
The Haemophilia Society's submission to NICE for the appraisal of hepatitis C (mild to moderate) — pegylated interferons, ribavirin and alpha interferon

John Morris, services development manager 22 April 2005

Petersham House, 57A Hatton Garden, London, EC1N 8JG

Formerly at Chesterfield House, 385 Euston Road, London, NW1 3AU

The Haemophilia Society Registered charity no. 288260 Registered as a Limited Company in England no. 1763614.

Summary

The Haemophilia Society is the national patient organisation for over 20,000 registered patients with haemophilia, von Willebrand's and related inherited bleeding disorders. It has much experience of supporting and representing the 4,865 people who are believed to have been exposed to hepatitis C through clotting factor concentrates, many of whom have also been at risk of hepatitis B and HIV. It has a strong background of providing information and advice to many of the 2829 who are living today with past exposure to HCV, the majority of whom remain chronically infected. Around 360 people in this number are also living with HIV. A significant number of adults with haemophilia has experienced interferon-alpha monotherapy and an increasing number has currently or recently undergone combination therapy with pegylated interferon or standard interferon and ribavirin.

The Society's submission to the 2003 NICE consultation on pegylated interferon/interferon and ribavirin contained much useful data and qualitative experience of HCV and interferon-based treatment. This current submission updates this information and makes updated reference to mild infection.

The Society makes the following recommendations about treatment for people with mild HCV:

Recommendations

- 1. We support the availability of treatment to people with mild disease. People in this category may have quality of life issues and goals of therapy which merit medical intervention, and people with HIV have additional reason to attempt to clear the HCV virus whenever possible**
- 2. Unless there is good clinical evidence to the contrary, combination- or mono-therapy with pegylated interferon-alpha should be the treatment of choice**
- 3. We support further research into non-invasive assessment of the extent of liver disease to define "mild" in a group of people for whom liver biopsy is often contraindicated, in order to further informed patient choice in treatment decision-making**

1 Introduction: Hepatitis C and the haemophilia community

The Haemophilia Society is the national patient organisation for over 20,000 registered patients with haemophilia, von Willebrand's and related inherited bleeding disorders. Now in existence for 55 years, it has much experience of supporting and representing the 4,865 people who are believed to have been exposed to hepatitis C through clotting factor concentrates, many of whom have also been at risk of hepatitis B and HIV. Approximately 5,000 are registered on its database. It has a vast experience of providing information and advice to many of the 2829 who are living today with past exposure to HCV, the majority of whom remain chronically infected (end 1999 figure). Of these 2027 have haemophilia A, 584 have haemophilia B and 218 have von Willebrand's. The ratio of men to women is 91:9. A total of 241 people have suffered liver failure at the time of death¹. The Society estimates 40 people have undergone liver transplants for HCV-related liver damage. A significant number of adults with haemophilia have experienced interferon alpha monotherapy and an increasing number has currently or recently undergone combination therapy with pegylated interferon or standard interferon and ribavirin.

The Society runs a telephone helpline, a network of regional groups and a series of hepatitis information events, ensuring that the hepatitis worker receives considerable numbers of treatment-related calls and letters. In 2002, 450 e-mails and letters on the subject of HCV were made by people affected by haemophilia and haemophilia professionals. Of these 161 were taken by the HCV worker on the subject of HCV-related health and lifestyle issues. An additional 52 enquiries were taken by the HIV/HCV coinfection worker on HCV treatment issues for people with both HIV and HCV. The average time spent dealing with each enquiry is estimated to be twelve minutes.

The Society has produced a variety of information booklets and factsheets on HCV, including *Meeting the challenge*, a booklet for adults with haemophilia which recently won a BMA award for Patient Information. A quarterly newsletter, *H3*, is sent to members and other contacts affected by haemophilia, as well as interested professions. The current circulation is around 2000 copies.

The Society has always worked in collaboration with medical/nursing and patient representatives from other HCV communities to gain a wider understanding of the issues involved. Additionally it is a leading voice in advocacy for patients co-infected with HIV and HCV, of whom about 360 are currently living and registrants of the Macfarlane Trust for financial assistance. It held two conferences for professionals on HIV/HCV co-infection in 2001 and 2003, attended by 122 and 93 delegates, and five HIV/HCV co-infection information evenings in 2002 throughout UK, attended by 91 professionals and people affected by haemophilia.

