calcium and energy intakes, and who did and did not take a regular physical therapy ($p>0.05$). Although the ambulatory status, quantity of calcium and energy intakes, and the presence or absence of a physical therapy program had no effects on bone mineral density values of the children with cerebral palsy in this study, the exact factors and mechanisms responsible for the reduced bone mineral density in children with cerebral palsy should be investigated in further large-scale studies considering the increased risk of pathological fractures in these patients.

Key words: ambulation, bone mineral density, calcium, cerebral palsy, energy, hemiplegy, nutrition, physical therapy, tetraplegy.

Many factors may contribute to poor bone mineralization in children with cerebral palsy. Duration of immobilization and some physical problems may cause deficiency in bone mineralization[1,2]. These patients are not infrequently subjected to several surgical operations. Poor feeding and oral motor dysfunction may lead to inadequate caloric, protein and calcium intake[3,4]. Anticonvulsant medication and limited sunlight exposure may further cause low serum vitamin D levels[5], and thus, calcium content of bone may be decreased. Most children with cerebral palsy have many of these risk factors and are at increased risk for the development of metabolic bone disease through a combination of potential mechanisms. It would be beneficial to determine the effects of various risk factors frequently present in these children on bone mineralization. We therefore aimed in this study to identify the risk factors that may affect bone mineralization and to assess their association with bone mineral density in children with cerebral palsy.

Material and Methods

Between June 1997 and April 2000, 40 cerebral palsied patients (15 males, 25 females) with a mean age of 5.1 years (range, 2.7 to 14.2 years)

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were studied. Forty healthy children (20 males, 20 females) with a mean age of 5.3 years (range, 3 to 14 years) were chosen as the control group. Patients were eligible if they had hemiplegic, diplegic, or tetraplegic cerebral palsy without major athetoid or ataxic behavior, or any significant medical or operative histories. Informed consent was obtained from the parents or legal guardians, and the study was approved by the local ethical committee.

Every patient was screened with a thorough clinical history and physical examination. Nutritional status was assessed by height, weight, triceps skinfold thickness and body mass index (weight [kg]/height [m]^2). Height was measured with a Harpenden portable stadiometer to the nearest 0.1 cm and weight with a Seca scale to the nearest 0.1 kg. Skinfold thickness was measured to 0.1 mm on the non-dominant side of the body at the triceps sites, using Harpenden calipers. Each skinfold measurement was taken in triplicate. The mean of the three skinfold measurements was calculated and used in the analysis. Each patient completed a questionnaire asking about their physical therapy status. Peripheral venous blood samples were obtained for measurements of calcium, phosphorus and alkaline phosphatase (Menarini Diagnostics Kits, Italy; Technicon RA-1000 autoanalyzer). Levels of 25 OH vitamin D were measured with an enzyme immunoassay, in an IMX (Abbott, USA).

Bone mineral density in the lumbar spine was measured with dual-energy X-ray absorptiometry (DXA Norland, XR-36). All scans were taken using general scan software at a scan speed of 10 mm/s and with pixel size 1.0x1.0 mm^2. The scan width was 5 cm and the total effective dose remained <1 μSv. The subject sometimes moved excessively during scanning, but it was usually possible to calm the child and repeat the scan. Only five patients were sedated during measurement (hydroxyzine HCI, 1 mg/kg).

Patients received nutritional counseling from the same nutritionist (NI). Dietary assessment and individual food consumption questionnaire were administered by the nutritionist in a 30-minute interview. The interview included the primary caregiver and the child, if the child's age and intellect were appropriate. The total energy and calcium intake were compared with a standard food consumption table of Turkish children[6].

Results were expressed as mean and standard deviation. Comparisons were made using the Student's test, and significance was established at $p<0.05$.

Results

Characteristics of the patients in the study group with respect to ambulation and pattern of involvement are given in Table I. Although weight, height, skinfold thickness and body mass index measurements of the study group were lower than those of the control group, there were no significant differences ($p>0.05$) (Table II).

Table I. Characteristics of the Patients in the Study Group with Respect to Ambulation and Pattern of Involvement

Characteristics	No of patients (%)
Type of involvement	
Hemiplegic	11 (27.5)
Diplegic	2 (5)
Tetraplegic	27 (67.5)
Ambulation pattern	
Ambulant (normal)	18 (45)
Non-ambulant	22 (55)

Mean serum levels of 25 OH vitamin D, calcium, phosphorus and alkaline phosphatase did not differ significantly between the study and control groups.

The mean bone mineral density value of the study group was significantly lower than that of the control group ($p<0.05$) (Table III). When the patients in the study group were assessed

Table II. Anthropometric Measurements of the Study and Control Groups*

	Study group	Control group	p-value
Weight (kg)	16.8±1.30	18.2±1.40	>0.05
Height (cm)	107.3±3.37	111.0±3.20	>0.05
Triceps skinfold (cm)	8.4±0.92	9.2±1.03	>0.05
Body-mass index (kg/m^2)	14.7±1.12	15.5±1.07	>0.05

* Values are given as mean ± standard deviation.

with respect to ambulation status, pattern of involvement, calcium and energy intakes, and whether or not they had taken and/or were taking a regular physical therapy program, there was a significant difference only between the hemiplegic and tetraplegic patients ($p<0.05$), while there were no significant differences among the patients who were ambulant versus non-ambulant, who had sufficient versus insufficient calcium and energy intakes, and who did and did not take a regular physical therapy program ($p>0.05$) (Table III).

