Haemophilia Management: Achieving the Best Possible Care for Previously Untreated Patients

A Factor Think Tank Podcast Series

Slide summary

Disclaimer

- The Factor Think Tank is an educational activity funded by Sobi. The Factor Think Tank podcast series, Haemophilia Management: Achieving the Best Possible Care for Previously Untreated Patients, was developed by the Factor Think Tank working group
  - All views and opinions expressed in the podcasts are those of the participants only
  - As situations for families affected by haemophilia vary globally, information in the podcasts should be considered in relation to the situation prevailing in the country in which it is intended to be applied

- This accompanying slide deck complements the information in the podcasts and is only intended for HCPs; its content is based on an article by Astermark, et al., from which more detailed information can be obtained
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Date of preparation: June 2024

HCP, healthcare professional

Astermark J, et al. Ther Adv Hematol. 2023;14:20406207231165857

Introduction

- A review article,[1] published in *Therapeutic Advances in Hematology*, provides information to help guide management of PUPs with haemophilia

- The paper considers information for HCPs to provide to affected families to help facilitate shared decision making; it covers discussions relating to pregnancy and birth, as well as the early years of life for infants with haemophilia A or B who require primary prophylaxis

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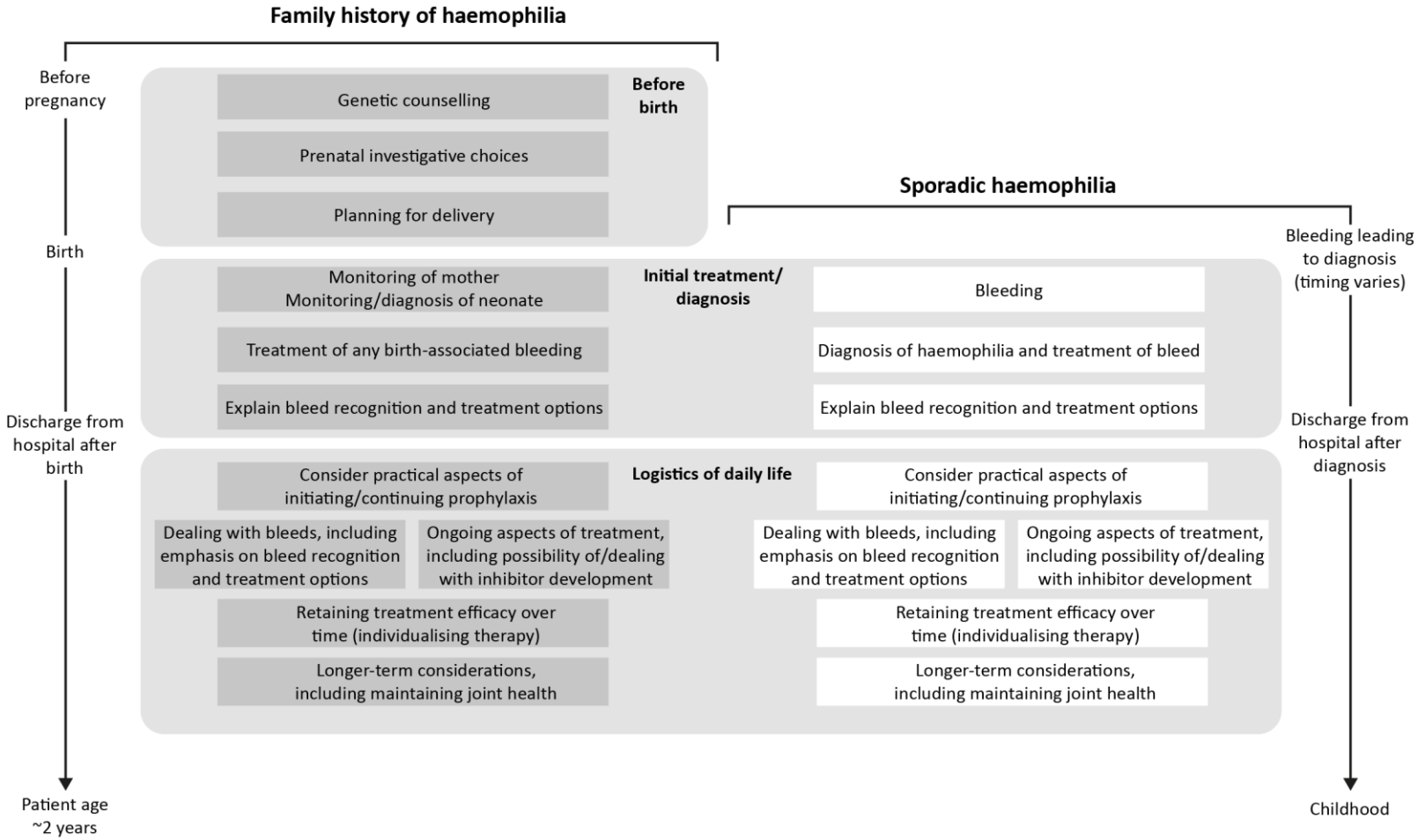
HCP, healthcare professional; PUP, previously untreated patient

