



Bone Mineral Density among Children with Cerebral Palsy

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Keywords

Cerebral palsy; Osteopenia; Osteoporosis

Abstract

Background: Reduction in bone mineral density (BMD) is one of the problems among children with cerebral palsy (CP). The pathophysiology is a complex field in which various factors are involved. The present study was conducted with the aim to evaluate BMD among children with CP.

Methods: In this descriptive-analytical cross-sectional study, 85 children with CP were studied in the Children's Hospital of Tabriz, Iran, for 12 months. BMD was measured in the patients in three vertebrae (L2-L4) and the pelvis using the dual-energy X-ray absorptiometry (DXA) method. The variables of age, sex, types and subclasses of CP, previous physiotherapy, standing and walking status, nutritional status, history of receiving anticonvulsant drugs, and functional status were investigated based on the Gross Motor Function Classification System (GMFCS).

Results: In the present study, 85 children including 44 boys and 41 girls with a mean age of 5.79 ± 2.39 (3 to 11) years were studied. Osteopenia and osteoporosis were present among 48.2% and 30.6% of the participants, respectively. The ability to walk and duration of standing during the day were directly

related to the increase in BMD in the vertebrae. In addition, there was an inverse relationship between BMD and GMFCS score; however, this relationship was not statistically significant.

Conclusion: Reduced BMD, osteopenia, and osteoporosis are common among children with CP. The relevant pathophysiology is multifactorial and complex.

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Introduction

Children with cerebral palsy (CP) are at increased risk of developing growth disorders, osteopenia, developing small and weak bones, and reduced muscle mass.¹⁻⁶ What seems more important in this regard is that growth disorders among children with CP may be due to various causes such as malnutrition, endocrine dysfunction, reduced duration of standing (weight tolerance), etc., which can all have negative outcomes.

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Osteopenia is one of these complications. The risk of incidence of fracture, especially in spontaneous forms, increases among these patients.⁷⁻¹⁰

Various factors have been associated with bone health disorders in children with CP, including motor impairment, muscle weakness, malnutrition, and the use of anticonvulsants. These children may suffer from growth hormone deficiency; in addition, growth related factors, such as insulin-like growth factor I (IGF-I) and IGF-I-binding protein-3, are usually lower among these children in comparison to their counterparts.^{11,12} There is evidence that some interventions can impede osteopenia or reduce its severity among children with CP.¹²⁻¹⁸ However, the exact mechanism of bone disorders is still not well known among these patients. Although numerous studies have been conducted in this area, the findings are not consistent and definitive.¹⁹⁻²² This issue, and the lack of studies in this regard in our region so far, as well as the lack of knowledge on bone density status have caused limitations in the implementation of rehabilitation programs in terms of stretching exercises due to the risk of pathologic fractures. Thus, the researchers in the present study decided to examine bone mineral density (BMD) among children with CP and determine the role of some parameters in osteopenia and osteoporosis among these patients.

Methods

In this descriptive-analytical and cross-sectional study, 85 children with CP diagnosis were studied. BMD and the presence of osteopenia and osteoporosis were evaluated among this group of patients and the possible relationship of various variables with these conditions was evaluated. The study was carried out in the Children's Hospital of Tabriz City, Iran, during a period of 12 months, and the data collection and analysis were carried out since late October 2010 to late April 2011. Convenience sampling was implemented among the

statistical population of the study that consisted of children with CP referred to the Children's Hospital of Tabriz. The study exclusion criteria were age of older than 11 years, history of previous treatment for osteoporosis or receiving medications effective on BMD, history of major diseases and surgery operations [such as malignancy, diabetes mellitus (DM), and hip surgery], history of hip fracture, and presence of deformity in the hip in such a way that densitometry was not possible.

A history of the disease was obtained from the patients and they were subjected to complete physical examination. Bone densitometry was performed through dual-energy X-ray absorptiometry (DXA) method in the two L2-L4 lumbar regions and proximal femur (pelvic) area. The rate of reduction of X-ray intensity by the scanned bone was considered as bone mineral content (BMC) and, by dividing it by the surface area, BMD was determined in both areas and adjusted according to the age and sex of the patients (calculation of Z-score).

