Bleeding Disorders - Hepatitis Infection and Vaccination - Full Clinical Guideline

Reference no.: CG-HAEM/2023/015

1. Introduction

The emergence and transmission of hepatitis B and C viruses (and HIV) through clotting factor products resulted in high mortality of people with haemophilia and other bleeding disorders in the 1980s and early 1990s. Many studies conducted all over the world indicate that hepatitis transmission through factor concentrate has been almost completely eliminated. This has been achieved through the implementation of several risk-mitigating steps, which include careful selection of donors and screening of plasma and effective virucidal steps in the manufacturing process. Recombinant factor concentrates have been adopted (mainly for haemophilia) over the past two decades, and have contributed significantly to infection risk reduction.

It is highly unlikely therefore that new patients treated in the UK will contract hepatitis as a result of clotting factor concentrate treatment. However, this possibility must always be considered, particularly in patients previously lost to follow up, or arriving from low resource countries.

There are a significant number of individuals who were infected during the original high risk period with hepatitis C and a smaller number with hepatitis. Many individuals have been successfully treated to eradicate infection. However, some developed liver disease prior to treatment being available and may require long term surveillance for complications of this. Others may have not yet been successfully treated or have been unable to access treatment (perhaps because they were formally living in a low resource country). It is essential that any individual affected by hepatitis in association with a bleeding disorder can access services to ensure optimal treatment and support.

2. Aim and Purpose

To enable the detection, prevention (where possible) and effective treatment of hepatitis B and C in people with bleeding disorders.

3. Definitions, Keywords

Haemophilia A - Congenital deficiency of clotting factor VIII; Haemophilia B - Congenital deficiency of clotting factor IX. Severe haemophilia is associated with spontaneous bleeding into joints, muscles and organs e.g. the brain.

Clotting Factor Concentrate – this is given therapeutically to replace the clotting factor that is missing or low. Most CFC's are recombinant. However it is still necessary to use plasma derived CFC in some circumstances e.g. type 2 von Willebrands. Also, some of the rare bleeding disorders are treated with FFP (solvent detergent FFP) e.g. factor XI and factor V deficiency; or Cryoprecipitate (Octaplas -methylene blue treated) – a/hypo or dysfibrinogenaemia (if fibrinogen concentrate is not available)

4. Main body of Guidelines

Hepatitis testing in individuals with bleeding disorders

1. Patients who will only receive recombinant products do not need testing for hepatitis B or C, unless indicated by clinical symptoms or where otherwise recommended by current guidelines[1]
2. Baseline hepatitis A, B and C (HAV, HBV, HCV) testing should be considered in patients who are likely to, or will definitely receive a plasma derived product.
3. Hepatitis B and C testing should be offered in patients who have previously received plasma products and are potentially at risk. For example, a potential scenario would be a patient arriving from a low resource country who has received plasma products in the past and has not previously been tested.
4. Any individual with a bleeding disorder treated with plasma derived products that are not adequately virus-inactivated should be tested for hepatitis B and C at least every 6-12 months and whenever clinically indicated.

Prior to hepatitis B and C testing, a discussion should happen about the reasons for testing; the potential benefit to the individual from testing; and how the results will be communicated.

Hepatitis vaccination in individuals with bleeding disorders

- Patients with haemophilia A and B and factor VII deficiency, whose planned therapy is with recombinant concentrates should not receive routine vaccination against hepatitis A and B (unless the patient is a child born after 2017 for whom HBV vaccination is part of routine childhood immunisation). The need for protection against hepatitis A and B, however, must take into account other risks for acquiring these viruses and be in line with the recommendations by the Department of Health's 'Green Book' [2].
- Patients with haemophilia A and B who are likely to receive plasma-derived coagulation factor concentrates and who are not immune to HAV and HBV should be vaccinated using established schedules. This may arise because of:
    - the development of an inhibitor,
    - side effects of recombinant concentrate
    - an imminent change in residence to an area where recombinant concentrates are not available and so exposure to plasma derived concentrates, cryoprecipitate or fresh frozen plasma is likely.
- Patients with other clotting factor deficiencies thought likely to require treatment with plasma-derived concentrate who are not immune to HAV and HBV should be routinely offered vaccination against these.
- HBV vaccination is now part of the routine childhood immunisation schedule (since late 2017). Children born before 2017 will not have been routinely immunised so will require assessment as above. As HAV vaccination is not included in the childhood schedule, the need for HAV immunisation should be assessed and delivered in accordance with the guidance above and delivered as per guidance in the Green Book.
- All vaccines must be given sub-cutaneously.
- Most patients will be immunised simultaneously with combined HAV and HBV vaccine.The vaccine schedule in the Green Book should be followed appropriate to the age of the patient.

Testing for response to vaccination

Hepatitis B vaccines are highly effective; around 90% of adults respond to vaccines adequately. Poor responses are mostly associated with age over 40 years, obesity and smoking. Lower seroconversion rates have also been reported in people who have alcohol dependency, particularly those with advanced liver disease. Patients who are immunosuppressed or on renal dialysis may respond less well than healthy individuals and may require larger or more frequent doses of vaccine. The vaccine is not effective in patients with acute hepatitis B, and is not necessary for individuals known to have markers of current (HBsAg) or past (anti-HBc) infection.
However, immunisation should not be delayed while awaiting any test results for current or past infection.
Testing for evidence of immunity post immunisation (anti-HBs) is not routinely recommended in the Green Book except in health care and laboratory workers and individuals with renal failure. It has been common practice to check response to vaccination in patients with bleeding disorders.

- In the absence of evidence to the contrary, continuation of current practice to test response to vaccination is recommended.
- Re-vaccination of non-responders should be considered.

Re-inforcing (Booster immunisation)
The current UK recommendation is that those who have received a primary course of immunisation do not require a reinforcing dose of HepB-containing vaccine except in the following categories:

- The individual is a healthcare worker (including students and trainees), who should be offered a single booster dose of vaccine, once only, around five years after primary immunisation
- patients with renal failure
- at the time of a significant exposure

Care of patients with hepatitis B and C.
All people with bleeding disorders who are hepatitis B and/or C ab positive must be referred to Hepatology for eradication treatment. See CG-T/2012/199 and CG-GASTRO/2015/195-GASTROENTEROLOGY AND HEPATOLOGY on Trust intranet.

5. References (including any links to NICE Guidance etc.)

1. Guidelines for the management of haemophilia. A. Srivastava, A. K. Brewer, E. P. Mauser-Bunschoten, N. S. Key, S. Kitchen, A. Llinas, C. A. Ludlam, J. N. Mahlangu, K. Mulder, M. C. Poon And A. Street; Treatment Guidelines Working Group On Behalf Of The World Federation Of Hemophilia. Hemophilia 2013, 19, e1–e47

2. Immunisation against infectious disease (The Green Book) 2017 Public Health England.

3. Update to UKHCDO guidance on vaccination against hepatitis A and B viruses in patients with inherited coagulation factor deficiencies and von Willebrand disease. HG Watson,J T. Wilde, G Dolan, C Millar, T T Yee and M Makris on behalf of morbidity and mortality working party UKHCDO. Haemophilia (2013), 19, e174--e192

6. Documentation Controls

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Review Date:	Dec 2026
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