1. Astermark J, et al. Ther Adv Hematol. 2023;14:20406207231165857

Management of PUPs who will require prophylaxis



PUP, previously untreated patient

Figure from Astermark J, et al. Ther Adv Hematol. 2023;14:20406207231165857.

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Podcast series

- Based on the themes in the review article,[1] an educational podcast series has been produced for HCPs

This slide deck provides information to support this podcast series, entitled:
Haemophilia Management: Achieving the Best Possible Care for Previously Untreated Patients

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Haemophilia management: achieving the best possible care for previously untreated patients

- The podcast series, hosted by Assoc. Prof. Christoph Königs, contains four episodes, each with a different chair:

Episode 1. Counselling and diagnosis

Dr Jayashree Motwani: a Consultant Paediatric Haematologist at Birmingham Children's Hospital, and also the lead for haemostasis and thrombosis, and Centre Director at the Haemophilia Comprehensive Care Centre, Birmingham, UK

Listen to podcast

Episode 2. Initiation of treatment

Prof. Jan Blatný: a Consultant Haematologist at the Department of Paediatric Haematology and Biochemistry and Director of the Haemophilia Comprehensive Care Centre, University Hospital Brno, Czech Republic, Associate Professor of Paediatrics at Masaryk University, Brno, and a Clinical Lead for internal medicine outpatient services at Hospital Bory, Bratislava, Slovakia

Listen to podcast

Episode 3. Safety and logistical challenges

Assoc. Prof. Víctor Jiménez-Yuste: an Associate Professor of Medicine at the Autónoma University, Madrid, and Head of the Haematology Department at the Hospital Universitario La Paz, Madrid, Spain

Listen to podcast

Episode 4. Optimising the treatment

Assoc. Prof. Christoph Königs: works closely with patients and their families at the Paediatric Haemophilia Centre, University Hospital Frankfurt, Germany, where he leads the Clinical and Molecular Haemostasis research group

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The following slides include key points to be considered to help inform management decisions

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Counselling

- Different approaches are required for families with a history of haemophilia and those affected by sporadic cases (which comprise around one-third of affected individuals)
- Family history enables various prenatal considerations, including
  - Genetic counselling (and preimplantation diagnostics, if appropriate)
  - Prenatal investigations (available choices for which vary between different countries)
  - Management of women and unborn children during pregnancy
  - Planning for birth
- In cases of sporadic haemophilia, prompt diagnosis is important
  - The timing of diagnosis will vary according to bleed presentation
  - Sudden diagnosis is liable to compress timelines for parental discussion and disease education

Families of all children with haemophilia will benefit from appropriate psychological and practical support

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Pregnancy and birth (haemophilia family history)

- During pregnancy, regular assay of FVIII/FIX levels will inform knowledge of bleeding risk
  - Unlike FIX, FVIII increases during pregnancy but, together with VWF, can decrease rapidly after birth
- Advance delivery planning (which includes developing written plans) involves:
  - Providing a home supply of factor concentrate, to help address any relevant pre-term complications
  - Considering choice of hospital and atraumatic mode of delivery, as well as a mother's potential haemostatic treatment and route of anaesthesia; planning for treatment of the newborn, including in relation to heel pricks, routine vaccinations and vitamin K administration
- Babies should be carefully monitored during birth, thoroughly examined afterwards, using US to detect ICH, and mothers monitored to detect PPH, with any specialist treatment provided as necessary

Children with haemophilia are being born into a world where management and treatment options can help to achieve the best possible outcomes, aiming for quality of life comparable to individuals without haemophilia

FVIII, factor VIII; FIX, factor IX; ICH, intracranial haemorrhage; PPH, post-partum haemorrhage; US, ultrasound; VWF, von Willebrand factor

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Diagnosis

- In children born to those with a family history of haemophilia, cord blood testing can be used to facilitate diagnosis within hours of birth
  - Repeat testing, using blood from a peripheral vein, may be appropriate if there could be contamination from maternal blood or FVIII/FIX levels fall outside the expected range (considering a family index case)
  - For mild haemophilia A, as FVIII levels can rise due to the acute-phase response at birth, repeat testing may be necessary when a baby is around 6 months old; repeat testing may also be necessary to diagnose mild haemophilia B, due to reduced FIX levels at birth
- Sporadic haemophilia is diagnosed as a consequence of infant bleeding (variable timing)
- While attention has tended to focus on boys with haemophilia, there is now increased appreciation of the value of prompt diagnosis in both boys and girls

