Osteoporosis/Osteopenia and Hemophilic Arthropathy in Severe Hemophilic Patients

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Abstract

Background: Types A and B hemophilia are coagulation disorders associated with many complications. Osteoporosis is a skeletal condition characterized by the decreased density of normally mineralized bone. This study aims to determine the relationship between osteoporosis and hemophilic arthropathy in severe hemophilia patients over the age of 20 years in Kerman, Iran.

Methods: We performed a cross-sectional study of bone density among 40 male patients with severe hemophilia. Lumbar spine and femoral bone mineral density (BMDs) were measured using a Dual Energy X-ray Absorptiometry (DEXA) scan. The T-scores for BMDs were computed and values from -2.5 to -1 were considered as osteopenia. Those less than -2.5 were considered to be osteoporotic.

Results: About 42% of patients had normal BMD, 50% were osteopenic, and the rest were osteoporotic. The mean BMI, number of arthropathic joints, and the numbers of joint bleeding during the previous year were significantly higher in osteoporotic patients than osteopenic and normal groups (P = 0.05, = 0.003 and = 0.011, respectively). The mean for factor replacement, the number of joint bleeding episodes in the past year, and the number of arthropathic joints were significant independent predictors of both spinal and femoral BMD. Their odds ratios (OR) were 1.29 (factor replacement), 1.17 (numbers of joint bleeding episodes), and 1.73 (number of arthropathic joints), which were significant (P < 0.05).

Conclusion: Our results suggest that men with severe hemophilia have reduced BMD. Patients at risk are those with signs of hemophilic arthropathy. Because osteoporosis may complicate the future treatment of patients with hemophilia, screening of patients with hemophilic arthropathy for reduction of BMD and preventive therapies is highly recommended.

Keywords: Arthropathy, bone density, hemophilia A, hemophilia B, osteoporosis


Introduction

Two main types of severe hemophilia are attributed to the reduction of factor VIII (type A) and factor IX (type B) to an amount less than 1%. As a result of arthropathy and immobilization, osteopenia and osteoporosis are frequently seen in younger adult patients.¹

The Dual Energy X-ray Absorptiometry (DEXA) scan is the best non-invasive method for repeated measurements of bone mineral density (BMD) with a high accuracy rate. The absorption of X-rays is low when using this method.²⁻⁵

In Iran, the prevalence of osteopenia and osteoporosis is high because dairy consumption and physical activities are inadequate, yet consumption of carbonated drinks is high. The purpose of this study is to determine the relationship between osteoporosis and hemophilic arthropathy in patients above 20 years old that have been diagnosed with severe hemophilia (A and B), by using the DEXA scan and patient referrals to the Hemophilia Center in Kerman province, Iran.

Materials and Methods

Patients

A total of 40 severe hemophilic patients above 20 years old were selected for this cross-sectional study from Kerman Province, Iran. Patients with a history of endocrine diseases (thyroid, parathyroid, adrenal, pancreas, and gonads), patients with chronic renal failure, and those with congenital paralysis were excluded from this study.

We completed a form that included demographic characteristics, type of hemophilia (A or B), mean coagulation factor injections in the past year (u/kg), co-morbidity (AIDS, hepatitis B, and hepatitis C) and number of bleeding episodes during the last year. Joints with arthropathy were recorded on the form by physical examination results, and specified in accordance with the Colorado table.¹²

Anthropometric measurements

The weight and height of all patients were measured. Body mass index (BMI) was calculated using the standard formula [weight (kg)/height squared (m²)].

Bone densitometry

Measurement of BMD was performed using a DEXA scan. To assess BMD, the lumbar spine (second to fourth) from the front to the rear side in addition to the femoral neck bone were studied by the scanner, and density values expressed based on g/cm². In the present study, the criteria for osteoporosis as assessed by the World Health Organization (WHO) was used, which meant that a T score of less than -2.5 SD of the standard normal population was
considered as osteoporosis, a T score of -1 to -2.5 SD was classified as osteopenia, and finally those more than -1 were considered normal. T scores compare the maximum peak bone density of the normal population with patients based on reference values.6

Statistical analysis
Descriptive statistics (mean ± SD), student’s t-test, ANOVA test, and logistic regression [to obtain odds ratios (OR)] were used for the presentation of results, as well as to determine the association between BMD and potential risk factors. Data was analyzed by SPSS version 15 (Chicago, IL, U.S.) and P < 0.05 was considered significant.

Results
The range of hemophilic patients’ ages was 20 to 56 years. The average age of patients was 27.73 ± 9.5 years and average BMI was 21.55 ± 5.4 kg/m². There were 30 patients (75%) who had hemophilia A and 10 patients (25%) with hemophilia B. Arthropathic joints in the right elbow was observed in 45% of patients, the left elbow in 30%, the right knee in 82.5%, the left knee in 30%, the right ankle in 40%, and the left ankle in 12.5% of patients. Thus, the most common joint involved was the right knee, while the left ankle had the least involvement. Also, 11 patients (27.5%) had hepatitis C. In this study, 3 patients (7.5%) were osteoporotic, 20 (50%) were osteopenic, and 17 (42.5%) were normal based on BMD results in the femur. Of patients, 33 cases (82.5%) had normal bone density, 7 (17.5%) were osteopenic, and there was no case of osteoporosis noted in the lumbar spine densitometry.