Nutritional status of the patients was determined with the help of a nutritionist and through interviewing the parents of the patient regarding the total amount of energy received as well as the amount of calcium intake. Then, the patient's status was determined in terms of intake or lack of intake of anticonvulsant drugs. In addition, CP performance level was determined using the Gross Motor Function Classification System (GMFCS) score. This system consists of 5 levels that assess net motor performance based on the self-motivated movement of the child with CP with a focus on sitting, walking, and moving with the help of a wheelchair. High GMFCS scores indicated a poor performance and the CP type was determined based on physical examination. The condition of the patient was determined in terms of daily movement (in two forms of ability to walk and inability to walk) and the length of time of standing. The existence or absence of regular physiotherapy was also

determined (as 3 sessions per week). In the next step, the relationship between each of the above factors and BMD was examined, which was adjusted based on age (Z-score) ($-2 < Z\text{-score} < -1$ and $Z\text{-score} < -2$ were considered as osteopenia and osteoporosis, respectively). The presence of osteopenia or osteoporosis at least in one of the two examined regions was sufficient to detect the condition of the patient.²³⁻²⁵ Due to the need for radiation during densitometry, the study method was explained to the parents of the children prior to starting the study and a written consent form was obtained from those willing to participate in the study.

No financial charges were imposed on the patients and all their information remained confidential. This study has been approved by the ethics committee of Tabriz University of Medical Sciences.

The data obtained from the study were statistically investigated and analyzed using descriptive statistical methods including rate [percentage and mean \pm standard deviation (SD)], mean difference test for independent groups, and chi-square test or Fischer's exact test in SPSS software (version 15.0, SPSS Inc., Chicago, IL, USA). The quantitative data were evaluated in terms of the normal distribution of data using Kolmogorov-Smirnov (K-S) test and Q-Q curve, and the correlation between quantitative variables was determined using the Pearson coefficient. In all tests, the results were considered to be statistically significant in case of meeting the condition of $P > 0.05$.

Results

The mean age of the patients was 5.79 ± 2.39 years (3 to 11 years); in addition, 44 (51.8%) and 41 (48.2%) of the patients were boys and girls, respectively.

The type of involvement was spastic, hypotonic, dyskinetic, and mixed CP in 67 (78.8%), 6 (7.1%), 3 (3.5%), and 9 (10.6%) of the patients, respectively. Moreover, 20 (23.5%), 37 (43.5%), and 28 (32.9%) of the children were hemiplegic, quadriplegic, and

diplegic, respectively. The energy intake status was sufficient and insufficient among 27 (31.8%) and 58 (68.2%) of the participants, respectively. In addition, calcium intake was sufficient and insufficient in 34 (40.0%) and 51 (60.0%) of the patients, respectively. The history of physiotherapy was negative, regular, and irregular among 7 (8.2%), 47 (55.3%), and 31 (36.5%) of the subjects, respectively. The mean \pm SD of GMFCS was 2.68 ± 0.91 (1 to 5) among the patients. Among the patients, 41 (48.2%), 34 (40.0%), and 10 (11.8%) had no walking ability, were able to walk, and were able to walk with help, respectively. The mean \pm SD of duration of standing in the day was 112.84 ± 14.97 (10-480) minutes and the mean \pm SD of age of onset of walking was 3.78 ± 2.16 years (1-9 years) among the patients. There was a history of receiving anticonvulsant drugs in 23 (27.1%) of the patients. The mean \pm SD length of use of anticonvulsant drugs was 2.92 ± 1.05 years (1 month to 9 years) in these patients. The mean \pm SD of the Z-score was -1.35 ± 1.32 (-0.20 to -4.80) and 1.68 ± 1.18 (0 to -5.90) for the pelvis and vertebra of the patients, respectively.

Pelvic osteopenia, vertebral osteopenia, pelvic osteoporosis, and vertebral osteoporosis were present among 13, 33, 25, and 26 patients, respectively. The variables evaluated among the patients in the three groups of osteopenia, osteoporosis, and normal bone density have been compared in table 1.

