NICE Health Technology Appraisal: Interferon alfa and ribavirin for the treatment of mild chronic hepatitis C – part review of existing guidance no. 75

A personal view by John Morris, services development manager, on behalf of The Haemophilia Society UK

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I began working in the field of hepatitis C in January 2001 in the position of hepatitis worker at the Haemophilia Society. Prior to that my only experience of HCV was with a close friend with haemophilia and mild HCV, and a counselling client who was an intravenous drug use and newly diagnosed with the virus.

Since my induction at the Society I have attended numerous professional and patient conferences on hepatitis C, HIV/HCV coinfection and liver disease, had free and productive access to medical advisers, and conducted over two thousand telephone conversations or email exchanges about living with hepatitis C monoinfection. Other related calls have included discussions about the Society's campaigning activities or the Skipton Fund. Recent advances in interferon treatment, the ongoing campaign and the announcement of the Skipton Fund on 29 August 2003, have served to raise awareness of hepatitis C generally and help people take more notice of their condition, particularly if they are asymptomatic.

The difficulty with the subject of this appraisal and the haemophilia community is that in most pre-cirrhosis cases it is difficult to establish the extent of progression of liver disease. This is because performing a liver biopsy in patients with a bleeding disorder is so problematic, and, for that matter, expensive and time-consuming because of the need to bring clotting factor levels up to 100%. Leaving aside aspects and outcomes of treatment, the community tends to divide into those with direct symptoms of liver disease (usually cirrhotics), those with only associated symptoms such as fatigue and concentration impairment, and those without any symptoms. People with mild hepatitis C obviously fall into one of the last two categories. Those I speak to belonging to the second are likely to be keener to undergo treatment than those in the third.

We calculate that a total of around 2000 people with a bleeding disorder in the UK are living today with chronic infection, or past infection cleared on treatment. This may be an overestimate as only around 1700 of these have successfully claimed for a stage one Skipton Fund payment. (The figures for England and Wales are 89% of the UK totals, i.e. 1800). Originally 4865 developed acute or chronic HCV through factor concentrates between 1969 and 1985/87. Nearly 250 of these have died from liver failure. It is difficult to estimate the numbers who might be classified as having mild hepatitis C. In 20-35 years of infection there have been some deaths in people with

advanced liver disease, and the population is now aging and largely male. If a third of those living still have only mild liver disease, the England and Wales figure is 600, although this includes an unknown number who have already achieved an SVR on treatment. Aside from those who are monitored by liver biopsy, it is now rare to hear from a helpline caller that he or she has not been offered treatment at some time, since funding and liver services are at their most accessible. Even in 2003, a patient survey showed 61% of people (102) with HCV had been on treatment. Others who are still treatment-naïve are likely to belong to the sub-group with normal liver function tests, have HIV co-infection or have chosen to refuse treatment.

Amongst patients there is little interest in which of the two pegylated interferons product is prescribed in combination. A far more appreciated difference is between the once-weekly injections with PegIFN and the thrice-weekly with standard IFN. Unless there are significant clinical advantages in using standard IFN, it would be unthinkable to only recommend regimes including this treatment on cost grounds alone.

The presence of HIV/HCV co-infection (and to a lesser extent HBV/HCV infection) would appear to warrant early intervention to eradicate HCV whenever possible. A little over 350 people with haemophilia have been in this position. I fear that insufficient attention has been given to these groups, and the final recommendation should acknowledge the special needs of patients in this group. People may have an enhanced resolve to clear one virus complete, or alternatively might be over-consumed with managing HIV to be concerned with a mild HCV infection. However, if the presence of HIV speeds up the progression to cirrhosis, it would make sense to offer interferon treatment whenever this is practical.

There is a wealth of anecdotal and semi-quantitative evidence of the patient experience of living with HCV and interferon-based treatments available in the Society's submissions to NICE in 2005, 2003 and 2000. I have combined these qualitative and semi-quantitative surveys with five years' of helpline experience to compile the following patient-centred exhaustive list of factors influencing choice of treatment in adults with haemophilia and related bleeding disorders.