According to the femur BMD area
The difference between mean age and mean factor replacement during the previous year for osteoporotic patients in comparison with osteopenic and normal BMD patients was not significant (P value’s were = 0.24 and = 0.14). The mean BMI, the numbers of bleeding episodes during the last year, and the mean number of arthropathic joints in osteoporotic patients were significantly higher than in the osteopenic and normal BMD groups (P value’s were = 0.048, = 0.003, and = 0.011, respectively) (Table 1).

According to the lumbar spine BMD area
The mean age (P = 0.46), numbers of bleeding episodes during the previous year (P = 0.06), mean number for factor replacement (P = 0.36), and the numbers of arthropathic joints (P = 0.58) between the two groups (osteopenia vs. normal) were not significant. The mean BMI of osteopenic patients was significantly higher than normal patients (P = 0.011; Table 1).

Patients over 40 years old were 2.6 times higher than patients lower than 40 years old in term of the bone density reduction (OR = 2.6, 95%CI = 0.26 to 26.42, P value = 0.4). Patients with hemophilia B have reduced bone density 0.86 times more than type A (OR = 0.86, 95%CI = 0.2 to 3.67, P value = 0.85). We observed that hemophilic patients with hepatitis C were at risk of bone density reduction 1.73 times more than patients who had no other comorbidities (OR = 1.73, 95%CI = 0.6 to 2.9, P value = 0.41). Only three variables of the number of factors, the number of joint bleedings during the last year, and the number of arthropathic joints were significantly associated with bone density reduction. These three variable increased odds of bone density reduction in patients with osteopenia rather than normal patients (OR were equal to 1.29 (P = 0.035), 1.17 (P = 0.011) and 1.73 (P = 0.04, respectively for these three variables).

Discussion
In our study, 42.5% of the patients had normal BMD, 50% were osteopenic, and 7.5% had osteoporosis. In a Bernhard Hospital study in Germany, 43.5% of patients were osteopenic whereas 25.8% were osteoporotic as measured by DEXA scan.7 Also, in a Royal Children’s Hospital study on 19 American children with severe hemophilia, the BMD of their lower limbs were significantly reduced.8 The prevalence of osteoporosis in hemophilic males over 20 years old has been reported as 25.8% in many studies.9

In our study, the average number of hemorrhages during the past year and the number of arthropathic joints was significantly higher in patients with osteoporosis when compared to patients who were either osteopenic or had normal bone density. A total of 37 cases (92.5%) in our study had arthropathy that involved at least one joint. There were 47.5% of patients in our study who suffered from arthropathy in three or more joints. The highest and the lowest involvements were in the right knee joint (82.5%) and left ankle joint (12.5%). The Bernhard Hospital study showed that increased numbers of involved joints and the severity of arthropathy accompanied reductions of bone density in the femur neck. The main

<table>
<thead>
<tr>
<th>Areas</th>
<th>Variables</th>
<th>Normal</th>
<th>Osteopenia</th>
<th>Osteoporosis</th>
<th>P-value</th>
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<td>BMI</td>
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<td>17.7±6.1</td>
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<td>Mean factor replacement during the last year</td>
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<td>31±2.5</td>
<td>29.5±3.5</td>
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<td>Number of arthropathic joints</td>
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<td>2.7±1.1</td>
<td>4±1.82</td>
<td>0.011</td>
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<td>Age</td>
<td>28.2±10</td>
<td>25.3±7.1</td>
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<tr>
<td></td>
<td>BMI</td>
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<td>31.1±2</td>
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<tr>
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<td>Number of arthropathic joints</td>
<td>2.3±1.4</td>
<td>2.7±1.4</td>
<td></td>
<td>0.58</td>
</tr>
</tbody>
</table>

*Any cases based on the lumbar spine were not found in the osteoporosis group. † based on the ANOVA test; ‡ based on student’s t-test. Results shown.
reasons that arthropathy caused osteoporosis were chronic pain and reduction of performance. The Melbourne study showed that children with hemophilic arthropathy had less than normal physical activity that culminated in osteoporosis. Our study was undertaken on different age groups (< 40 years and > 40 years), different types of hemophilia, and patients with co-morbidity (hepatitis B and C, AIDS). Thus, we concluded that the OR between the two groups was not statistically significant. Also in an Indian study carried out on 50 severe hemophilic patients (ages 20–50), the researchers did not find any relationship between hepatitis C and reduced bone density. The Bernhard Hospital study showed that hepatitis C, decreased BMD, and increased age were risk factors for osteoporosis, but it also emphasized the necessity for further studies to clarify whether there was a role for hepatitis C and HIV in the progression of osteoporosis in hemophilia or not.

Osteoporotic patients in our study had significantly higher mean BMI compared to osteopenic and normal bone density patients. Various studies have shown that hemophilic patients have short height, low weight, low activity levels, and other risk factors (such as hepatitis C and HIV). These factors lead to a lower peak bone mass (PBM).

This study demonstrates the high prevalence of reduced bone density (osteopenia or osteoporosis) in hemophilic patients in Kerman, Iran. Annual monitoring of bone with densitometry, increasing physical activities, weight reduction, physiotherapy, surgery to re-mobilize joints, and receiving calcium and vitamin D supplements are highly recommended. Hormone replacement therapy and the use of inhibitors of bone destruction drugs (particularly bisphosphonates) are the treatment of choice, in cases of rapid reductions in PBM according to serial BMD measurements.

We can prevent the complications, reduce the risk, and delay, or prevent the progression of osteopenia to osteoporosis by providing supportive care services and educating patients and their families. We recommend conducting studies with greater numbers of patients in the future.

References