The Society's submission to the 2000 and 2003 NICE consultations on pegylated interferon, interferon and ribavirin contained much useful data and qualitative experience of HCV and interferon-based treatment. The table of contents for the 2003 submission is appended to this report and the both documents are available from the author of this submission. This current submission updates this information and makes updated reference to mild infection.

The 2003 submission made recommendations which are listed in the appendix.

2 The advantages of successful anti-HCV therapy

The motivation the group of people with mild liver disease to clear the virus gives useful insight into general goals of therapy from the patients' perspectives. Whatever the results of recent studies on treating people

¹ UK HCDO figures, 2000-02

with mild liver damage, some people in this position are anxious to clear the virus for quality of life reasons quite apart from halting liver damage. Individuals speak of removing the fear of infecting others, making the obtaining of life and travel insurance easier, reducing the stigma associated with HCV infection, freedom for possible travel restrictions on people with infectious diseases; perceptions about health prospects for the individuals and their family and friends, and inconvenience of attending regular HCV clinics. Some of these issues are more poignant for people with HIV or HBV co-infection. Many people with blood product and transfusion-acquired HCV feel they deserve the right to the best opportunity to clear a virus with which they were infected by their NHS treatment

3 Assessing the extent of liver disease

The practice of liver biopsy amongst patients with haemophilia varies enormously amongst the country's hepatologists. At one extreme patients are biopsied as frequently as every three years; at the other the practice is considered absolutely contraindicated. The majority of patients prefers the more cautious approach of not monitoring liver damage by biopsy because of the risk of prolonged post-operative bleeding which has led to at least two deaths in people with haemophilia: one in London and one in New York. Some consultants prefer the trans-jugular route as a safer compromise.

Having been life-long patients, people with haemophilia can be very informed and inquisitive about their care and many are very keen to know how the extent of their liver disease can be assessed. This is notoriously difficult in the absence of liver histology, but more recent developments in non-invasive markers such as the APRI test and Fibrotest have aroused interest, if only because of the need to assess if cirrhosis is present in order to qualify for the stage two Skipton Fund payment. For every person contacting the helpline and seeking a biopsy to ascertain the extent of his liver damage, there are five to ten more trying to avoid the procedure. In addition to the risk of haemorrhage, the procedure involves a two-to-three day stay in hospital because of considerable and expensive clotting factor use to maintain haemostasis.

4 Views of people with mild hepatitis C

Anecdotal evidence has been gathered from helpline enquiries. A total of 342 in 2003 and 295 in 2004 enquiries relating to HCV health and psychosocial issues, excluding the Skipton Fund, were received. In our estimation, of those who have had a liver biopsy which proves little or no fibrosis, most are content with the decision to delay treatment until the liver disease becomes more serious or better treatments become available. This decision is made invariably on a combination of the fear of the side-effects of interferon-based therapy and the modest success rates of therapy. It tends to be strongly influenced by the specialist managing the condition, who presumably has chosen to biopsy in order to make a decision about whether to recommend treatment. Those who have never had a biopsy are far more likely to want to try treatment unless they have been persuaded that their disease is only mild. Such decisions tend to be based on the personal fear of being HCV positive, experience of symptoms which are perceived to be related to the virus, and the opinion of their doctor.

In conclusion, there is a large group of people with haemophilia and von Willebrand's who have raised ALT/AST levels, fatigue and concentration problems, but little idea of how far the disease has progressed. We support their right to undergo treatment if they so wish and have been well informed.

5 2003 needs assessment survey of people with haemophilia

Our 2003 needs assessment survey featured 163 responses from people with a bleeding disorder and HCV. It was carried out after the 2003 NICE submission was made. It did not ask about the extent of disease progression.

A total of 163 (28%) people responding were affected by HCV. The total number of people responding to the needs assessment survey was 589, of whom 64 (11%) were affected by HIV and HCV. The ratio of bleeding order severities, high:medium:low was 80:28:54 (49%:17%:33%), reflecting the widespread prevalence of HCV amongst the haemophilia population. People with von Willebrand's are in a minority compared to haemophilia A and B (8%), reflecting the rarity of von Willebrand's diagnosis and treatment during the use of non-virally-inactivated factor concentrates (1969-1985).

5.1 Hepatitis C treatment for those with haemophilia and HCV mono-infection

102 (61%) of respondents had tried treatment. 68 (67%) said it was ineffective, 22 (22%) were awaiting the results, and 12 (12%) said it was successful. This probably reflects the large number of people who have been on interferon monotherapy which had an average success rate of only 15%. We believe this was indicated on the basis of raised liver enzymes alone. Those awaiting results were probably taking pegylated interferon and ribavirin or have recently finished a course of this combination. If 55% of these treatments are successful then at least a quarter of the respondents will have been cured of HCV or at the time were currently PCR negative and will remain so.