The mean BMD of the spinal and pelvic bone in the group with inadequate caloric intake and the mean BMD in the pelvis in the group with inadequate calcium intake were significantly lower. Mean pelvic BMD was significantly lower in the group with a history of receiving anticonvulsant drugs compared to the group receiving adequate calories and calcium. The mean BMD in the vertebrae and pelvis was significantly higher in the group with hypotonic CP and in cases with hemiplegic involvement in comparison to those with other types of CP.

Table 1. Variables examined in the normal, osteopenia, and osteoporosis groups

Variable	Group	Normal (n = 18)	Osteopenia (n = 41)	Osteoporosis (n = 26)	P
Age (year)		4.86 ± 2.04 (3-10)	5.15 ± 2.19 (3-11)	7.46 ± 2.14 (5-11)	< 0.001
Gender [rate (%)]	Boy	11 (61.1)	20 (48.8)	13 (50.0)	0.670
	Girl	7 (38.9)	21 (51.2)	13 (50.0)	
BMI		14.45 ± 3.12 (10.41-21.00)	13.24 ± 2.61 (7.09-19.34)	14.67 ± 2.65 (9.09-19.20)	0.080
CP type [rate (%)]	Spastic	15 (83.3)	31 (75.6)	21 (80.8)	0.770*
	Hypotonic	3 (16.7)	3 (7.3)	0 (0.0)	
	Dyskinetic	0 (0.0)	2 (4.9)	1 (3.8)	
	Mixed	0 (0.0)	5 (12.5)	4 (15.4)	
CP side [rate (%)]	Hemiplegic	5 (27.8)	12 (29.3)	3 (11.5)	0.520
	Quadriplegic	7 (38.9)	16 (39.0)	14 (53.8)	
	Diplegic	6 (33.3)	13 (31.7)	9 (34.6)	
GMFCS score		2.39 ± 0.70 (1-4)	2.71 ± 1.01 (1-5)	2.85 ± 0.83 (1-4)	0.250
History of physiotherapy [rate (%)]	Negative	3 (16.7)	3 (7.3)	1 (3.8)	-
	Regular	12 (66.7)	19 (46.3)	16 (61.5)	
Walking ability	Irregular	3 (16.7)	19 (46.3)	9 (34.6)	0.510**
	Negative	8 (44.4)	18 (43.9)	15 (57.7)	
	Positive	10 (55.6)	17 (41.5)	7 (26.9)	
	With help	0 (0.0)	6 (14.6)	4 (15.4)	

BMI: Body mass index; GMFCS: Gross Motor Function Classification System; CP: Cerebral palsy
Data have been presented as (maximum-minimum) mean ± SD or rate (%).

* Between the two spastic and other groups; ** Between the negative and positive groups

The mean age of onset of walking among patients in the osteoporotic group was significantly higher than the normal and osteopenic group. Moreover, there was an inverse relationship between BMD and GMFCS score; however, this relationship was not statistically significant.

Discussion

In the present study, BMD, osteopenia, osteoporosis, and their associated factors were investigated in children with CP.

In this study, the incidence rate of osteopenia and osteoporosis was 48.2% and 30.6%, respectively. Osteopenia and osteoporosis of the lumbar spine were present in 38.8% and 30.6% of the subjects, respectively; in addition, pelvic osteopenia and osteoporosis were observed among 15.3% and 29.4% of the subjects, in the same order. In a study performed by Henderson et al. on children and adolescents aged 2 to 19 years with moderate to severe CP, a 77% incidence rate of distal femoral osteopenia was reported.³ Mergler et al. summarized the results of 32 studies in a meta-analysis.²² According to their study, the incidence rate of fracture among children with different

degrees of CP varied from 2.7% to 23%. In addition, the prevalence of BMD varied from 27% to 77% among them compared to their healthy counterparts.²² Review of the existing information resources indicated that there was no similar study examining the same subject as the present study. Nevertheless, compared to the results of previous studies, the incidence of osteopenia and osteoporosis (in case of considering it to be equivalent to fracture) was within the reported range. As can be observed, these reports include a wide range of variables. Various reasons can be provided to justify this inconsistency, including the risk factors associated with decreasing BMD among children with CP.

