TREATMENT OPTIONS IN
THE MANAGEMENT OF
HEMOPHILIA IN
DEVELOPING COUNTRIES

Mammen Chandy
Hematology Department
Christian Medical College Hospital
Vellore, India
© World Federation of Hemophilia, 2005

The WFH encourages redistribution of its publications for educational purposes by not-for-profit hemophilia organizations. In order to obtain permission to reprint, redistribute, or translate this publication, please contact the Communications Department at the address below.

This publication is accessible from the World Federation of Hemophilia’s web site at www.wfh.org. Additional copies are also available from the WFH at:

World Federation of Hemophilia
1425 René Lévesque Boulevard West, Suite 1010
Montréal, Québec H3G 1T7
CANADA
Tel. : (514) 875-7944
Fax : (514) 875-8916
E-mail: wfh@wfh.org
Internet: www.wfh.org

The Treatment of Hemophilia series is intended to provide general information on the treatment and management of hemophilia. The World Federation of Hemophilia does not engage in the practice of medicine and under no circumstances recommends particular treatment for specific individuals. Dose schedules and other treatment regimes are continually revised and new side effects recognized. WFH makes no representation, express or implied, that drug doses or other treatment recommendations in this publication are correct. For these reasons it is strongly recommended that individuals seek the advice of a medical adviser and/or to consult printed instructions provided by the pharmaceutical company before administering any of the drugs referred to in this monograph.

Statements and opinions expressed here do not necessarily represent the opinions, policies, or recommendations of the World Federation of Hemophilia, its Executive Committee, or its staff.

Treatment of Hemophilia Monographs
Series Editor
Dr. Sam Schulman
Table of Contents

Introduction ............................................................................................................................................... 1

Education ................................................................................................................................................. 1
   Educating the family ................................................................................................................................. 1
   Educating healthcare workers and doctors .............................................................................................. 2

Laboratory Diagnosis ............................................................................................................................... 2
   Carrier detection and prenatal diagnosis .................................................................................................. 3

Treatment and Care .................................................................................................................................. 3
   Preventive care ......................................................................................................................................... 3
   Management of joint and muscle bleeds ................................................................................................. 3
   Management of life-threatening bleeds .................................................................................................... 4
   Management of mucous membrane bleeds (gum bleeding and nose bleeds) ........................................ 5
   Dental hygiene and extractions ............................................................................................................... 5

Pharmacologic Options for Controlling Bleeding .................................................................................. 5
   Tranexamic Acid .................................................................................................................................... 5
   Fibrin Sealant (glue) ................................................................................................................................. 5
   Calcium alginate ...................................................................................................................................... 5
   Desmopressin (DDAVP) ......................................................................................................................... 6
   Coagulation factor ................................................................................................................................. 6
   Cryoprecipitate and plasma .................................................................................................................... 7
   Danazol .................................................................................................................................................... 7
   Prednisone ............................................................................................................................................... 7
   Aminoglycosides ...................................................................................................................................... 7

Conclusion ............................................................................................................................................... 7

References ............................................................................................................................................... 8
Introduction

In the Western world today, it is possible for a child with hemophilia receiving adequate treatment to live a near normal life. An accurate diagnosis is quickly established, the family is educated on the management, and the child is put either on prophylactic factor replacement or on-demand replacement given at home. With this type of treatment most children with hemophilia (apart from the small number who develop inhibitors) can go to school, enjoy sports, and expect to have minimal or no joint bleeding.[1] This level of treatment is expensive. In Sweden, for example, it costs US$ 100,000 per year to provide prophylactic factor replacement for one child with hemophilia. However, the cost of providing prophylaxis for all children with hemophilia in the country represents only 0.2% of the national health budget.[2]

This is not the case in most developing countries where the government does not have the resources to buy the necessary quantities of coagulation factors in the face of more urgent health priorities and hardly any patients can afford to pay for their own treatment even for on-demand home therapy.

In this situation hemophilia is managed by using every available option that does not require expensive treatment products. This monograph highlights the various options available when treatment products are extremely scarce, supplementing an earlier WFH monograph entitled The Treatment of Hemophilia Bleeding with Limited Resources, by Dr Shelby Dietrich.[3]

The three major problems with regard to hemophilia care in developing countries are:

- inadequate knowledge;
- lack of facilities for a proper laboratory diagnosis; and
- inadequate supply of affordable, safe factor.