According to UKHCDO data for 1999, 2829 people with a bleeding disorder are antibody positive. Of these an estimated 15% (leaving 2405) will have cleared the virus in the acute phase (and may have little interest in the Society's surveys). Of the remaining 85%, 12% have undergone successful treatment, leaving 2116 with chronic HCV or on treatment to eradicate it. The population declines by 3% each year, so at the time of the survey, the size of the group of antibody positive people will be 10% smaller (1904). Of this group 400 are Macfarlane Trust registrants, of whom an estimated 350 are living with chronic HCV. Therefore the current (2003) size of the chronic HCV mono-infection service-user group is currently estimated to be 1550.

5.2 Hepatitis C treatment for those with haemophilia and HIV/HCV co-infection

There were 64 responses from people with HIV, and all were co-infected with hepatitis C.

There was a significant difference in those undergoing HCV treatment in the two groups with only 44% of the coinfected group treated, compared to 61% of the mono-infected group. The treatment outcomes were very similar for both groups. Only 23% of the coinfected group had cleared the virus, however 17% were awaiting their result. For 60% the treatment was not successful.

Appendix 1: Contents of the Haemophilia Society 2003 submission to NICE for the appraisal of pegylated interferon and ribavirin combination therapy for the treatment of hepatitis C

1. Patient Experience

1.1 Semi-quantitative data

- 1.1.1 HCV Treatment Survey, 2003
- 1.1.2 Oxford and Sheffield survey, 2001
- 1.1.3 *C Issues* Opinion Poll of readership

1.2 Qualitative data

- 1.2.1 Comments recorded in Oxford and Sheffield survey
- 1.2.2 Personal stories published in *C Issues* and *Haemophilia Quarterly*

1.3 Other Issues

- 1.3.1 HIV/HCV Coinfection
- 1.3.2 HBV co-infection
- 1.3.3 Relapse and non-response to standard interferon therapy
- 1.3.4 Genotypes 4-6
- 1.3.5 The advantages of successful anti-HCV therapy
- 1.3.6 Early Viral Response
- 1.3.7 Liver Biopsy

1.4 Other concerns

- 1.4.1 Postcode prescribing
- 1.4.2 Availability of nursing and 'counselling' support whilst on treatment

2. Clinical Evidence

2.1 Guidelines on the Diagnosis, Management and Prevention of Hepatitis in Haemophilia

- 2.1.1 Communication
- 2.1.2 Treatment
- 2.1.3 Liver Transplantation
- 2.1.4 Co-infection with HIV

2.2 HIV and HCV Co-infection

2.3 Results of published studies on anti-HCV treatment on people with haemophilia

2.4 Genotypes 4-6

3. Conclusion

4. Recommendations

1. **The pegylated combination or monotherapy therapy for HCV should be available for people with all genotypes because of its improved efficacy and ease of administration over standard interferon-based treatment.**
2. **The potential severity of the side-effects of the treatment require that a significant amount of nursing and counselling support be given before and during the treatment in order for patients to have the best chance to complete the treatment.**
3. **We support the availability of treatment to people with mild disease. People in this category may have quality of life issues and goals of therapy which merit medical intervention, and people with HIV have good reason to clear the HCV virus whenever possible.**
4. **Attention should be paid to non-1,2,3 HCV genotypes and a full (48 week) course of treatment offered if there is doubt about the optimum length of treatment.**
5. **People who do not get an early viral response (12 week EVR) should be offered the opportunity to continue treatment for 24 weeks if they so choose.**
7. **A non-response/relapse on non-pegylated mono and combination therapy should not bar an individual from being considered for pegylated interferon-based therapy.**

5. Appended reports

Appendix 1 Haemophilia Society 2000 submission to NICE for the appraisal of interferon and ribavirin combination therapy for the treatment of hepatitis C (HCV)

Appendix 2 Pegylated interferon survey, 2003

Appendix 3 Oxford and Sheffield survey, 2001

Appendix 4 *C Issues* Opinion Poll of readership

Appendix 5 Personal stories of people affected by HCV

Appendix 6 L Garvican, *National Survey of provision of care for patients with HIV and Hepatitis by Haemophilia Centres*, 2001.