Pattern of Haemarthrosis in Haemophilia

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Abstract

Background: To study the pattern of haemarthrosis and its related complications in patients of Haemophilia A and B.

Methods: Fifty one patients of Haemophilia A and B were evaluated on the basis of patient’s demographic data, history (family, medication, past) and parameters like age, clinical features (pallor, number of joint involved, ankylosis and pain). Blood complete picture, coagulation screening tests, bleeding time, PT, APTT, mixing studies and factor assays were documented.

Results: Haemarthrosis was seen in 86% of the patients, 15.7% patients had single joint involvement. Three to six joints were involved in 43.1%of patients while 11 (21.6%) patients had no joint involvement. Right Knee was the most commonly involved joint(53%). Ankylosis was documented in 12%. Eight percent were using crutches. Haemarthrosis was directly proportional to severity of disease and children under the age of 5 years did not show significant arthropathy.

Conclusion: Haemarthrosis with joint deformities is the commonest manifestation of haemophilia. Treatment with factor concentrate, prophylaxis and physiotherapy can help to prevent new bleeds and allow the synovitis to resolve.

Key Words: Haemarthrosis; Haemophilia A and B

Introduction

Haemophiliias are a group of hereditary genetic disorders characterized by the body's inability to control blood coagulation resulting in bleeding either spontaneously or after a trauma. The estimated number of Haemophiliacs worldwide is 400,000. Haemophiliias being X linked recessive disorders, affect males. Females are carriers which transmit the disease to their sons. Clinically patients present with recurrent, spontaneous, and usually posttraumatic hemorrhages which may involve deep muscles, resulting in hematoma formation, hemarthrosis, and easy bruising. Infants may develop excessive bleeding after circumcision. 1-4

Bleeding in Haemophilia has a special predilection for the joints which may be due to synthesis of tissue factor pathway inhibitor (TFPI) in synovial tissue. Another possible suggestion is low level of tissue factor (TF) expression in synovial tissue. In patients with severe haemophilia the spontaneous bleeding into joints initiates a vicious cycle of bleeding followed by partial healing with synovial thickening and cartilage damage. It leads to a sequence of events of acute and chronic haemarthrosis and acute and chronic synovitis which results in disabling arthropathy. Hemarthrosis (intra articular bleeding) is the most common clinical manifestation of severe hemophilia (70%-%-80%). Although any joint can be involved but typically, hinge joints like knees, elbows, and ankles are most frequently affected as they are weight bearing joints, but bleeds may also occur in the wrist or shoulder joint. Bleeding into the hip joint is unusual. The affected joint is swollen and warm, and held in a position of flexion, with no external discoloration or bruising around the joint (ankylosis).5-8

It is of critical importance to prevent initial joint bleeds, and the resulting synovial hypertrophy and joint destruction. Management of all patients involves a team approach led by the haematologist but including input from orthopaedic surgeons and physiotherapists.9-13

Optimal treatment involves a combination of factor replacement, cryoprecipitate, fresh frozen plasma, rest, ice, and supervised rehabilitation. In certain cases, joint aspiration may be considered under cover of replacement of deficient factor.14,15

In chronic cases radiation synovectomy is recommended. Radiation synovectomy is considered a choice for patients with persistent synovitis of the knee and synovitis of the elbow unresponsive to a 3-month trial of prophylactic factor replacement. If two to three consecutive synoviortheses with 3 to 6 months intervals have been ineffective, or when the radiographic score is more than two points, an open synovectomy is indicated.15 Patients with severe haemophilia, who began prophylactic treatment with clotting factors between 1 and 2 years of age, are likely to have normal joints and able to lead normal lives. 16,17
The target ankle joint is a special challenge as it often develops in very young children when the articular cartilage is susceptible and compliance with conservative treatment is difficult. Continuous prophylaxis from age of 2 to 18 years has been claimed to reduce the incidence of chronic hemophilic synovitis and joint damage. 14

**Patients and Methods**

A total of 51 patients of haemophilia A and B, who attended haemophilia clinic of Pakistan Institute of Medical Sciences, Islamabad, were included. Clinical presentation of the patient which included pallor, pain, the type and site of bleeding, joint involvement, number of joints involved and complications like ankylosis were recorded. Baseline Laboratory tests included blood complete picture, coagulation screening tests including bleeding time, prothrombin time and activated partial thromboplastin time, mixing studies and factor assays were performed. For coagulation assays, venous blood samples were collected in 0.109 mol/L (3.2%) tri sodium citrate in a ratio of 9 parts blood to 1 part anticoagulant and then centrifuged without delay at 1500g for 15 minutes. Prothrombin time (PT), activated partial thromboplastin time (APTT) were carried out on this platelet poor plasma by manual method. Mixing studies were performed using aged and adsorbed plasma, APTT was measured after making 1:1 ratio of patient’s plasma with aged and adsorbed plasma. In mixing studies Hemophilia A patients showed correction of APTT by adsorbed plasma but no correction with aged plasma while correction with aged serum was documented in Haemophilia B patients. Factor assays were performed on automated blood coagulation analyzer CA-500 series.

