ORIGINAL ARTICLE

Bone mineral density in children. 
Association with musculoskeletal pain and/or joint hypermobility

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Abstract

Objective: joint hypermobility can be associated with benign musculoskeletal pain. The relation between hypermobility and low bone mineral density is still unknown. Osteoporosis can be observed in some genetic syndromes associated with joint hypermobility. The aim of our study was to detect the possible relation between joint hypermobility, benign musculoskeletal pain and bone mineral density in children. Patients and methods: ninety-three children from 5 to 10 years of age were evaluated concerning the presence of joint hypermobility and the presence of musculoskeletal pain based on a questionnaire directed to parents. We also performed densitometry to measure bone mineral density. All children underwent an L2-L4 lumbar bone densitometry.

Results: children were distributed into four groups according to the presence or not of joint hypermobility associated or not with musculoskeletal pain: 29 (31.2%) with hypermobility and pain, 20 (21.5%) with hypermobility and without pain, 22 (23.6%) without hypermobility and with pain and 22 (23.6%) without hypermobility and without pain (control group). Twenty-four children (25.8%) presented reduction in bone mineral density over 10% related to the adequate bone mineral density for age and gender. Bone mineral density was significantly lower in relation to the controls in the following groups: with hypermobility (independently of the presence of pain), with pain (independently of hypermobility), with hypermobility and without pain and without hypermobility and with pain.

Conclusion: bone mineral density may be lower in children with joint hypermobility (independently of musculoskeletal pain) and in children with pain (independently of hypermobility) when compared to controls.


Introduction

Musculoskeletal pain is a common complaint in pediatric practice. Generally it is extra-articular, occurring more often in the lower limbs, typically bilaterally, with deep and diffuse location, and manifests in the evening or at night, having a variable relationship to physical activity and stress.1-3 A family history of benign musculoskeletal pain is usually present.2,4,5 Physical examination as well as laboratory and radiological tests are normal.3
Oster & Nielsen report a prevalence of 15.4% in schoolchildren.\(^1\) The incidence of musculoskeletal pain is greater in the female sex and has its onset during childhood, generally before the age of 5 and with increased intensity between 3 and 5 years of age.\(^2\)

Benign musculoskeletal pain is a diagnosis of exclusion. Organic causes (hematologic, oncological, endocrine, rheumatic, infectious, orthopedic) should be ruled out first.\(^6\) Joint hypermobility is defined as the capacity to perform a series of joint movements with a greater range than normal.\(^7,8\) This can be normal or a benign condition in children\(^6,9\) or can be associated with hereditary diseases of connective tissues such as the Marfan and Ehlers-Danlos syndromes.\(^9-11\)

A number of different criteria and scoring systems have been used in diverse studies for the diagnosis of joint hypermobility. Currently, the criteria defined by Carter and Wilkinson, partially modified by Beighton and Horan, are widely recognized.\(^12,13\) A score of five or more of the nine available points (four bilateral points and one unilateral point) indicates a diagnosis of hypermobility.\(^14\) Forléo et al. observed a joint hypermobility frequency of 36% in 1,005 Brazilian schools.\(^15\)

The hypermobility syndrome is defined by the British Society for Rheumatology (1992) as the presence of arthralgia or musculoskeletal pain with an evolution of at least three months associated with hypermobility.\(^16\) This syndrome has been predominantly recognized in children.\(^9,17-20\) According to Lewkonia, the hypermobility syndrome is one of the most frequent causes of musculoskeletal symptoms in adolescents, particularly girls, aged between 13 and 19 years old.\(^21\)

The association between low bone mineral density (BMD) values and joint hypermobility is still under discussion. Genetic syndromes such as homocystinuria and the Ehlers-Danlos syndrome, which associate with joint hypermobility, can present reduced bone mass.\(^22\) To our knowledge, no evaluative studies of BMD in children with joint hypermobility exist, which is our motivation for performing this study.

Our objective was to detect the possible association between joint hypermobility and changes in the BMD of children with and without musculoskeletal pain.

**Patients and methods**

**Patients**

Ninety-three children between 5 and 10 years old who had received medical care between June 1997 and June 1998 were included consecutively in the case-control study. The children used as control were paired according to sex and age.

