Clinical Management of Hemophilia in Developing Countries

Ampaiwan Chuansumrit, M.D.

Department of Pediatrics, Faculty of Medicine
Ramathibodi Hospital, Mahidol University,
Bangkok, Thailand
Disclosures for:

<table>
<thead>
<tr>
<th>CONFLICT</th>
<th>DISCLOSURE — IF CONFLICT OF INTEREST EXISTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>RESEARCH SUPPORT</td>
<td>Novo Nordisk, Baxalta</td>
</tr>
<tr>
<td>DIRECTOR, OFFICER, EMPLOYEE</td>
<td></td>
</tr>
<tr>
<td>SHAREHOLDER</td>
<td></td>
</tr>
<tr>
<td>HONORARIA</td>
<td>Novo Nordisk, Baxalta, TEM</td>
</tr>
<tr>
<td>ADVISORY COMMITTEE</td>
<td>Novo Nordisk, Baxalta</td>
</tr>
<tr>
<td>CONSULTANT</td>
<td></td>
</tr>
</tbody>
</table>
Hemophilia: Not Uncommonly Found

- Incidence 1: 10,000 population
- Estimated 420,000 patients with hemophilia globally
- 180,000 patients are diagnosed
- Only 50% of all diagnosed patients receiving replacement therapy of factor concentrate
Hemophilia: Not Uncommonly Found

- X-linked recessive inheritance, found in males
- Lack of factor VIII or IX resulting in frequent bleeding at the muscles and joints
- In cases of inadequate replacement therapy, patients often die during childhood period. They cannot reach the adulthood.
Replacement Therapy

Fresh frozen plasma, cryoprecipitate

Heat-treated lyophilized cryoprecipitate

Solvent-detergent treated cryoprecipitate

Factor concentrate
Management of Hemophilia in Developing Countries

- Poor awareness
- Inadequate diagnostic facilities
- Scarce factor concentrates for therapy
- Self-reliance and positive attitude
- Modified strategy of ‘lower-cost treatment’ and ‘low-tech’ intervention
Management of Hemophilia in Developing Countries

• It is difficult to persuade government to use resources for hemophilia. Advocacy based on humanity, solidarity or emotion is not sufficient

• There is a real need to demonstrate that the resources utilized are justified and the treatment regimens are working
Laboratory Diagnosis of Hemophilia A & B

- Prolonged APTT
- Low level of FVIII:C or FIX:C
- Bedside diagnostic kit
Important Issues

• Provide knowledge to patients and parents

• Effective bleeding prevention through daily life-style should be emphasized

• Although replacement therapy is often not available, simple and effective intervention with ‘RICE” can lessen the pain of hemophilic children who have bleeding into the muscles and joints
First Aid Management for Bleeding Episode

R = Rest
I = Ice
C = Compression
E = Elevation
Principle of Treatment

• Prevention of bleeding
  - Avoid trauma, contact sport

• Replacement therapy

• Comprehensive care
  - Rehabilitation
  - Dental care
  - Immunization
  - Infectious & inhibitor screening
  - Genetic counseling
Healthy Diet

- Healthy diet is important, not to gain too much weight that will burden the joint function and create difficulty in venipuncture.
Replacement Therapy

- Episodic bleeding treated in the hospital
- Early bleeding treated at home, nearby health stations or hospitals
- Prophylactic treatment
Replacement Therapy

• Episodic bleeding treated in the hospital
• Early bleeding treated at home, nearby health stations or hospitals
• Prophylactic treatment
Episodic Treatment

Hemophilia without inhibitor

- Using lower dose compared to standard regimen based on guideline of World Federation of Hemophilia (WFH)
- Replacement therapy was initiated when the patients were hospitalized
- Requiring a larger amount of blood components compared to early treatment
Episodic Treatment

Hemophilia without inhibitor

- In cases of emergency surgeries or serious bleeding, risk to volume over load if only FFP were used as replacement therapy

- Risk to recurrent bleeding complication if the raised levels of factor VIII and factor IX were lower than standard levels
# Treatment Guideline

<table>
<thead>
<tr>
<th>Type of bleeding</th>
<th>Level of factor (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
<td>Maintenance</td>
</tr>
<tr>
<td>1. Bleeding at muscle, suture wound, dental procedure*</td>
<td>20-30</td>
<td>–</td>
</tr>
<tr>
<td>2. Deep hematoma, hemarthrosis, large wound</td>
<td>40-60</td>
<td>20-30 (3-7 days)</td>
</tr>
<tr>
<td>3. Bleeding in vital organs, CNS, GI, ileopsoas muscle, and general surgery e.g. appendectomy</td>
<td>80-100</td>
<td>40-50 (1 week)</td>
</tr>
<tr>
<td>4. Major surgery of musculoskeletal, brain surgery</td>
<td>80-100</td>
<td>40-50 (1-3 weeks)</td>
</tr>
</tbody>
</table>

*In case of using fibrin splint, replacement therapy may not be needed*
Episodic Treatment

Hemophilia with inhibitor

- Bypassing agents of activated prothrombin complex concentrate (APCC) and recombinant activated factor VII (rFVIIa) are more expensive compared to factor VIII and IX concentrates
- Using lower dose and few doses of bypassing agents
- Risk to more serious bleeding complications
- Predisposing patients to more morbidity and mortality
- Causing higher treatment cost
Replacement Therapy

