ABSTRACT

Objective: To compare the chronological age and bone age among cerebral palsy patients in the outpatient clinic and its correlation with the type of neurological involvement, gender and functional status.

Methods: 401 patients with spastic cerebral palsy, and ages ranging from three months to 20 years old, submitted to radiological examination for bone age and analyzed by two independent observers according Greulich & Pyle.

Results: In the topographic distribution, there was a significant delay (p<0.005) in tetraparetic (17.7 months), hemiparetic (10.1 months), and diparetic patients (7.9 months). In the hemiparetic group, the mean bone age in the affected side was 96.88 months and the uncompromised side was 101.13 months (p<0.005). Regarding functional status, the ambulatory group showed a delay of 18.73 months in bone age (p<0.005). Comparing bone age between genders, it was observed a greater delay in males (13.59 months) than in females (9.63 months), but not statistically significant (p = 0.54).

Conclusion: There is a delay in bone age compared to chronological age influenced by the topography of spasticity, functional level and gender in patients with cerebral palsy.

Level of Evidence IV, Case Series.

Keywords: Cerebral palsy. Bone age. Age.
chronological age, correlated with the effects of different topographies of spastic CP (tetraparetic, hemiparetic and diparetic), with the influence of functional capacity (community-ambulating, home-ambulating, and not-ambulating) and gender. We also intend to compare the delay in bone age of the affected side compared to the unaffected side in patients with hemiparetic cerebral palsy.

CASUISTRY AND METHODS

Case series

We evaluated children with spastic CP, who were being followed at the Neuromuscular Diseases Clinic and underwent radiographs of the right and left wrists and hands, in anteroposterior incidence. The research was evaluated and approved by the Hospital's Ethics Research Committee (439/09). Radiographs and collection of patient data was authorized by a parent or guardian for each patient. Inclusion criteria were patients with spastic CP, skeletally immature, and therefore excluded children who completed the bone maturity, and presence of those with severe deformities that impair radiographic evaluation. The sample was represented by 450 patients without prior evaluation, of which 49 were excluded due to poor quality or absence of radiographic data in medical records. Of the 401 patients analyzed, 214 (53.3%) males and 187 (46.7%) females. Chronological ages ranged from 3 months to 20 years old (mean and median). Regarding the type of spastic lesion, patients were as follows: 149 were hemiparetic (37.2%), 128 diparetic (31.9%) and 124 quadriparietic (30.9%). Regarding the motor functional status, 182 were community-ambulating (45.4%), 52 home-ambulating (13%) and 167 non-ambulating (41.6%). (Table 1)

Table 1. Distribution of deambulating status among types of CP.

| Type      | CD   | HD   | ND   | Total (%) |
|-----------|------|------|------|-----------|
| Hemi      | 99   | 19   | 31   | 149 (37.2%) |
| Di        | 80   | 30   | 18   | 128 (31.9%) |
| Tetra     | 3    | 3    | 118  | 124 (30.9%) |
| Total     | 182 (45.4%) | 52 (13%) | 167 (41.6%) | 182 |

Source: SAME.

CD: community-ambulating, HD: home-ambulating, ND: not-ambulating, Hemi: hemiparetic, Di: diparetic, Tetra: tetraparetic.

METHODS

The radiographs were evaluated by two independent observers, the bone age of the left and right wrist was determined according to the atlas Greulich and Pyle. The arithmetic mean of the measurements of the two observers was used for comparisons with chronological age. The collected data were distributed in a spreadsheet: hospital records, initial, date of birth, gender, functional status (community-ambulating, home-ambulating, and not-ambulating), chronological age (in months), bone age of the right and left wrist rated by observer 1, and the same for observer 2, the arithmetic mean between observers 1 and 2 regarding bone age of the wrist and the left and right kind of spasticity (hemiparesis, diparesis, and tetraparesis).

Regarding the hemiparetic patients there were recorded separately the affected and not affected sides, since the side without spasticity would be the control group. The status of ambulation was the criterion to assess the severity of spasticity, therefore the impairment in increasing order of severity would be: community-ambulating (1), home-ambulating (2) and non-ambulating (3). It was also determined the influence of gender on the delayed bone age. To assess the qualitative variables, we calculated absolute and relative frequencies; for quantitative variables, we calculated summary measurements. A comparison of the differences between chronological and bone age was performed using the Student’s t test or variance analysis, and the comparison between the bone ages of affected and unaffected sides in hemiparetic patients was performed using the Student’s t test for paired data. Assessment of inter-observer matching was made through the intra-class correlation coefficient. The level of significance adopted was 5% (p < 0.05). The software used was SPSS (Statistical Package for the Social Sciences) version 13.0 for Windows.