The children with musculoskeletal pain (n = 51) were selected from amongst those attending the Pediatric Rheumatology Clinic at our service. The children without pain (n = 42) were screened at the Pediatric Emergency Room of the same institution during consultations for acute pediatric complaints (upper respiratory tract infection, acute gastroenterocolitis, etc).

The children’s guardians were questioned as to the presence of musculoskeletal pain (articular or extra-articular) for more than 3 months, the presence of current or previous illness and the use of medication. Illnesses which affect the calcium metabolism were ruled out, as were hereditary diseases such as the Marfan and Ehlers-Danlos syndrome and chronic pathologies (detected by anamnesis or physical examination). Other exclusion criteria included the use of medications which affect bone mass, children with any degree of pubertal development and those over 10 years old.

**Methods**

**Evaluation of joint hypermobility and of musculoskeletal pain**

For the diagnosis of joint hypermobility Carter and Wilkinson’s criteria, partially modified by Beighton and Horan, were adopted: \(^12,13\)

- a) passive apposition of the thumbs to the flexor aspect of the forearm (two points);
- b) passive dorsiflexion of the little fingers beyond 90 degrees (two points);
- c) hyperextension of the elbows beyond 10 degrees; (two points)
- d) hyperextension of the knees beyond 10 degrees; (two points)
- e) forward flexion of the trunk with knees fully extended so that the palms of the hand rest flat on the floor (one point).

The clinical assessment was performed by two independent examiners in order to increase the reliability of diagnosis. For criteria 3 and 4 a goniometer was used to measure the range of joint movement. The presence of at least five points was considered criterion for the diagnosis of joint hypermobility.\(^15\)

For the diagnosis of musculoskeletal pain a questionnaire was used containing questions about the location, duration and frequency of pain.

The children were distributed into eight groups according to sex and to the presence or absence of joint hypermobility and/or musculoskeletal pain.

**Bone Densitometry**

After clinical assessment, bone densitometry was performed for lumbar vertebrae L2-L4 of each child. The bone mineral density measurements, expressed in grams per square centimeter (g/cm²) and those for the vertebral body area of the lumbar segment L2-L4 expressed in square centimeters (cm²), were obtained using a DEXA unit (Model: DPX, Lunar Radiation Corporation, Madison, Wisconsin,
USA. The densitometer was calibrated daily, with a variation coefficient of 2.0% for the lumbar vertebrae in adults\textsuperscript{23} and the accuracy of the apparatus ranged between 0.5% and 2%. The scan was performed with the patient in a supine position with the lower limbs supported and a 90 degree flexion at the hips.

In order to calculate ideal BMD values for lumbar vertebrae (vertebrae L2-L4) the following formulae were used for all children, as defined in the study by Fonseca et al. who corrected BMD for vertebral area and age\textsuperscript{24}:

\[
\begin{align*}
\text{a) females:} & \quad \text{BMD} = 0.225 + 0.012 \times \text{vertebral area (L2-L4)} + 0.025 \times \text{age (years)}; \\
\text{b) males:} & \quad \text{BMD} = 0.336 + 0.009 \times \text{vertebral area (L2-L4)} + 0.017 \times \text{age (years)}. \\
\end{align*}
\]

The age match control limit (as a percentage of the ideal) was calculated taking into account the relationship between the observed BMD and the ideal one. BMD losses greater than 10% of the ideal BMD, corresponding to osteopenia or osteoporosis, were considered pathological, and each 10% of loss corresponded to one standard deviation.\textsuperscript{25} This study was approved by the local Ethics Committee and performed only after the consent of parents who had previously been informed of its nature was obtained.

The statistical analysis was based on the Mann-Whitney, chi-squared or Fischer tests.

**Results**

Ninety-three preschool and school-aged children participated in the study. Forty-nine (52.7%) of them were female and their ages varied from 5 to 10 years (mean average of 7.3 years). There was a predominance of the Caucasian race (93.5%). Table 1 shows the presence or absence of joint hypermobility associated or not with musculoskeletal pain, according to age and sex.

