



Synovitis in Haemophilia: A Factor Think Tank Podcast Series

Episode 5. Prevention and treatment
Slide summary

Disclaimer

- The Factor Think Tank is an educational activity funded by Sobi. Synovitis in Haemophilia: A Factor Think Tank Podcast Series was developed by the Factor Think Tank working group and the accompanying slide deck is only intended for healthcare professionals
- Slides 7–10 summarise content from the e-Delphi consensus article by Mancuso et al.;¹ wording closely resembles that of the article to reflect the e-Delphi consensus discussions
- All views and opinions expressed in the podcast are those of the participants only
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Synovitis in Haemophilia: A Factor Think Tank Podcast Series (1)

- Findings from the e-Delphi consensus study on synovitis and joint health in haemophilia have been published in [Haemophilia](#) and provide the basis for the podcast series

HAEMOPHILIA

Synovitis and joint health in patients with haemophilia:
Statements from a European e-Delphi consensus study

*Maria Elisa Mancuso, Katharina Holstein, James S. O'Donnell,
Sébastien Lobet, Robert Klamroth, the FVIII Think Tank Study Group*

Synovitis in Haemophilia: A Factor Think Tank Podcast Series (2)

- The e-Delphi consensus examined five key domains relevant to synovitis in haemophilia:
 - Definition and pathophysiology
 - Diagnosis
 - Impact on joint health
 - Monitoring and follow-up
 - Prevention and treatment
- Based on these key domains an educational [series of five podcasts](#), featuring lead author Dr Maria Elisa Mancuso and co-authors or expert guest speakers, is available to healthcare professionals

This slide deck provides supporting information for [Episode 5. Prevention and treatment](#) of the podcast series on synovitis in haemophilia



An overview of synovitis in haemophilia

- Synovitis is defined as inflammation of synovial tissue within the joint¹
- It is common in patients with haemophilia in response to blood within joints and is the first step towards the development of chronic arthropathy¹
- One bleeding episode can initiate synovial inflammation, which may develop into chronic synovitis if bleeds recur frequently and are not adequately prevented²
- Synovitis is highly relevant to joint health in haemophilia; however, knowledge gaps exist regarding definition, pathophysiology, diagnosis, prevention, follow-up and treatment³
- Delphi methodology, which is often used to produce best-practice guidelines where evidence is missing, was employed to conduct a European e-Delphi consensus study on synovitis in haemophilia³

1. van Vulpen L, et al. Haemophilia. 2021;27(Suppl. 3):96–102; 2. van Vulpen L, et al. Osteoarthritis Cartilage. 2015;23:63–9;
3. Mancuso M, et al. Haemophilia. 2023;29:619–28

e-Delphi consensus article

Domain: Prevention and treatment of synovitis (statements 17–22)

Prevention and treatment of synovitis in haemophilia e-Delphi consensus statements 17–22: Background

- Synovitis prevention is key to protect joints from long-term irreversible structural damage¹
- Early prophylaxis has been shown to preserve joint structure and reduce bleeds in individuals with severe haemophilia²
- Joint damage may also occur in those with moderate disease, with progression only slightly delayed compared with severe haemophilia^{3,4}
 - This underlines the need to extend prophylaxis to patients with moderate haemophilia, irrespective of baseline levels, as well as the recommendation to increase trough levels from 1–3% to ≥ 3 –5% during prophylaxis⁵
- Treatment tailoring and individualisation of prophylaxis regimens can also be beneficial in the prevention of synovitis⁶

1. van Vulpen LFD, et al. Haemophilia. 2021;27(Suppl. 3):96–102; 2. Manco-Johnson MJ, et al. N Engl J Med. 2007;357:535–44; 3. Ling M, et al. Thromb Haemost. 2011;105:261–8; 4. Scott MJ, et al. Haemophilia. 2019;25:205–12; 5. Srivastava A, et al. Haemophilia. 2020;26(Suppl. 6):1–158; 6. Mancuso ME, et al. Haemophilia. 2023;29:619–28

Prevention and treatment of synovitis in haemophilia

e-Delphi consensus statements 17–22: Background

- The detection of joint damage in a significant proportion of patients treated with standard prophylaxis¹ highlights the need for treatment optimisation
- Optimisation can be achieved through prophylactic regimens that maintain higher factor levels such as clotting factors with improved pharmacokinetic profiles (i.e., extended half-life products), or from non-replacement therapies²
- Conservative treatments, such as anti-inflammatory drugs and physiotherapy, may also be considered in addition to factor replacement^{3,4}
- For synovitis not controlled/reverted by factor replacement plus conservative therapies, surgery* may solve the mechanical impingement caused by hypertrophic synovium in the joint space (which cannot be controlled by medical treatment)

*Ranging from selective arterial embolisation to open surgical synovectomy including chemical, radioisotopic and arthroscopic synovectomy^{5–11}

1. Oldenburg J, et al. *Blood*. 2015;125:2038–44; 2. Collins PW, et al. *Haemophilia*. 2021;27:192–8; 3. Rattray B, et al. *Haemophilia*. 2006;12:514–7; 4. Lobet S, et al. *J Blood Med*. 2014;5:207–18; 5. Klamroth R, et al. *Haemophilia*. 2009;15:247–52; 6. Galli E, et al. *Cardiovasc Intervent Radiol*. 2013;36:964–9; 7. Rivard GE. *Haemophilia*. 2001;7(Suppl. 2):16–19; 8. Rodriguez-Merchan EC. *Blood Rev*. 2019;35:1–6; 9. Dunn AL, et al. *J Pediatr Orthop*. 2004;24:414–26; 10. Wiedel JD. *Haemophilia*. 2002;8:372–4; 11. Mingo-Robinet J, et al. *Haemophilia*. 2015;21:e306–11