Prompt diagnosis is important to ensure optimal management and ameliorate consequences of bleeding

FVIII, factor VIII; FIX, factor IX

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Bleeds

- In neonates and infants, bleeds manifest differently than in older children
- Bleeds in early infancy include
  - Soft tissue/intramuscular haematomas, which can be difficult to recognise, but may present with pain, swelling and/or loss of movement
  - Oral/nasal bleeding, in which those affected can swallow a lot of blood
  - Head injuries, which may be evident as a consequence of somnolence or feeding difficulties, and for which immediate attention should be sought
- Joint bleeds, characteristic of haemophilia, tend to occur after young children become more mobile (for example, after starting to crawl)
  - These can affect patterns of movement or have less specific symptoms such as inconsolable crying

If parents have any doubt about bleeding, they should seek prompt advice, including out-of-hours assessment

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Initiating treatment

- For haemophilia patients with a severe bleeding phenotype, primary prophylaxis is the standard of care; this should start before a clinical joint bleed or detectable joint damage is evident, and before 2 years of age
- Parents should be helped to understand the benefits of this, in terms of bleed protection, joint health and long-term consequences for quality of life
  - Discussions about prophylaxis may include mention of venous access, possible use of central venous access devices, and home treatment
  - Parents should also be aware that although prophylaxis reduces the risk of bleeding, it does not completely abolish this; physicians can help parents to recognise breakthrough bleeds and appreciate the importance of early intervention

By providing appropriate information to families, HCPs can help to facilitate timely initiation of prophylaxis in countries where this is available

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Treatment options

- HCPs can help to educate parents by informing them of the treatment options for their child in relation to both prophylaxis and bleed treatment, with reference to local/national guidelines and product availability
- Options include standard half-life clotting factors, extended half-life clotting factors and non-factor therapy
  - It is important to explain the different mechanisms of action of these products, as well as their modes of administration and other practical differences relating to use
  - Product availability should be taken into account
- Therapeutic choice can be guided by individuals' preferences

Educating parents of young children helps to inform shared decision making

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Safety

- While available treatment options have reassuring safety profiles, as shown by clinical trial and real-world data, for the youngest individuals supporting evidence is more limited
  - Compared with well-characterised treatments, further information is required relating to adverse events associated with newer therapies
- As a relevant serious treatment complication of replacement therapy, parents should be informed of the possibility of inhibitor development and consequent therapeutic compromise
- As factor therapy is required to treat bleeds, tolerance is important
  - Early intervention to reverse inhibitors via immune tolerance induction is encouraged
- There is also potential for antibody-neutralising effects with non-factor treatment

Safety profiles help to inform decision making

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Logistical challenges

- It is important to equip families to deal with the practical aspects of day-to-day life with haemophilia

- Logistic considerations will change over time
  - Support can prevent overprotection, facilitating access to routine childcare
    - Parents can be empowered to inform others who care for their child when attending nursery/school, enabling staff to confidently recognise any need to seek help, if required
    - Engaging in appropriate physical activity will help facilitate inclusion of children affected by haemophilia
  - Education can help to provide families with short- and medium-term views for their children, and aid management transitions when progressing through various life stages

HCPs can help families to navigate the journey through life, with shared decision making

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Optimising the treatment

- HCPs should provide families with information to help facilitate changes over time; as children get older, management considerations change
  - As individuals grow and mature, there may be a desire for increased levels of physical activity, while personal development and emerging lifestyle choices may be associated with greater independence
- Nevertheless, there should be a focus on maintaining joint health
- With the current therapeutic landscape, where such choices are available, treatment can be tailored to recognise changing needs, taking into account, for example, treatment burden and the importance of ensuring adherence
- Possibilities for individualising therapy include treatment switching and tailoring prophylaxis with factor replacement products, which can help to maintain adherence

Informed decision making will help to retain treatment efficacy

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Future prospects

- As the treatment landscape continues to evolve, guidance should be continually updated
- Families should be apprised of new innovations, aiding understanding of both benefits and potential risks
- For those affected by haemophilia, choices are greater than ever before

With the choices now available, health equity has now become a consideration

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In summary…

'It is important to provide parents, and ultimately those individuals living with haemophilia as they become older, with the information required to facilitate truly informed decision making to achieve the best possible health equity and quality of life'

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