**Joint hypermobility**

The presence of joint hypermobility was observed in 49 (52.7%) children, of whom 27 (55.2%) were female, with a mean age of seven years, and 91.2% were Caucasian. Five hypermobility points were observed in 14 children (28.6%), six points in 18 (36.8%), seven points in six (12.2%), eight points in eight (16.3%) and 9 points in three children (6.1%) (with a mean of 6.3 points). The mean average of hypermobility points was equal for both sexes (6.3 points).

We did not find any significant difference between the different age groups and the number of joint hypermobility points. Nevertheless, we observed a tendency towards a greater number of points in younger children (less than seven years old).

Amongst the diagnostic criteria for joint hypermobility, the most frequently fulfilled criteria were, in descending order: “passive apposition of the thumbs to the flexor aspect of the forearm” (49 children), “passive dorsiflexion of the little fingers beyond 90 degrees” (48 children) and “hyperextension of the elbows beyond 10 degrees” (45 children).

There was no divergence between the results observed by the two examiners who assessed joint hypermobility.

**Musculoskeletal pain**

Fifty-one children (54.8%) presented musculoskeletal pain, 27 of which were girls (52.9%), with a mean age of 7.4 years and a 90% predominance of the Caucasian race.

With respect to location, 21 children (41.1%) presented diffused pain without any definite location, 11 (21.6%) knee pain, six (11.7%) pain at knees and ankles, three (5.9%) ankle pain, two (3.9%) pain at elbows and ankles and one child (2.0%) presented hip pain. Seven children (13.7%) were unable to specify the location of their pain.

Pain duration was a matter of hours for 15 children (29.4%), of days for 26 (50.9%), and for three children (6.0%) pain lasted weeks. Seven children were unable to specify the duration of their pain.

<table>
<thead>
<tr>
<th>Pain</th>
<th>Hypermobility (n) / mean age (years)</th>
<th>No hypermobility (n) / mean age (years)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M / F</td>
<td>M / F</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 / 6.8 17 / 7.4</td>
<td>12 / 7.8 10 / 7.5</td>
<td>51</td>
</tr>
<tr>
<td>No</td>
<td>10 / 7.3 10 / 6.5</td>
<td>10 / 7.3 12 / 8.0</td>
<td>42</td>
</tr>
<tr>
<td>Total</td>
<td>22 / 7.0 27 / 7.0</td>
<td>22 / 7.5 22 / 7.7</td>
<td>93</td>
</tr>
</tbody>
</table>

Table 1 - Distribution of children regarding the presence or absence of joint hypermobility associated or not with musculoskeletal pain according to sex and age (n = 93)
The frequency at which pain occurred was daily for two children (4.0%), weekly for 11 (21.5%), and between one and three times a month for 31 children (60.8%). Seven children (13.7%) were unable to specify the frequency of occurrence of their pain.

**Bone mineral density**

The BMD (g/cm²) and the average age match level (%) calculated for each group were as follows: group 1 - 0.648/96%; group 2 - 0.635/96.5%; group 3 - 0.677/94.8% and group 4 - 0.674/105.1%.

As we found no significant differences between the two sexes, both were combined for purposes of statistical analysis. Table 2 shows BMD age match levels according to presence or absence of joint hypermobility and of musculoskeletal pain. The comparison between hypermobility and musculoskeletal pain showed that children without hypermobility but with pain exhibit a BMD significantly lower than those without pain. The equivalent comparison when made with the hypermobility group showed no difference. However, by comparing children with and without hypermobility, no significant BMD difference was found for the subgroups with and without pain.

Twenty-four children (25.8%) presented a BMD reduction greater than 10% with respect to the BMD match level for their age and sex (Table 3). The statistical analysis did not reveal any difference between the children with and without hypermobility or between those with and without musculoskeletal pain. However, by applying the chi-squared or Fischer tests to compare each subgroup, we observed that the BMD values were significantly lower in the following groups in relation to the control group (f): with joint hypermobility (a) (p = 0.02), with musculoskeletal pain (c + e) (p = 0.014), with hypermobility but without musculoskeletal pain (d) (p = 0.005) and without hypermobility but with musculoskeletal pain (e) (p = 0.004).