However, even with a limited amount of coagulation factor, it is possible to improve the lives of people with hemophilia in the developing world using some aspects of “ancillary care” that are discussed in this monograph.

Education

When resources are scarce, education is the cornerstone of hemophilia care. This should be the first major emphasis when organizing hemophilia services in developing countries. This includes education for the person with hemophilia and his family, as well as healthcare providers and the population in general. It is not expensive to do and much of the morbidity related to hemophilia in developing countries can be reduced if the person with hemophilia, his family, and his physician know enough about the disease. The World Federation of Hemophilia (WFH) website, at www.wfh.org, is a good source for information both for healthcare providers and people with hemophilia and their families.

Educating the family

After a child is diagnosed with hemophilia, the family should be given a detailed explanation of the nature of the disease and its genetic basis. The WFH publication Hemophilia in Pictures is a good resource for this.[4]

The news that their baby has a genetic disorder with a life long risk of bleeding for which there is “no cure” is devastating for parents, and the family requires a great deal of support and counselling.

After the child has been diagnosed, parents should look at their home anew to see what could be new dangers for their child.
When the child is under three years old the parents should:
- Have the child sleep on a mattress on the floor rather than in a bed when the caregiver is busy in another part of the house;
- In a two-storey home, make sure the stairwell is blocked at the top with a locked half door or safety gate, when the child is upstairs;
- Check that toys have no sharp edges and ensure that there are no sharp instruments, such as scissors, accessible to the child; and
- Use helmets as well as protective pads for knees and elbows to help avoid bleeds.

A child with hemophilia must not receive injections into a muscle. Immunizations are usually given in this way, but can also be given under the skin (subcutaneously). Children with hemophilia should receive all immunizations subcutaneously using a 26-gauge needle with firm pressure applied to the injection site for 3-5 minutes.

When the child is over three years old:
- Use support struts or stabilizers with wheels on either side of the bicycle so that the child does not fall until he can keep his balance, and have the child always wear a helmet.
- Avoid contact sports, encourage the child to take up swimming, badminton, or table tennis instead.

When the child starts school, remember to:
- Always tell the principal and class teacher that the child has a bleeding disorder; and
- Arrange for appropriate activities during the games period.

Living with Haemophilia, by Dr Peter Jones, is an excellent source of information about hemophilia and its management.[5] It should be essential reading not only for people with hemophilia and their families but also for teachers, healthcare workers, and doctors.

Educating healthcare workers and doctors
Most doctors in developing countries do not have enough information on the management of a child with a bleeding disorder. This can be improved by:
- Including a module on hemostasis and the prevention and management of bleeding in the undergraduate curriculum in all medical schools.
- Having guidelines for management of hemophilia, such as the WFH Guidelines for the Management of Hemophilia.[6]

Hematologists in developing countries should use every opportunity (seminars, conferences) to educate other medical personnel on hemostasis and the diagnosis and management of bleeding disorders.

Key points for healthcare workers to remember:
- Treat bleeds quickly (within two hours if possible) to recover more quickly and prevent permanent damage later in life.
- Avoid intramuscular injections, difficult phlebotomy, and arterial punctures.
- Patients should avoid drugs that affect platelet function, particularly acetylsalicylic acid (ASA) and non-steroidal anti-inflammatory drugs (NSAIDs) except certain COX-2 inhibitors.
- Bleeding episodes in the head, neck, chest, and gastrointestinal and abdominal regions are life-threatening and should be treated with clotting factor concentrates immediately if available.

Laboratory Diagnosis
Correct diagnosis of a bleeding disorder can be provided at a cost of US$20 in developing countries if basic laboratory services are available. These services can be developed on a regional basis with limited investment, but training of technical staff and quality control are essential. The WFH offers laboratory training workshops and runs an external quality assurance scheme to help improve laboratory skills. The WFH lab manual Diagnosis of Haemophilia and Other Bleeding Disorders is a useful resource that outlines the basic methods and techniques of various coagulation tests and assays.[7]

Prothrombin time (PT), activated partial thromboplastin time (APTT), and platelet count are the basic screening tests in anyone suspected of having a bleeding disorder. If these are abnormal, the patient should be referred to a hemophilia treatment centre that can make a
complete diagnosis with factor assays, inhibitor screens, and, where necessary, platelet function studies.