Reasons to choose treatment	**Reasons not to choose treatment**
Genotypes 2 and 3	Genotype 1
HIV (or HBV) co-infection	Impaired health and QoL resulting from HIV, particularly triple therapy
	RBN is contraindicated so predicted success rates are poor
Fear of transmitting the virus to sexual partners and household members	
Desire to try for a baby once PCR –ve (particularly female patients)	
Fear of hostility from local community	
Difficulty in forging relationships	

Hoped-for renewed energy, ability to get more financially-rewarding work, and cheaper life insurance premiums	Reluctant to risk needing time off work
	Unable to keep 24/48 weeks clear
	Lack of ambition, perhaps through being of pensionable age, or co-morbidities reducing self-esteem
Desire to reduce frequency of appointments with liver specialist	Anticipating better drugs to tackle virus in near future
Wish to bring an end to frequent liver biopsies	Waiting to qualify for stage 2 Skipton Fund payment
Uncertainty about future health and life expectancy	In denial about having a virus
Simply hating the feeling of carrying a virus	Absorbed by health issues arising from haemophilia or another condition
Relief from fatigue, concentration impairment and memory loss	Completely free of any symptoms of chronic infection
Encouragement from having relapsed on mono-therapy	Complete non-response to standard IFN combination therapy
	Bad experience of side-effects on earlier interferon therapy in self or family member/friend
	Aversion to needles or taking pills
Over-encouragement from clinical team who regard SVR as ultimate outcome	Encouraged by specialist's preference for 'watchful waiting', particularly with frequent biopsies
Regard NHS as having a duty to make all efforts to clear the infection	Feeling pushed into undergoing treatment to salve consciences of clinical team

Taking an overview of the whole haemophilia and wider community, I would like to add my own impressions:

- It seems daft to run an HCV awareness campaign, obtain new diagnoses as a result and then explain to people that they are barred from treatment because their disease is only mild, hence causing puzzlement, despair and anger
- Many of the 38,000 diagnosed are current drug users who fall into the category of mild disease. The risk of infecting others would be minimised by offering treatment to all.
- People are probably at their most motivated to embark on treatment and cope with the side-effects when they are newly-diagnosed, especially if they have not had to wait for a liver biopsy to open the gate to treatment
- Offering newly-diagnosed patients (and hence often mild disease) the choice of treatment is a positive start to empowering them to self-manage what may become a lifelong condition

- Those who acquired HCV through blood or blood products deserve to be given the best possible opportunity to be rid of the virus. Anything less causes resentment and mistrust of clinicians and the wider health service.

In conclusion, I and the Society fully support that pegylated interferon treatment be available to all who want to clear the hepatitis C virus, irrespective of the progression of chronic disease. It would be grossly unjust for the healthcare system which is responsible for their viral infections to refuse gold standard treatment to clear HCV on the grounds of cost. In the case of mild disease it is particularly important to offer good counselling to enable patients to take a decision about embarking on this unpleasant treatment regime, since the alternative of 'watching waiting' is entirely viable, at least in the short term. We recommend that before the prescription is signed, treatment be discussed over at least two appointments to give time for the patient to come to the best decision.

Clearly this appraisal is concerned with a far smaller issue than the subject of the 2003 appraisal, as it concerns a smaller group of patients with, by definition, no clinical symptoms or immediate fear of advanced liver disease. A change in decision about treating those with mild hepatitis C would bring only a trickle of new patients with haemophilia. No-one replied in response to my newsletter request for individual feedback on the issue of treating mild HCV. The newsletter is sent or emailed to over 1000 people living with hepatitis C. I also am fully aware that historically, people with haemophilia have been in a much better position to access HCV services, however, certain important principles are at stake (particularly the issue of liver biopsy) and I have tried to address these.

Having reflected on the whole issue of treating pre-cirrhotic disease, I have come to the conclusion that one simple piece of advice is sadly absent from the consulting room. If a patient fears the side-effects of the drug and the treatment is not urgent, why should he or she not try the drugs for a few weeks and see how manageable the side-effects are? A review after, say, four to twelve weeks, would be the time to commit to the full course of the treatment or drop out with less of a feeling of failure. Early indications as to the potential success of the treatment from viral load measurements would enhance this decision-making process. So many people think that by signing up to the treatment they are agreeing to a full course, with the only exceptions being when the side-effects become absolutely unmanageable or certain blood tests indicate that it is time to stop or at least reduce the dose.