**Results**

Factor VIII deficiency was documented in 80.3% patients (Hemophilia A), while 9.6% were deficient in Factor IX (Hemophilia B). Thirteen (25%) patients were less than 5 years of age, while maximum number 15 (29%) patients were between 11 to 15 years of age. Haemarthrosis (bleeding in the joints) was the commonest clinical presentation noted in 86% of the patients. Right Knee was the most commonly involved joint, in 52.9% (Table 1). In our study, 5.7% patients had single joint involvement while 27.4% patients had two joints involved. Involvement of 3 to 6 joints was recorded in 43.1%, while 21.6% had no joint involvement (Table 2). Ankylosis was found in 11.8%. Only 7.84% patients were using crutches (Table 3).

<table>
<thead>
<tr>
<th>Joint involvement</th>
<th>Right No(%)</th>
<th>Left No(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip</td>
<td>1(2)</td>
<td>1(2)</td>
</tr>
<tr>
<td>Knee</td>
<td>27(52.9)</td>
<td>20(39.2)</td>
</tr>
<tr>
<td>Ankle</td>
<td>17(33.3)</td>
<td>9(17.6)</td>
</tr>
<tr>
<td>Shoulder</td>
<td>7(13.7)</td>
<td>5(9.8)</td>
</tr>
<tr>
<td>Elbow</td>
<td>19(37.3)</td>
<td>13(35.5)</td>
</tr>
<tr>
<td>Wrist</td>
<td>1(2)</td>
<td>3(5.9)</td>
</tr>
</tbody>
</table>

**Table 1: Involvement of joints in patients of hemophilia (n=51)**

<table>
<thead>
<tr>
<th>Joint involvement</th>
<th>No of patients</th>
<th>Haemarthrosis</th>
<th>No. of Joints involved</th>
<th>Ankylosis</th>
<th>use of crutches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe (&lt;1%)</td>
<td>22</td>
<td>20</td>
<td>2-6(13)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Moderate(1-5%)</td>
<td>19</td>
<td>15</td>
<td>2-6(12)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Mild (&gt;5%)</td>
<td>10</td>
<td>9</td>
<td>2-6(4)</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

*Factor level; p value=0.003%

**Discussion**

Haemophilias A and B are most common inherited bleeding disorder, affecting individuals from all geographical areas. Haemophilia A is more common than B and both cannot be distinguished from each other on clinical grounds. In Pakistan approximately twenty thousand people are living with hemophilia. Lack of awareness among general public, illiteracy, poverty and social taboos are the influences which create gap of access to diagnosis and treatment of Hemophilia. Deficiency in training of medical and paramedical staff and unavailability of factor
Haemophilia B in a study by Borhany et al. 4 Mohsin S patients of Haemophilia A and 23 patients of cases. Hemarthrosis was also documented in 102 patients and permanent disability was seen in 31.62% document that arthropathy was found in 75.21% of the most commonly involved joint(52.9%). Zafar et al also 68.0% were experiencing pain. Right Knee was the in 8.3% of the patients only, while 44.4% of patients from Egypt showed that joint involvement was present of the haemophilia patients. Aznar JA et al, 2009 in Spain observed that 30 % of patients had established hemophilic arthropathy in at least one joint. The reason for this difference in the frequency of arthropathy is the early diagnosis and prophylactic treatment in developed countries.

Haemophilic arthropathy results from mismanagement and under treatment with factor concentrates in developing countries like Pakistan. In our study 86.2% patients had either single or multiple joint involvement. Ankylosis was found in 11.8% and 68.0% were experiencing pain. Right Knee was the most commonly involved joint(52.9%). Zafar et al also document that arthropathy was found in 75.21% of the patients and permanent disability was seen in 31.62% of cases. Hemarthrosis was also documented in 102 patients of Haemophilia A and 23 patients of Haemophilia B in a study by Borhany et al. 4 Mohsin et al reported that Arthropathy was the most frequently (76.4%) occurring complication. Studies from Egypt showed that joint involvement was present in 8.3% of the patients only, while 44.4% of patients had no complication. This was due to prophylaxis given to most of the haemophilia patients. Aznar JA et al, 2009 in Spain observed that 30% of patients had established hemophilic arthropathy in at least one joint. The reason for this difference in the frequency of arthropathy is the early diagnosis and prophylactic treatment in developed countries.

2. Awareness of the problem in general public, medical personnel and paramedics on grass root as well as higher levels and prophylactic factor replacement are the keys to decrease the morbidity and mortality and to achieve the targets in management of haemophilia in the society.

Table 4: Association of factor (FVIII & FIX) levels with age at diagnosis (yrs) in patients of Haemophilia A & B

<table>
<thead>
<tr>
<th>Age at diagnosis (years)</th>
<th>Severe (&lt;1%)</th>
<th>Moderate(1-5%)</th>
<th>Mild(&gt;5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5 years</td>
<td>22</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>6-10</td>
<td>00</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>11-15</td>
<td>00</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>16-20</td>
<td>00</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>21-25</td>
<td>00</td>
<td>00</td>
<td>3</td>
</tr>
<tr>
<td>Total patients</td>
<td>22</td>
<td>19</td>
<td>10</td>
</tr>
</tbody>
</table>

References