**Carrier detection and prenatal diagnosis**
In developed countries, where hemophilia care has progressed to such an extent that a child can live a near normal life with safe and effective therapy, the need for carrier detection and prenatal diagnosis may be less important. However, these services are necessary in developing countries so that individuals and families can be evaluated, informed of their carrier status, and be allowed to make an informed choice on whether they will risk having a baby with hemophilia or not.

If there is an affected family member then the molecular defect can be easily confirmed by DNA studies in the person with hemophilia. This information is used to determine whether the female family member is a carrier.

If a carrier is keen to have prenatal diagnosis because she is sure that she does not want to have a baby with hemophilia then a chorionic villous biopsy is performed at 8-10 weeks of gestation and DNA tests are performed on the tissue to confirm whether the baby is normal, a carrier, or affected. If the baby is affected then the pregnancy is terminated. It is possible to provide a molecular diagnosis of the genetic defect in hemophilia A and B by polymerase chain reaction (PCR) testing and conformation sensitive gel electrophoresis and sequencing at a cost of US$50.[8] Reference centres which can provide genetic services for hemophilia must be established in developing countries and services must be extended to other rare bleeding disorders.

**Treatment and Care**
Since factor replacement therapy is scarce in developing countries, other options for treating and preventing bleeds are necessary.

**Preventive care**
Prevention of bleeding should be the goal. Staying healthy also helps prevents bleeds. This includes:
- Getting regular exercise to promote strong muscles, protect joints, and improve fitness;
- Wearing protection (helmets, protective padding) that is appropriate for the sport or activity;
- Getting regular checkups that include joint and muscle examinations;
- Getting all vaccinations is recommended, including hepatitis A and B;
- Maintaining a healthy body weight to avoid extra stress on joints; and
- Avoiding contact sports, but swimming and cycling with appropriate gear should be encouraged. See the WFH publication *Go for It* for recommended sports.[9]

Physiotherapy to develop strong muscles and thereby prevent bleeding into the joints is an important component of hemophilia care in developing countries.

All patients and their families should have a book of simple exercises and the child as he grows should learn that regular exercise, even when there is no bleeding, is the best prevention. Detailed information is provided in *Physiotherapy in Hemophilia- Exercises to Do at Home* by Genny Dwyer and Alicia Hosking.[10] These exercises do not require any expensive equipment, are very simple to do, and if done regularly can make all the difference.

**Management of joint and muscle bleeds**
When factor replacement therapy is not an option, bleeds can be treated with first aid (rest, ice, and compression) and analgesics. First aid should be started as soon as possible to limit the amount of bleeding and damage.

**First Aid**
**Rest:** Rest in the position of function (a sling for any upper limb bleeds and bed rest for lower limb bleeds). The person should not move the bleeding joint or walk on it.

**Ice:** Data from sports medicine and an experimental study in rats show that ice therapy helps to decrease inflammation and swelling by decreasing leukocyte-endothelial interactions.[11] Ice must be applied over a wet towel intermittently for periods of 5 minutes to achieve a 10-15º C lowering of temperature in the deeper tissues. Ice should not be applied directly to the skin as it can “burn” the skin.
Technique of Ice Application

- Put ice cubes in a cloth and crush.
- Apply on the skin with a thick towel as a wet under-layer.
- Leave for 5 minutes.
- Remove for 10 minutes and repeat.

Application of ice is not useful after 48 hours.

Compression: Joints can be wrapped in a tensor bandage or elastic stocking. This gentle pressure may help limit bleeding and support the joint. Use compression carefully with muscle bleeds if a nerve injury is suspected.

Analgesics
Acetaminophen (paracetamol) can be used at home to relieve acute pain. If the pain is not relieved with acetaminophen alone then any one of the following can be added: propoxyphene, codeine, buprenorphine, or tramadol. See Table 1 for dosage.

Aspirin and NSAIDs should be avoided.