Prevention and treatment of synovitis in haemophilia e-Delphi consensus statements 17–22

17 Synovitis can be prevented by early primary prophylaxis started before or at least soon after the first joint bleed

18 Patients with moderate haemophilia A, with a baseline FVIII of 1–3 IU/dL, are at risk of synovitis and deserve prophylaxis

19.1 To prevent synovitis, joint bleeds and microbleeds need to be avoided through effective prophylaxis*

19.2.1 Levels of 3% FVIII are not adequate to fully prevent synovitis in all patients*

*The statement, 'To prevent synovitis time spent within the normal range of FVIII levels and FVIII trough levels above 3–5 IU/dL are needed', was split into two following a second and third e-Delphi round
FVIII, factor VIII

Prevention and treatment of synovitis in haemophilia e-Delphi consensus statements 17–22

20 Treatment tailoring and prophylaxis intensification with factor replacement is needed in the presence of synovitis

21 Management of synovitis always requires conservative treatments (i.e., anti-inflammatory drugs, physiotherapy) beyond prophylaxis with factor replacement

22 For chronic synovitis resistant to intensified factor replacement and appropriate conservative treatment, radio- or chemical synoviorthesis, arthroscopic/surgical synovectomy or selective arterial embolisation are recommended

Podcast discussion points

Synovitis in Haemophilia: A Factor Think Tank Podcast Series
Episode 5. Prevention and treatment

Episode 5. Prevention and treatment

- This episode focuses on four topics relevant to the prevention and treatment of synovitis in haemophilia:
 - Patients at risk of developing synovitis
 - Prevention of synovitis
 - Target FVIII levels for prevention
 - Haemostatic treatment
- Host Dr Maria Elisa Mancuso leads the discussion with guest Dr Gianluigi Pasta



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Dr Gianluigi Pasta is an orthopaedic surgeon at the Department of Orthopaedics and Traumatology, Fondazione Policlinico IRCCS San Matteo of Pavia, Italy

FVIII, factor VIII

Topic 1. Patients at risk of developing synovitis

- No direct correlation between clotting factor levels and synovitis incidence has been demonstrated
- Onset of synovitis and haemophilic arthropathy is not only influenced by factor levels
- Non-haemophilia-specific risk factors related to MSK health, such as posture, feet loading and flat feet, also influence the development of synovitis
- MSK health should be assessed to identify patients at risk of developing synovitis

“All haemophilia patients are at risk of developing synovitis”

MSK, musculoskeletal

Topic 2. Prevention of synovitis

- Synovitis prevention is key to protect joints from long-term irreversible structural damage
- Beyond preventing clinically relevant joint bleeds, microbleeds should also be avoided through prophylaxis
- Although early prophylaxis is crucial, it may not be sufficient to fully prevent synovitis
- Additional preventative measures are also needed, especially those that account for the importance of MSK health; these include education, physical activity and physiotherapy
- Consider the functional damage, as well as the structural damage, related to haemophilia

“Prevention is crucial...it is key to protect joints from long-term irreversible structural damage”

MSK, musculoskeletal

Topic 3. Target FVIII levels for prevention

- Trough levels above 3–5% may be useful to prevent synovitis
 - But there is a paucity of data on this topic
 - There may not be a universal value for all patients
- The movement towards more personalised care in haemophilia applies to both trough levels and musculoskeletal health

“Trough levels above 3–5% may be useful to prevent synovitis...but it is not true for all patients”

FVIII, factor VIII

Topic 4. Haemostatic treatment

- Beyond haemostatic therapy additional strategies are needed to treat synovitis
- Conservative treatments with anti-inflammatory drugs and physiotherapy are often needed
- Invasive treatments, such as radio- or chemical synoviorthesis, can be performed in outpatient and surgical settings
- Surgery can be performed at a later stage or at the point of diagnosis
 - Benefits of arthroscopic synovectomy extend beyond the management of inflammation and bleeding
 - Successful surgical treatment can delay or even halt disease progression, increasing patients' functional levels and thus improving their quality of life

“Haemophilia is a multidisciplinary disease, and treatment has to be multidisciplinary”

Conclusions

- Synovitis development can be the consequence of non-protective prophylaxis
- There is limited information on the correlation between factor levels and synovitis; however, prevention of bleeds, including silent bleeds, is crucial in this setting because untreated synovitis can lead to overt and irreversible joint damage
- When haemostatic treatment is not enough to solve synovitis, there are other treatment strategies that could be applied, such as radio- or chemical synoviorthesis, or synovectomy

Listen to the whole series

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More in the series

- If you enjoyed this podcast and want to find out more about the Factor Think Tank, please visit the website: www.factorthinktank.com
- All episodes in the series can be found here:
 - Episode 1. Definition and pathophysiology (Dr Maria Elisa Mancuso and Dr Robert Klamroth)
 - Episode 2. Diagnosis (Dr Maria Elisa Mancuso and Prof Dario Di Minno)
 - Episode 3. Impact on joint health (Dr Maria Elisa Mancuso and Dr Sébastien Lobet)
 - Episode 4. Monitoring and follow-up (Dr Maria Elisa Mancuso and Dr Katharina Holstein)
 - Episode 5. Prevention and treatment (Dr Maria Elisa Mancuso and Dr Gianluigi Pasta)