Table III. Comparison of the Bone Mineral Density Values of the Cases in the Study and Control Groups

	No of subjects	BMD (g/cm^2)*	p-value
Study group	40	0.393±0.13	<0.05
Control group	40	0.502±0.15	
Ambulation			
Ambulant (normal)	18	0.438±0.17	>0.05
Non-ambulant	22	0.361±0.12	
Physical therapy			
None	19	0.380±0.04	>0.05
Regular	21	0.400±0.04	
Involvement			
Hemiplegic	11	0.444±0.03	<0.05
Tetraplegic	27	0.373±0.02	
Energy intake			
Sufficient	9	0.407±0.03	>0.05
Insufficient	31	0.395±0.02	
Calcium intake			
Sufficient	19	0.400±0.02	>0.05
Insufficient	21	0.380±0.14	

* Bone mineral density (BMD) values are given as mean ± standard deviation.

Discussion

One of the most important medical problems of severely retarded and physically handicapped children is the risk of pathological fracture due to inadequate mineralization[7,8]. We therefore aimed to identify factors that may affect bone mineralization and to assess their association with bone mineral density, and results of the present study demonstrated that decrease in bone mineral density is significant in children with cerebral palsy. Suggested mechanisms responsible for the reduction in bone density in these children are poor nutritional status, insufficient calcium intake, immobilization and anticonvulsant use[9-12]. Bone mineralization is a complex process that requires adequate nutrition; protein for osteoid formation; calcium and phosphorus for calcification; weight bearing and muscle use; and modulation by thyroid, parathyroid, gonadal, and pituitary hormones[13]. Reduced bone mineral density values of the patients in the study group when compared to the healthy cases in the control group as measured by dual-energy X-ray absorptiometry method in the present study further confirmed the presence of inadequate mineralization in children with cerebral palsy.

Of the factors analyzed with respect to the effect on bone mineralization in the present study, ambulatory status and the presence or absence of physical and neurophysiological therapy had no significant effect on bone mineral density in children with cerebral palsy. In a study investigating the bone mineral density of both ambulant and non-ambulant cerebral palsied children, higher values have been reported in ambulatory patients[14]. In another study, children with impaired ambulation due to myelomenigocele had decreased bone mineral density values[15]. Mazess et al.[2] reported temporarily immobilized patients had lower bone mineral density values, and they suggested that bone mineral density increases with ambulation.

The type of involvement had a significant effect on the bone density of the cerebral palsied children in this study. Henderson et al.[9] found that there was no difference between the bone mineral density values of the diplegic and heliplegic patients, but both groups had greater bone density than tetraplegic patients[9]. Hemiplegic patients in our study also had greater bone mineral density values than tetraplegic patients. The cause of decreased bone density in tetraplegic patients is unclear. One possibility is a direct neuropathic effect of cerebral palsy, manifested in abnormal mineralization of bone and decreased muscle mass. Muscle mass and strength are diminished in neurologically affected extremities and this may contribute to the lower bone mineral density.

Some physical handicaps which have been found to be related directly to the eating habits of the cerebral palsied children include poor

occlusion, frequent dental caries, inability to feed self, inability to chew normally, difficulty in swallowing and poor appetite[3,16]. These factors lead to inadequate caloric, protein and calcium intake. Poor nutritional status may also affect growth and development[17]. Several studies have suggested that height and weight were reduced in cerebral palsied children[3,13]. We also found that all anthropometric parameters (height, weight, triceps skinfold, body-mass index) of the children with cerebral palsy were lower than age-matched controls, although the differences were not statistically significant. Poor nutrition contributes to the common problem of diminished linear growth, but other undefined factors also may play a major role.

The retrospective studies reporting a greater bone mass later in life among subjects who had high calcium intakes during childhood suggest that the differences do persist although this persistence may be due to a greater life-long calcium intake[18,19]. In a prospective and blinded study in normal children, calcium supplementation to a maximum intake did result in greater increases in bone mineral density[11]. The quantity of calcium intake (sufficient versus insufficient) had no effect on bone density of the children with cerebral palsy in our study.

Results of the present study demonstrate that bone mineral density of the children with cerebral palsy was significantly lower when compared to the healthy children, and that tetraplegic patients were more significantly prone to have decreased bone mineralization than hemiplegic patients. Although the ambulatory status, quantity of calcium and energy intakes, and the presence or absence of a physical therapy program had no effects on bone mineral density values of the children with cerebral palsy in this study, the exact factors and mechanisms responsible for the reduced bone mineral density in children with cerebral palsy should be investigated in further large-scale studies considering the increased risk of pathological fractures in these patients.

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