Table 1

<table>
<thead>
<tr>
<th>DRUG</th>
<th>ADULT DOSE</th>
<th>PEDIATRIC DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen (Paracetamol)</td>
<td>500mg -1 g every 4-6 hours</td>
<td>10-15 mg/kg every 4-6 hours (available as syrup)</td>
</tr>
</tbody>
</table>

If the pain is not relieved with acetaminophen alone then add any one of the following:

<table>
<thead>
<tr>
<th>DRUG</th>
<th>ADULT DOSE</th>
<th>PEDIATRIC DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propoxyphene</td>
<td>65 mg every 4-6 hours</td>
<td>Not recommended for children</td>
</tr>
<tr>
<td>Codeine</td>
<td>180-200 mg every 4-6 hours</td>
<td>0.5 –1 mg/kg every 4 hours</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>0.8 mg every 6 hours</td>
<td>Not recommended for children</td>
</tr>
<tr>
<td>Sub-lingual</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol</td>
<td>50-100 mg every 6 hours</td>
<td>Not recommended for children</td>
</tr>
</tbody>
</table>

Factor concentrates
Where some factor is available, a single dose of factor VIII or factor IX (10 IU/kg) may be adequate to stop the bleed. If concentrates are not available then two bags of cryoprecipitate can be given for factor VIII deficiency or one unit of plasma (250 ml) for factor IX deficiency.

Rehabilitation
Once pain and swelling have subsided it is very important to start physiotherapy initially with static exercises. Muscle wasting leads to joint instability and recurrent bleeding in the joint, which can lead to chronic hemophilic arthropathy with synovial thickening and later destruction of the joint surface. In many patients, this can be prevented by physiotherapy.

The use of walking aids (crutches, cane) can also help speed recovery.

Daily exercise to improve muscle strength and maintain joint motion can greatly reduce the frequency and damage caused by joint bleeds.

Chronic joint bleeds
Once a patient develops recurrent bleeding episodes in a particular joint (target joint), permanent damage begins and worsens with each bleeding episode. In the early stages, the synovium becomes chronically inflamed and eventually hypertrophies, causing the joint to appear grossly swollen. If recurrent bleeding continues and is not controlled by other means, synovectomy should be considered.

Radioisotopic synovectomy is the most effective and least invasive procedure. It has the fewest side effects and is done in an out-patient setting. It also requires minimal, if any follow-up physiotherapy. Minimal clotting factor is required.

Management of life-threatening bleeds
Bleeding episodes in the head, neck, chest, and gastrointestinal and abdominal regions are potentially life-threatening and should be treated with factor concentrates immediately.
Management of mucous membrane bleeds (gum bleeding and nose bleeds)
Whenever a clot forms, the body attempts to break it down within the vessel so that blood flow can be restored. This process of clot breakdown called fibrinolysis is very active on mucous membrane surfaces. In people with hemophilia this process can prevent a bleed from stopping. Fibrinolysis can be inhibited by drugs, and of these tranexamic acid is the most widely used.

Most mucous membrane bleeds can be controlled with the correct use of this agent. Since the drug is absorbed from the buccal mucous membrane and then secreted into the saliva, hemostasis is better achieved with a mouthwash than if the tablet is swallowed. Where the mouthwash is not available, tablets can be dissolved in 10 ml of water and the solution kept in the mouth for as long as possible and then swallowed. For an adult 1 g is administered every 6 hours and the dose for a child is 20 mg/kg.

Cost-effective use of tranexamic acid to control oral bleeding in hemophilia

1. Crush two 500-mg tablets in 10 ml of water.
2. Keep the solution in the mouth for as long as possible (approximately 5 minutes).
3. Swallow the solution.

For very young children the tablet can be made into a paste and applied directly to the site of bleeding.

Nose bleeds can be controlled by gently packing the nostril with gauze soaked in a solution of tranexamic acid made from the tablet as for gum bleeding. When the nasal bleeding has stopped the gauze must be thoroughly soaked with saline and gently removed. Bleeding will start again if the gauze is removed forcibly so it must be so well soaked with saline that it literally falls out on its own.

Dental Hygiene and Extractions
Patients with hemophilia in developing countries must recognize very early that dental hygiene is extremely important. Regular brushing of teeth twice daily, even if there is mild bleeding, will help to prevent dental caries.

Dental extractions can be performed with a single dose of 15 units/kg of factor VIII and tranexamic acid (see dose above) administered before and for 5 days after the extraction.[13]

Fibrin sealant can prevent bleeding after tooth extraction, reducing the need for clotting factor administration.