RESULTS

Assessment of inter-observer matching resulted in high correlation coefficients with values of 0.995 and 0.994 on the right and left sides, respectively. Given this result, it was possible to confirm the reproducibility of the method to obtain bone age in patients with cerebral palsy between different observers and correlate them with several factors. (Table 2)

When comparing chronological age with the average bone age between the right and left wrist, according to the gender, we observed a delay in males of 13.59 months and in females of 9.63 months, showing only a tendency to a greater difference in males, without statistical significance (p = 0.54). (Table 3)

Table 2. Analysis of matching between observers.

| Type | Mean | St. Dev. | Minimum | Maximum |
|------|------|----------|---------|---------|
| RO 1 | 100.26 | 50.99 | 3 | 228 |
| RO 2 | 100.03 | 51.51 | 3 | 228 |
| LO 1 | 101.49 | 51.00 | 3 | 228 |
| LO 2 | 101.12 | 50.56 | 3 | 228 |

Source: SAME.

RO: right side observer, LO: left side observer. St. Dev.: standard deviation. IOMI: inter-observers matching index.

Table 3. Comparison of bone age and chronological age (in months) distributed by gender.

| Gender | N | CA | RBA | LBA | CA-RBA | CA-LBA | CA-MBA |
|--------|---|----|-----|-----|--------|--------|---------|
| M      | 214 | 115.11 (St.Dev. =47.83) | 101.16 (St.Dev. =51.27) | 101.88 (St.Dev. =50.76) | 13.96 (St.Dev. =23.00) | 13.23 (St.Dev. =22.32) | 13.59 (St.Dev. =22.34) |
| F      | 187 | 109.44 (St.Dev. =48.45) | 98.96 (St.Dev. =51.01) | 100.68 (St.Dev. =50.64) | 10.48 (St.Dev. =18.24) | 8.75 (St.Dev. =18.31) | 9.63 (St.Dev. =18.05) |

Source: SAME.

M: male, F: female, N: number of patients, CA: chronological age, RBA: right bone age, LBA: left bone age, MBA: mean bone age, CA-RBA: difference between chronological age and right bone age, CA-LBA: difference between chronological age and left bone age, CA-MBA: difference between chronological age and mean bone age.
Regarding the topographic distribution of the CP there was a significant delay (p < 0.005) in tetraparetic (17.7 months), hemiparetic (10.1 months) and diparetic (7.9 months) patients. It was also evident a shorter delay in diparetic than in hemiparetic. (Table 4)

In the hemiparetic group, the mean bone age in the affected side was 96.88 months and in the unaffected side 101.13 months. The difference between both sides is statistically significant (p < 0.005). (Table 5)

Regarding the functional status, the non-ambulating demonstrated a significant delay in bone age over the chronological age of 18.73 months (p < 0.005). The delay in community-ambulating was 6.72 months and in the home-ambulating 6.93 months, both showing no statistically significant difference (p=1 in both). (Table 6)

### Table 4. Difference between chronological and bone age (in months) distribution by type of cerebral palsy.

|   | N  | CA         | RBA        | LBA        | CA-RBA     | CA-LBA     | CA-MBA    |
|---|----|------------|------------|------------|------------|------------|-----------|
| Hemi | 149 | 109.10 (St.Dev. =48.29) | 97.73 (St.Dev. =53.24) | 100.28 (St.Dev. =52.20) | 11.37 (St.Dev. =16.87) | 8.88 (St.Dev. =16.00) | 10.10 (St.Dev. =14.94) |
| Di  | 128 | 112.74 (St.Dev. =47.22) | 104.82 (St.Dev. =51.60) | 104.86 (St.Dev. =51.41) | 7.93 (St.Dev. =21.66) | 7.88 (St.Dev. =21.53) | 7.90 (St.Dev. =21.54) |
| Tetra | 124 | 116.25 (St.Dev. =49.02) | 98.18 (St.Dev. =47.93) | 98.92 (St.Dev. =48.11) | 18.06* (St.Dev. =23.41) | 17.33* (St.Dev. =23.31) | 17.70* (St.Dev. =23.02) |

Source: SAME.

### Table 5. Comparison of bone age (in months) between the compromised and non-compromised sides on hemiparetic patients group.

|   | N  | Bone age | Std. Deviation |
|---|----|----------|----------------|
| Compromised | 149 | 96.88 | 53.05 |
| Non Compromised | 149 | 101.13 | 52.33 |

Difference Compromised-Non Compromised 149 -4.26* 7.26

Source: SAME.

