WFH
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Chapter 6 PROPHYLAXIS IN HEMOPHILIA

Manuel Carcao, H. Marijke van den Berg, Emna Gouider, Kate Khair, Manuel A. Baarslag, Lisa Bagley, Francisco de Paula Careta, Rolf C. R. Ljung, Margaret V. Ragni, Elena Santagostino, Glenn F. Pierce, Alok Srivastava

RECOMMENDATIONS

6.1 | Introduction

Recommendation 6.1.1

For patients with hemophilia A or B with a severe phenotype (note that this may include patients with moderate hemophilia with a severe phenotype), the WFH strongly recommends that such patients be on prophylaxis sufficient to prevent bleeds at all times, but that prophylaxis should be individualized, taking into consideration patient bleeding phenotype, joint status, individual pharmacokinetics, and patient self-assessment and preference.

• REMARK: Individualizing prophylaxis means that if patients continue to experience bleeds, their prophylaxis regimen should be escalated (in dose/frequency or both) to prevent bleeding.

• REMARK: In countries with significant healthcare constraints, the WFH still advocates for the use of prophylaxis over episodic therapy but recognizes that less intensive prophylaxis may be used. **CB**

Recommendation 6.1.2

For pediatric patients with severe hemophilia A or B, the WFH recommends early initiation of prophylaxis with clotting factor concentrates (standard or extended half-life FVIII/FIX) or other hemostatic agent(s) prior to the onset of joint disease and ideally before age 3, in order to prevent spontaneous and breakthrough bleeding including hemarthroses which can lead to joint disease. **CB**

Recommendation 6.1.3

For adolescents and adults with hemophilia who show evidence of joint damage and have not as yet been on prophylaxis, the WFH recommends commencing tertiary prophylaxis in order to reduce the number of hemarthroses, spontaneous and breakthrough bleeding, and slow down the progression of hemophilic arthropathy. **CB**

6.2 | Benefits of prophylaxis

Recommendation 6.2.1

For patients with severe phenotype hemophilia A or B, especially children, the WFH recommends regular long-term prophylaxis as the standard of care to prevent hemarthrosis and other spontaneous and breakthrough bleeding, maintain musculoskeletal health, and promote quality of life. When prophylaxis is not feasible, episodic therapy is essential treatment for acute hemorrhages, but it will not prevent long-term joint damage.

• REMARK: In the long term, early and regular prophylaxis for children reduces hemarthrosis and other hemophilic bleeding, produces better health and joint outcomes, reduces the number of hospital visits and admissions, and may avert the need for orthopedic interventions, including surgery, in the future. **CB**

6.3 | Standard half-life factor prophylaxis

Recommendation 6.3.1

For patients with severe phenotype hemophilia A or B, prophylaxis with clotting factor concentrates (either standard or extended half-life) is recommended at a dose and dosing interval (dependent on the pharmacokinetic [PK] properties of the clotting factor concentrate) that allow them to at all times have sufficient circulating factor to prevent hemarthrosis, and spontaneous and breakthrough bleeding, based on their individual needs and lifestyles and preserve musculoskeletal function.

• REMARK: In the past, a trough factor level of 1 IU/dL (1%) was deemed an adequate goal. Now recognizing that with a 1% trough level, patients remain at risk of bleeding, most clinicians would prefer to target higher trough levels (>3%-5%, or higher). Recent studies show that such trough levels achieve less bleeding. However, the trade-off is that higher trough levels may require higher doses or more frequent infusions of clotting factor concentrates. This should therefore be personalized based on the individual ' s activities, lifestyle, and PK handling of factor. **CB**

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Recommendation 6.3.2

For patients who are adherent to their prescribed prophylaxis regimen but still experience breakthrough bleeds, the WFH recommends escalation of prophylaxis with measurement of trough levels and, if required, orthopedic interventions as appropriate.

• REMARK: Any patient who fails to respond to adequate factor replacement therapy after past responsiveness should be tested for inhibitor development prior to escalation of therapy. CB

6.4 | Extended half-life factor prophylaxis

Recommendation 6.4.1

For patients with severe phenotype hemophilia A or B using EHL FVIII or FIX concentrates, the WFH recommends prophylaxis with EHL clotting factor concentrates at sufficient doses and dosing intervals to prevent hemarthroses and spontaneous and breakthrough bleeding and preserve joint function. CB

6.5 | Prophylaxis with non-factor replacement therapy

Recommendation 6.5.1

For patients with severe phenotype hemophilia A without inhibitors, prophylaxis with emicizumab will prevent hemarthrosis, spontaneous, and breakthrough bleeding.

• REMARK: The WFH however notes that there are very little longterm data on patient outcomes with such an approach and recommends that such data be obtained. CB

6.6 | Fixed/non-tailored factor prophylaxis regimens

Recommendation 6.6.1

For patients with moderate/severe hemophilia A or B, especially those who have experienced a life-threatening bleed (e.g., intracranial hemorrhage [ICH]), the WFH recommends prophylaxis with FVIII or FIX concentrates or with a non-factor therapy (e.g., emicizumab for hemophilia A) in order to prevent a recurrent life-threatening bleed. This is particularly important during the first 3-6 months following an ICH as the risk of recurrence is highest during this period.

• REMARK: As inhibitor development is associated with intense exposure as would occur in the setting of an ICH, such patients require good clinical monitoring of treatment response and frequent laboratory testing for inhibitors. CB

Recommendation 6.6.2

For patients with hemophilia and venous access difficulties that impede regular clotting factor concentrate infusions, the WFH recommends insertion of a central venous access device (CVAD) to facilitate prophylactic clotting factor concentrate infusions. Another currently available option is the use of emicizumab while in the future there may be other subcutaneous non-factor therapies that become available. CB

6.8 | Adherence and patient/caregiver education

Recommendation 6.8.1

For patients with severe phenotype hemophilia A or B on prophylaxis, the WFH recommends that patients/caregivers be taught to maintain timely and accurate records of bleeding episodes and treatment and be followed in hemophilia treatment centres. CB

6.10 | Low- dose prophylaxis for patients with limited access to CFCs

Recommendation 6.10.1

For patients with severe phenotype hemophilia A or B in countries with healthcare constraints, the WFH still strongly recommends prophylaxis (even when the only option is using lower factor doses) over episodic factor therapy to reduce hemarthroses and other spontaneous and breakthrough bleeding and better preserve joint function. CB

CB, consensus based; CVAD, central venous access device; PK, pharmacokinetics; EHL, extended half-life.

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