Pharmacologic Options for Controlling Bleeding

Tranexamic Acid
Tranexamic acid is an antifibrinolytic agent that inhibits the activation of plasminogen to plasmin. It promotes clot stability and is useful as adjunctive therapy in hemophilia. It is valuable in controlling bleeding from mucosal surfaces (e.g., oral bleeding, epistaxis, menorrhagia) in hemophilia. (see “Management of mucous membrane bleeds” section for dosage.)

In a study by Sindet-Pedersen et al, 29 patients on oral anticoagulants following cardiac surgery were randomized: 19 received treatment with a 4.8% solution of tranexamic acid as a mouth wash and 20 received a placebo prior to dental extraction. There was only one episode of bleeding in the treated group compared to 10 episodes in the placebo group.[13,14,15]

Fibrin sealant (glue)
Fibrin sealant has hemostatic, sealing, and healing properties. It is made by mixing fibrinogen and thrombin, which mimics the last step in the blood coagulation cascade. A semi-rigid fibrin clot consolidates and adheres to the application site and acts as a fluid-tight sealing agent able to stop bleeding.[16]

Fibrin sealant can be used for dental extraction,[17] circumcision,[18] and to stop bleeding from mucous membranes. Commercially available fibrin sealants (Tisseel – Baxter, Beriplast – Aventis) are prohibitively expensive at around US$130 for a 1-ml kit. However, it is possible to devise a simple delivery system and use cryoprecipitate as the
source of fibrinogen and “manufacture” fibrin sealant at a much lower cost.[19]

**Cost-effective method for local manufacture fibrin sealant**

1. Seven ml of wet cryoprecipitate is taken with 3 ml of a 500 mg/10 ml solution of tranexamic acid in one syringe.
2. Bovine thrombin in 10 ml of water for injection concentration of 50-1000 units/ml is taken with 6 ml of calcium chloride and 100 mg of gentamicin in the other syringe.
3. The two syringes are fixed onto a dual delivery system which simultaneously injects the contents of both syringes to the bleeding/surgical site.

**Calcium alginate**

There are several hemostatic agents in the dry form. Sailors and seaweed collectors have known for ages of calcium alginate’s ability to stop bleeding and heal wounds. Calcium alginate is a polysaccharide that can be extracted from brown seaweed and made into fibers for swabs. When this material comes into contact with biological fluids, calcium alginate exchanges its Ca++ ions with Na+ ions from the blood and gels. Several studies have shown a hemostatic effect of this material, which can be used for epistaxis.

**Desmopressin (DDAVP)**

DDAVP is a synthetic analogue to the natural hormone arginine-vasopressin 1-deamino-8-D-arginine vasopressin (desmopressin). It causes release of von Willebrand factor (vWF) from endogenous stores in the endothelial cells and is effective in mild/moderate hemophilia and Type 1 von Willebrand disease (vWD) but is not effective in Type 2 and Type 3 vWD as there is no functional vWF. It is contraindicated in 2B and pseudo vWD.

The main advantage is that it is inexpensive and there is no risk of blood-borne viral infections. The effect lasts for 6-8 hours and in a given patient is consistent on different occasions. It is available in intranasal or intravenous (IV) forms. IV preparation strength is 4 µg/ml and this can also be given subcutaneously with the same effect. There is a two- to sixfold increase in the vWF activity and factor VIII level within 15-30 minutes after administration. The usual dose is 0.2-0.3 µg/kg IV in a volume of 50-100 ml over 30 minutes. For subcutaneous injection it is given at the same dose with a volume of <1.5 ml/site.

Two intranasal preparations are available: 100 µg/ml used for Diabetes Insipidus (no significant increase in vWF) and 1.5 mg/ml used in vWD (dispensed as 2.5 ml which contains 25 doses of 150 µg). The intranasal dose for patients <50 kg is 150 µg (one spray) and for patients over 50 kg ~300 µg (two sprays). Thirty minutes after administration, the bleeding time or closure time is to be checked to document the effectiveness. The intranasal dose produces an effect which is equivalent to the IV preparation.

The main side effects of DDAVP include: flushing, fluid retention, hyponatremia, seizure activity in infants, thrombocytopenia in Type 2B and platelet type vWD, palpitations, and abdominal cramps. Tachyphylaxis may occur on repeated dosing. DDAVP should not be administered in people with coronary artery disease, elderly persons, and pregnant women.