* p < 0.005

### Table 6. Difference between chronological age and bone age (in months) by ambulating status.

|   | N  | CA         | RBA        | LBA        | CA-RBA     | CA-LBA     | CA-MBA    |
|---|----|------------|------------|------------|------------|------------|-----------|
| CD  | 182 | 117.32 (St.Dev. =46.65) | 109.86 (St.Dev. =51.18) | 111.35 (St.Dev. =50.31) | 7.46 (St.Dev. =19.21) | 5.98 (St.Dev. =16.66) | 6.72 (St.Dev. =18.64) |
| HD  | 52  | 113.92 (St.Dev. =50.29) | 106.45 (St.Dev. =50.03) | 107.54 (St.Dev. =53.50) | 7.47 (St.Dev. =18.64) | 6.38 (St.Dev. =18.05) | 6.93 (St.Dev. =18.16) |
| ND  | 167 | 106.73 (St.Dev. =48.76) | 84.56 (St.Dev. =47.58) | 88.46 (St.Dev. =47.65) | 19.18* (St.Dev. =21.66) | 18.27* (St.Dev. =21.44) | 18.73* (St.Dev. =21.22) |

Source: SAME.

CD: community-ambulating, HD: home-ambulating, ND: not-ambulating, CA: chronological age, RBA: right bone age, LBA: left bone age, MBA: mean bone age, CA-RBA: difference between chronological age and right bone age, CA-LBA: difference between chronological age and left bone age, CA-MBA: difference between chronological age and mean bone age. (*): p<0.005.

### DISCUSSION

Analyzing the results obtained, we observe that patients with spastic CP showed delayed bone age compared with chronological age. However, these data were based on the book from Greulich and Pyle which could assume that our healthy population could also present this delay due to the socio-economic and cultural reasons. But the fact that we have studied patients with hemiplegia, in which the normal side was the control group, and the fact that we have also observed a delay in the affected side compared to the unaffected, not only corroborates this statement, but we can also correlate with the involvement of non-nutritional factors.

Regarding the severity of spasticity we ranked patients according to ambulating status, despite other methods are available, such as quantifying the degree of skills in the upper limb (QUEST - Quality of Upper Extremity Skills Test). The GMFCS test, one of the most commonly used method in functional ranking of patients with spastic cerebral palsy, was not included in this paper because it is a retrospective study with data collection from the patient’s charts. We are aware about the difficulty to to differentiate between home-ambulating patients and community-ambulating in some cases, but it is a fact for not-ambulating patients. Therefore, we observe a longer delay in bone age of non-ambulating in comparison to ambulating, without evident difference between home- and community-ambulating. Regarding the type of spastic CP we observed a significant delay in bone age between the hemiparetic and tetraparetic and a smaller delay in diparetic. Regarding the non-ambulating status we observe a higher occurrence among tetraparetic (95%) than in hemiparetic (21%) and diparetic (14%). Therefore, the delay in bone age may be related to the fact that the patient does not walk, thus influencing the final outcome of such a comparison. Even so, tetraparetic patients showed a longer development delay, and this may be related to nutritional and non-nutritional factors.

Erickson et al. in a study with 38 patients with hemiparetic CP found no statistically significant difference between chronological age and bone age using the method of Greulich and Pyle, unlike our results. However, the study had a small sample and only one observer. In another study, Gilbert et al. observed no statistical difference between bone and chronological age in patients with tetraplegic paralysis. The authors used to the Fels method to determine bone age, considered by them complex and difficult to apply. Will sometime during the growth bone age in patients spastic CP reaches the normal chronological age? Questions like this point out the need for a longitudinal study to further clarification. Although statistically not significant (p=0.54), males showed a delay compared to females, as described by Marcondes et al. and by Castro et al., probably related to pubertal sexual development in CP affected children. In patients with cerebral palsy spastic hemiparesis has been observed longer delay in the affected side compared to the unaffected.

The results are important, since indications of clinical and surgical treatment should take into account the real bone age, and provide interventions to reduce the backlog of patients with cerebral palsy compared with the general population. For a more detailed study of the causes that potentially influence the rate of development of CP patients it would be necessary to develop an experimental model that controls the inherent defects and neurological impairment.
CONCLUSION

There is a delay in bone age compared with chronological age in patients with spastic CP, influenced by the topographic distribution of spasticity, functional level and gender. Tetraparetic patients had higher delayed bone age compared to hemiparetic and diparetic. It was observed a tendency to a greater delay in males compared to females.

Regarding the functional level, non-ambulating patients showed greater delay in bone age in relation to the chronological age, but no such difference was observed in community-ambulating and home-ambulating patients. We can infer the influence of nutritional and non-nutritional factors on developmental delay in bone age in patients with spastic cerebral palsy.

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