**Discussion**

For this study we selected only children (between 5 and 10 years old) in order to avoid the influence of puberty over bone mass acquisition.

<table>
<thead>
<tr>
<th>Joint hypermobility</th>
<th>Pain (n = 29)</th>
<th>No pain (n = 20)</th>
<th>No joint hypermobility</th>
<th>Pain (n = 22)</th>
<th>No pain (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>F</td>
<td>M</td>
</tr>
<tr>
<td>101.6</td>
<td>93.3</td>
<td>102.4</td>
<td>116.6</td>
<td>89.1</td>
<td>94.6</td>
</tr>
<tr>
<td>94.2</td>
<td>125.2</td>
<td>98.8</td>
<td>121.0</td>
<td>88.5</td>
<td>99.3</td>
</tr>
<tr>
<td>99.3</td>
<td>93.1</td>
<td>91.7</td>
<td>100.0</td>
<td>73.5</td>
<td>115.0</td>
</tr>
<tr>
<td>71.4</td>
<td>110.0</td>
<td>75.6</td>
<td>98.4</td>
<td>104.1</td>
<td>105.9</td>
</tr>
<tr>
<td>103.0</td>
<td>97.0</td>
<td>88.4</td>
<td>115.5</td>
<td>101.9</td>
<td>87.5</td>
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<tr>
<td>94.4</td>
<td>98.1</td>
<td>114.5</td>
<td>88.6</td>
<td>101.8</td>
<td>108.0</td>
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<tr>
<td>86.2</td>
<td>104.6</td>
<td>113.3</td>
<td>74.3</td>
<td>95.3</td>
<td>99.0</td>
</tr>
<tr>
<td>103.3</td>
<td>90.6</td>
<td>79.2</td>
<td>114.5</td>
<td>109.5</td>
<td>81.9</td>
</tr>
<tr>
<td>97.7</td>
<td>107.2</td>
<td>105.3</td>
<td>76.5</td>
<td>102.6</td>
<td>86.3</td>
</tr>
<tr>
<td>84.4</td>
<td>86.8</td>
<td>78.0</td>
<td>79.2</td>
<td>110.1</td>
<td>54.0</td>
</tr>
<tr>
<td>107.4</td>
<td>94.3</td>
<td>92.8</td>
<td>101.9</td>
<td>92.5</td>
<td>85.3</td>
</tr>
<tr>
<td>101.3</td>
<td>100.7</td>
<td>88.5</td>
<td>103.7</td>
<td>98.1</td>
<td>108.7</td>
</tr>
</tbody>
</table>

**Table 2** - Adequacy of bone mineral density according to the presence or absence of joint hypermobility and musculoskeletal pain

Mann-Whitney test (critical z = 1.96), M = male, F = female.

<table>
<thead>
<tr>
<th>Pain</th>
<th>No pain (M+F)</th>
<th>Hypermobility p &gt; 0.05</th>
<th>No hypermobility p &lt; 0.05</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
</tbody>
</table>
The frequency of joint hypermobility found in literature varies from 10 to 36%. The differences between these results could be attributed to ethnic variations, the different age groups studied and the lack of uniformity of the criteria and scoring systems employed.

In the study conducted by Forlêo et al. the frequency of hypermobility varied according to the score employed. When using four or more points, positivity was greatly increased (65.9%), scores of five or more points and three or more criteria yielded frequencies close to those for joint hypermobility (36.3% and 28.1% respectively). For our study we opted to use a five-point score, following the example set by other authors.

With regard to the frequency of the number of hypermobility points, Forlêo et al. observed that just nine in 1,005 schoolchildren (0.9%) presented nine positive points. In our study, we too found a low frequency of nine positive points. As described in literature we observed a tendency towards a greater number of points for younger children. This occurs by virtue of the laxity of ligaments which is a characteristic of this age group.

As to musculoskeletal pain, its association with joint hypermobility was found in other studies. Gedalia et al. found 66% hypermobility in 32 children with “arthralgia/ juvenile episodic arthritis”. In our study, musculoskeletal pain was present in 51 children (54.8%). Of these, 29 (56.9%) also presented hypermobility while 22 (43.1%) only had pain. With relation to the characteristics of the pain, it was diffuse in the majority of the cases (41%). This is in agreement with extant literature which refers to pain which is most frequently extra-articular and to children who cannot specify the precise location of their pain.