DDAVP can be used to control minor bleeds and to control menorrhagia in vWD. Tranexamic acid should be administered concomitantly since plasminogen activators are also released from the endothelial cells by DDAVP.[20] The platelet closure time (PCT) may be a good way to monitor response to DDAVP in Type 1 vWD.[21,22]

**Coagulation factor**

Provision of some safe and affordable coagulation factor concentrates is essential for major bleeding and surgery. Life-threatening bleeds in the central nervous system, upper airways, etc. cannot be adequately managed without coagulation factor concentrates. Low dose strategies for surgery in developing countries have been shown to be effective with acceptable rates of bleeding.[23]

When the purchase of large amounts of factor is negotiated through governments in developing countries, it is possible to procure intermediate-purity concentrates at a cost of US 10-20 cents per unit.
Cryoprecipitate and plasma
Cryoprecipitate, fresh frozen plasma (FFP), and cryo-poor plasma are the only affordable treatment options in many developing countries. However, they are usually not treated to eliminate blood-borne viruses. (It is possible to apply some forms of virucidal treatment to packs of FFP, and the use of treated packs is recommended.) Because of the risk of transmitting disease, the use of plasma and cryoprecipitate which has not been viral inactivated should be considered a temporary measure until adequate amounts of safe concentrates can be procured.

Danazol
In a study by Gralnik et al, 200 mg of danazol was administered three times daily to 4 adults, 2 with hemophilia A and 2 with hemophilia B. In those with hemophilia A, their factor VIII level rose from 1-3% to 3-8% and in those with hemophilia B the factor IX level rose from 5% to 14%. The level rose within 5-7 days and peaked at 7-13 days.[24] This agent may be useful for short-term administration following a central nervous system (CNS) bleed when recurrence risk is high and for a target joint with recurrent hemarthrosis. It is also useful to control intractable uterine bleeding in females with vWD.

Prednisone
Macroscopic upper hematuria, i.e. originating from the kidneys, can be resolved with corticosteroids. This was shown in a series of cases in 1965.[25] and there are also anecdotal positive experiences from other centres, however a more recent study failed to show any benefit of adding steroids to treatment with factor concentrate.[26] Treatment can be given as prednisone 0.5 mg/kg bodyweight daily for 5 days, then 0.25 mg/kg for another 5 days. The advantages of prednisone compared to factor concentrates are the much lower cost and absence of renal colic from blood clots passing down via the ureter.

Aminoglycosides
Clinical severity of hemophilia depends on the nature of the underlying mutations. Nonsense mutations account for about 11.5% of all hemophilia A and B, resulting in a premature stop codon. In addition, 5% of the mutations are frameshifts that can possibly lead to a premature stop codon. A slight increase in factor level (>1% of normal coagulant activity) can result in marked clinical improvement.

Aminoglycosides, such as gentamycin, can increase factor levels in patients with point mutations, especially those with nonsense/frameshift mutations due to premature stop codons. Aminoglycosides act by incorporation of alternative amino acids at stop codons, thereby producing some normal functional protein. The efficiency of ‘read through’ depends on the type of stop codon (TAA, TAG, TGA).

Aminoglycosides have been proven effective in cystic fibrosis and Duchenne’s muscular dystrophy. At present they are being tried in hemophilia at a dose of 7.5 mg/kg/day for children and 5 mg/kg/day for adults for 14 days.

Side effects include colonization with resistant organisms and renal and auditory toxicity. These have to be monitored closely. These drugs may elevate factor levels in the short term to cover specific periods like physiotherapy after joint surgery. The use of aminoglycosides and similar small molecules is still experimental, only tested in mouse models[27] and in limited clinical trials,[28] and cannot be recommended for use outside of a clinical trial.

Conclusion
Even with a limited amount of coagulation factor concentrates, it is possible to improve the lives of people with hemophilia in developing countries through education, prevention, and ancillary care. National hemophilia societies in developing countries have a great role to play in increasing awareness, education, and family support of patients with hemophilia. Doctors and other healthcare providers can maximize care by coordinating a national plan for hemophilia services that emphasizes education, physiotherapy, laboratory diagnosis, and simple measures to manage bleeds, along with a supply of safe concentrates.[29] This will go a long way to improving the lives of people with hemophilia in developing countries.[30,31]
References