• Episodic bleeding treated in the hospital
• Early bleeding treated at home, nearby health stations or hospitals
• Prophylactic treatment
Early Treatment

• At the first sign of tingling sensation associated with early bleeding into muscles or joints

• Immediate after trauma

• When treatment is given early, less blood product was used and less further bleeding occurs compared to delayed treatment
Hospitalized 3-7 days

Absence from work & school

Direct cost: IPD

Indirect cost

Suffering from pain

Morbidity

Transfusion-transmitted diseases

10-24 h before receiving blood components

Significant bleeding

Transport to hospital

ER / OPD

IPD

Early bleeding episode

Infusing factor concentrate at home/nearby hospital

15-60 min

3-12 h

6-12 h

1-3 h

Register at Hemophilia Comprehensive Care Center

Intervention

Process Mapping of Treating Bleeding Episode

Hospitalized 3-7 d

- Absence from work & school
- Direct cost: IPD
- Indirect cost
Exercise to Have Prominent Vein
Patients and Parents

- Exercise to have prominent vein
- Select the venipuncture site and remove the needle while hospitalized
- Practice venipuncture on a model and real vein
Simple Tool for Practicing Venipuncture
Practice Venipuncture in the Hospital
Case Study from Ramathibodi Hospital

- Parents provide proper care to prevent bleeding episodes
- Provide early bleeding treatment at home, nearby health stations or hospitals
  
  - 1-10 years: 250 units every 7 days
  - 11-15 years: 500 units every 10 days
  - 16-20 years: 500 units every 15 days
- Hospitalization
  
  - 1-15 years: 3 hospitalizations per year
  - 16-20 years: 2 hospitalizations per year
# Benefit of Early Treatment among Thai Hemophilia

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients</strong></td>
<td>47</td>
<td>58</td>
<td>59</td>
</tr>
<tr>
<td><strong>Number of patients</strong></td>
<td>15 (31.9%)</td>
<td>30 (51.7%)</td>
<td>40 (67.8%)</td>
</tr>
<tr>
<td>receiving home treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Number of patients</strong></td>
<td>27 (62.8%)</td>
<td>43 (75.4%)</td>
<td>49 (84.5%)</td>
</tr>
<tr>
<td>with unaided proper walking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Proportion of death</strong></td>
<td>14 (29.8%)</td>
<td>8 (13.8%)</td>
<td>3 (5.1%)</td>
</tr>
</tbody>
</table>

I. Evaluation Before and After Receiving Factor Concentrate for Treating Early Bleeding in 2007

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total episode of hospitalization</td>
<td>681</td>
<td>445*</td>
</tr>
<tr>
<td>Episode of hospitalization/case</td>
<td>2.7 ± 3.1</td>
<td>1.8 ± 2.4*</td>
</tr>
<tr>
<td>Days of total hospitalization</td>
<td>3230</td>
<td>1724*</td>
</tr>
<tr>
<td>Days of hospitalization/case</td>
<td>12.8 ± 14.3</td>
<td>6.8 ± 10.7*</td>
</tr>
<tr>
<td>Days of hospitalization/bleed</td>
<td>4.7</td>
<td>3.9*</td>
</tr>
</tbody>
</table>

*P < 0.001

II. Evaluation Before and After Receiving Factor Concentrate for Treating Early Bleeding in 2012

<table>
<thead>
<tr>
<th>Severity</th>
<th>Policy</th>
<th>Life time cost of treatment (THB)</th>
<th>QALY</th>
<th>Cost per QALY</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>No home base care</td>
<td>4,998,017</td>
<td>23.29</td>
<td>214,595</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Home base care</td>
<td>5,225,394</td>
<td>26.11</td>
<td>200,103</td>
<td>80,542</td>
</tr>
<tr>
<td>Moderate</td>
<td>No home base care</td>
<td>13,659,490</td>
<td>16.47</td>
<td>829,504</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Home base care</td>
<td>11,198,618</td>
<td>22.44</td>
<td>499,157</td>
<td>Cost saving</td>
</tr>
<tr>
<td>Severe</td>
<td>No home base care</td>
<td>25,908,099</td>
<td>12.21</td>
<td>2,122,085</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Home base care</td>
<td>20,189,367</td>
<td>20.61</td>
<td>979,557</td>
<td>Cost saving</td>
</tr>
</tbody>
</table>

Replacement Therapy

- Episodic bleeding treated in the hospital
- Early bleeding treated at home, nearby health stations or hospitals

- Prophylactic treatment
  - single dose prophylaxis
  - secondary prophylaxis for 1-3 months
  - long term prophylaxis
Prophylactic Treatment

- Standard dose of prophylaxis 25-40 units/kg three times per week for hemophilia A and twice a week for hemophilia B
- Escalated regimen of 50 units/kg once a week, 30 units/kg twice a week and 25 units/kg three times per week
- Low dose prophylaxis of 8-10 units/kg twice a week* or daily 5 units/kg

Inhibitor to Factor VIII Clotting Activity

Thank you for your attention