Hemophilia A: Pathophysiology and Treatment Strategies

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Hemophilia A: Pathophysiology and Treatment Strategies
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Otterbein University, Westerville, Ohio

Introduction
Hemophilia is a sex-linked recessive disorder that varies in severity. The implications and complications of hemophilia can be life-threatening; pathologic bleeding is usually diagnosed during childhood and adequate management is essential in maintaining health. Advanced practice nurses treat a variety of hemophilia care roles throughout the lifespan as a constant and provide vigilance.

Pathophysiology

Signs and Symptoms
- Common early manifestations are easy bruising in infancy with joint hematomas, upon development to the crawling/walking stages (Srivastava, Brewer, A.K., Mauser-Bunschoten, E.P., et al., 2013; Bleeding can occur in multiple sites, and treatment is adjusted accordingly.

Pathophysiology cont.

At Risk Populations
- Epidemiologic data suggest hemophilia A generally affects males, as it is a sex linked recessive disorder. Signs and symptoms usually are related to ease of housing hemostasis formation early in the lifespan especially during the crawling/walking phase of development (Srivastava, Brewer, A.K., Mauser-Bunschoten, E.P., et al., 2013). The majority of cases are related to inherited bleeding, but 1/3 of new cases are the result of spontaneous genetic mutation without prior family history (Srivastava, Brewer, A.K., Mauser-Bunschoten, E.P., et al., 2013).

Prophylactic Therapy
- Patients with hemophilia A are generally prophylactically treated with intravenous factor VIII with a goal of maintaining factor VIII levels at approximately 50%/d, as this level is associated with significantly decreased risk of spontaneous bleeding (Srivastava, Brewer, A.K., Mauser-Bunschoten, E.P., et al., 2013). The majority goal of hemophilia treatment through early adulthood is to maintain preserved musculoskeletal function and prevent any other sources of major bleeding (Srivastava, Brewer, A.K., Mauser-Bunschoten, E.P., et al., 2013).

Acute Management of Bleeding
- First line treatment of patients with hemophilia A is intravenous factor VIII replacement, and Table I represents the World Federation of Hemophilia's recommended initial target factor VIII levels for specific bleeding processes.

Table 1. Suggested Plasma Factor VIII Peak Level and Duration of Administration, from: Srivastava, A.K., Brewer, A.K., Mauser-Bunschoten, E.P., et al., 2013

<table>
<thead>
<tr>
<th>Type of Hemorrhage</th>
<th>Normal Level (IU/dL)</th>
<th>Time (min)</th>
<th>Peak Level (IU/dL)</th>
<th>Replacement Time (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery (major)</td>
<td>80-100</td>
<td>30-60</td>
<td>80-100</td>
<td>30-60</td>
</tr>
<tr>
<td>Neck/throat</td>
<td>40-50</td>
<td>30-60</td>
<td>40-50</td>
<td>30-60</td>
</tr>
</tbody>
</table>

Table 2. Approximate Frequency of Bleeding at Different Sites, from: Srivastava, A.K., Brewer, A.K., Mauser-Bunschoten, E.P., et al., 2013

<table>
<thead>
<tr>
<th>Site of Bleeding</th>
<th>Approximate Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal</td>
<td>10-20</td>
</tr>
<tr>
<td>Joints (hemorrhagic)</td>
<td>50-100</td>
</tr>
<tr>
<td>Muscles</td>
<td>10-50</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>50-100</td>
</tr>
</tbody>
</table>

Underlying Pathophysiology
Hemophilia A is a sex-linked recessive disorder that affects approximately 1 in 5,000 males born in Europe and North America (Anantheui, 2009). The portion of the gene that correlates to factor VIII production is quite large, and severity of disease is linked to the portion of the gene affected; a functional factor VIII level 1% or less than normal results from drastic deletions of genetic material (Srivastava, 2004).

Clotting Factor VIII
This protein is produced in the liver that plays a major role in the intrinsic pathway of the clotting cascade, and is essentially in activating factor X within the development of prothrombin (Bunschoten & Hall, 2011). Without adequate coagulation and clot formation, hemostasis cannot be achieved and can lead to clotting/blood loss.

Pharmacologic Stress
Table 2 illustrates the relationship of bleeding and factor level. As stated, factor VIII is critically important to the completion of the intrinsic coagulation pathway of hemostasis; without intrinsic activation, the only means of adequate coagulation is dependent upon activation of the extrinsic pathway, namely factor VII (Srivastava, 2011).

Table 3. Relationship of Bleeding Severity to Clotting Factor Levels, from: Srivastava, A.K., Brewer, A.K., Mauser-Bunschoten, E.P., et al., 2013

<table>
<thead>
<tr>
<th>Severity</th>
<th>Clotting Factor Level</th>
<th>Bleeding Episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe</td>
<td>&lt;1 IU/dL (&lt;0.01 mg/L)</td>
<td>spontaneous bleeding into joints or muscles, producing with absence of identifiable hemostatic challenge</td>
</tr>
<tr>
<td>Moderate</td>
<td>1-5 IU/dL (0.01-0.05 mg/L)</td>
<td>occasional spontaneous bleeding: prolonged bleeding with minor trauma or surgery</td>
</tr>
<tr>
<td>Mild</td>
<td>5-40 IU/dL (0.05-0.25 mg/L) or 5-40% of normal</td>
<td>spontaneous bleeding is rare</td>
</tr>
</tbody>
</table>

Additional Considerations/Modalities for Managing
- If administered factor VIII via plasma or recombinant source fails to increase serum factor VIII levels, the patient may require additional therapy.
- If acute bleeding cannot be controlled by the administration of factor VIII, administration of FPP, activated factor VII, and activated partial thromboplastin time is indicated to achieve hemostasis (Kasper, 2004).

Conclusion
Hemophilia A is a disease requiring medical care throughout the lifespan with the possibility of acute exacerbations and accompanying serious illness and disability. As advancements in medical treatment occur, vigilance is needed to adequately manage each patient’s health and wellness. Primary treatment is focused on replacing factor VIII levels and constant collaboration amongst the entire healthcare team and patient.

References