The literature does not describe an association between the hypermobility syndrome and bone fractures or alterations in BMD.

This study only assessed healthy children with no use of corticosteroids. Despite this, a reduction of BMD greater than 10% was found for 24 children (25.8%), of whom, 14 (58.3%) had joint hypermobility (six with musculoskeletal pain) and 10 (41.7%) did not present hypermobility (nine with musculoskeletal pain).

Bone mass was considered pathological below one standard deviation, since such losses are indicative of osteopenia.

For the children with hypermobility, we did not find any correlation between a larger number of points and a greater frequency of bone mass reduction or a greater frequency of musculoskeletal pain.

With relation to the control group, we observed statistical differences, i.e. the reduction of BMD occurs predominantly in children with joint hypermobility (independently of pain) and with musculoskeletal pain (independently of joint hypermobility). The comparison of the groups in isolation showed a significant difference in BMD within the group with pain but without hypermobility and in the group with hypermobility but without pain in relation to the control. This leads us to think that, in isolation, both hypermobility and pain can be predisposing factors to a reduction in bone mass.

Table 3 - Adequacy of bone mineral density (%) with reduction greater than 10% in children according to the presence or absence of joint hypermobility and musculoskeletal pain

<table>
<thead>
<tr>
<th></th>
<th>With hypermobility</th>
<th>Without hypermobility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With pain</td>
<td>Without pain</td>
</tr>
<tr>
<td></td>
<td>n=6</td>
<td>n=8</td>
</tr>
<tr>
<td>71.4</td>
<td>86.8</td>
<td>75.6</td>
</tr>
<tr>
<td>86.2</td>
<td>85.3</td>
<td>88.4</td>
</tr>
<tr>
<td>84.4</td>
<td>67.9</td>
<td>79.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>78.0</td>
</tr>
<tr>
<td>Mean</td>
<td>80.3</td>
<td>79.9</td>
</tr>
<tr>
<td>±SD</td>
<td>±8.4</td>
<td>±5.5</td>
</tr>
</tbody>
</table>

Mann-Whitney test

<table>
<thead>
<tr>
<th></th>
<th>With pain x Without pain (M+F)</th>
<th>Without hypermobility p &gt; 0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>With hypermobility</td>
<td>With pain + Without pain p &gt; 0.05</td>
<td></td>
</tr>
</tbody>
</table>

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The statistically lower BMD for children with musculoskeletal pain (independently of hypermobility) comparatively to the control group could be related to a lower level of physical activity, primarily because the child’s family tends to protect them from physical activity in order to attenuate pain or avoid it.

The fact that BMD is statistically lower in children with hypermobility (independently of pain) when compared to the control children, leads us to suppose that structural alterations to connective tissues could be responsible for this fact.

A small number of studies exist about BMD in patients with the Ehlers-Danlos syndrome.22,29,30 Dolan et al. (1998) studied 23 adults with the Ehlers-Danlos syndrome and observed a significant BMD reduction at the head of the femur and in the lumbar vertebrae comparatively to the 23 control patients. These authors justified their findings by ascribing multifactorial causes to them, amongst which are structural alterations to the connective tissues in addition to the reduction of physical activity, which is often recommended by doctors for individuals with this syndrome.22

To our knowledge no studies exist which deal with BMD in children with benign joint hypermobility. In a study with 58 adults with benign joint hypermobility syndrome, despite not having found statistically significant reductions in BMD in relation to the 30 control patients, the authors observed a tendency towards lower values for the head of the femur and lumbar vertebrae in individuals with benign hypermobility syndrome, and this difference was more pronounced below 45 years of age.32

In conclusion, we observed lower bone mineral density in children with hypermobility (independently of the presence of musculoskeletal pain) and in children with musculoskeletal pain (independently of the presence of hypermobility) with respect to the controls. It is possible that structural alterations to the collagen of children with joint hypermobility (independently of the presence of pain) are responsible for these results.

References

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