Although in the present study, a control group homogeneous with the patient group has not been considered (which is one of the drawbacks of this study), according to the definitions, the reports of the incidence of osteopenia and osteoporosis (based on Z-score) indicate the comparison with healthy groups. In the present study, the ability to walk and length of standing during the day were directly related to the increase in BMD in the vertebrae. Houlihan and Stevenson,²⁰ and Wilmschurst et al.²¹ reported

the inability to stand and move as the most important risk factor associated with decreasing BMD among this group of patients. In the present study, the mean BMD of the lumbar spine was significantly lower among the group with the lack of ability to walk as well. Furthermore, the length of standing during the day was inversely and significantly related to BMD in the lumbar spine. In an investigation on 9 children with CP lacking the ability to move, Shaw et al. considered a combination of factors such as inactivity, nutritional status, and history of use of anticonvulsants to be effective in reducing BMD.² The findings of the present study are consistent with the results of the study by Shaw et al.² in terms of nutritional status (energy and calcium intake) and the use of anticonvulsant drugs.

In a study conducted by Unay et al., 40 children with CP and 40 similar healthy children were examined.²⁶ The mean BMD in the CP group was significantly lower than that of the control group.²⁶

Intra-group comparisons showed that activity and inactivity, calcium intake, and regular and irregular physiotherapy were not related with BMD, and only the mean BMD in the hemiplegic group was reported to be significantly higher compared to that of the group with quadriplegic involvement.²⁶ In the present study, history of previous physiotherapy was also not related to BMD. Since the investigation of this situation has been carried out according to parents' statements, the results may not be accurate enough. Insignificant higher value of mean BMD in the group with hemiplegic involvement is consistent with the above report.

In another study carried out by Henderson et al. on 117 children with moderate to severe CP, a statistically significant relationship was presented between BMD of distal femur and GMFCS, malnutrition, and use of anticonvulsants.³ In addition, in the present study, there was an inversely insignificant relationship between

BMD and GMFCS score. In another study by Henderson et al. on 69 children with moderate to severe CP, a statistically significant relationship was found between BMD and severity of CP, GMFCS, and malnutrition.¹⁹ The results of this study are in agreement with the findings of the present study. Tasdemir et al. examined 24 children with CP.²⁷ They reported that the mean of BMD in the patient group was significantly lower compared to that of the control group; however, no difference was reported among the groups in terms of mobility status.²⁷ The results of their study contradict the findings of the present study.

Considering the above-mentioned studies and results, the results of different studies on the risk factors associated with decreasing BMD among children with CP are highly variable and non-deterministic. Accordingly, the findings of the present study were consistent with the results of other studies in some cases, but were contradictory in other cases. In this study, the variables were evaluated in terms of the presence or absence of osteopenia and osteoporosis. Therefore, regarding the comparison of the two groups with and without osteopenia, variables with significant statistical differences included patient's age, age of onset of walking, calorie intake status, and history of use of anticonvulsants. In a study performed by Caulton et al. on the role of standing programs among children with CP, it was revealed that BMD changes varied based on location.¹⁴ In this study, the rate of changes in BMD after the program was significant in the lumbar spine and insignificant in the proximal tibia.¹⁴ The findings of the present study, along with those of the mentioned study, revealed differences in the location of the measurement of BMD.

Regarding the effect of anticonvulsant drugs on BMD, as was previously mentioned, the results varied. The negative effect of these drugs on BMD has been generally proven. This adverse effect was particularly severe at younger ages.^{28,29}

Conclusion

Based on the results of the present study, the incidence of osteopenia and osteoporosis among children with CP is significant and various risk factors are involved in this regard. Therefore, the following suggestions can be made for this category of children:

1. Examining and controlling children with CP and severe delay in walking for BMD and associated disorders
2. Physical and rehabilitation programs, particularly in terms of standing, walking, and other activities associated with weight tolerance
3. Paying particular attention to their performance level, nutrition, and history of anticonvulsant therapy
4. Conducting a study in this regard with treatment interventions to correct nutritional status, implement a standing program, and re-control BMD

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Conflict of Interest

Authors have no conflict of interest.

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