

Adherence to hepatitis C treatment: unraveling the complexities

Rob Camp, Keith Alcorn

13 December 2012

Successful adherence to hepatitis C treatment may require physicians and care teams to address a wide range of factors, according to research from the United States and Germany presented at The Liver Meeting 2012, the 63rd annual meeting of the American Association for the Study of Liver Diseases (AASLD) in Boston last month.

Hepatitis C treatment presents a number of adherence challenges that are distinct from other disease areas, due to the use of pegylated interferon, which causes both physical and psychological side-effects that affect numerous areas of a patient's life during a treatment course that may last up to 48 weeks, and which may be undergone several times if the first course is unsuccessful.

Non-adherence to pegylated interferon and ribavirin often consists of non-completion of the treatment course, but a large cohort study of US veterans has also observed that adherence to ribavirin (as measured by prescription refills) declined after the first 12 weeks of therapy, even if the treatment course was completed, and that sustained virologic response was associated with higher levels of ribavirin adherence throughout the 48-week treatment course.

New direct-acting antivirals (DAAs) also present adherence challenges, because they must be taken up to three times a day for 12 to 24 weeks in most cases, and can cause side-effects that also interfere with daily functioning.

In addition to non-completion of the treatment course, missing doses of antivirals is a problematic form of non-adherence to DAA treatment, because it presents a risk of loss of virological control, resulting either in failure to achieve a rapid virologic response during the first four weeks of treatment (RVR), or in viral breakthrough after initial suppression has been achieved. This may lead to drug resistance to the antiviral agent.

Maximising people's ability to adhere to treatment requires an understanding of behavioural as well as biological factors, including socioeconomic status, access to treatment, the disease stage, a patient's individual ability to adapt and moderate behaviour, the treatment itself, its side-effects and cost.

Lauren Rover of George Mason University, Virginia, and Inova Health Systems, a large non-profit healthcare provider in northern Virginia, told a conference session that, for short-term treatment regimens, adherence rates of 70 to 80% are often achieved. For longer-term treatments, adherence rates drop to 40 to 50%, while adherence rates for therapies that also include an element of behaviour change are stuck at around 20 to 30%.

It is worth noting, however, that in one disease area – HIV infection – long-term adherence rates are closer to those for short-term medication courses than for chronic medication, due in part to the simplification of therapy and the provision of intensive adherence support.

Rover and colleagues carried out a study to examine the correlation between a range of psycho-behavioural measures and adherence to pegylated interferon and ribavirin in 63 people. Sociodemographic information included sex, race, substance use history, state of marriage and employment. Economic status and education were not measured.

Adherence scores were based on:

showing up to appointments

“adherence to doctor’s orders” and

filling out forms correctly.

Standardised patient-reported outcomes were assessed at baseline: expressing anger verbally or physically, level of angry reactions, anger as part of personality (“trait anger”), and expression of anger, all of which were higher in those who were already taking antidepressants at baseline; higher levels of emotions and worry were expressed by the same group all the way through the study. Of those patients (84%) who completed all patient reports, 45 individuals (71%) adhered to treatment (as defined) and 18 (29%) did not. Adherence was significantly lower in those who reported more frequently that they felt like expressing anger verbally ($p < 0.01$), and patients who reported more anger and worry at baseline were less likely to adhere to the course of treatment.

The research group concluded that it may be helpful to assess levels of anger and worry before treatment, and to use psycho-behavioural measures as a tool for monitoring people during treatment and to address need for specific interventions.

One issue not reported on was how many people started antidepressants during the study (a not-uncommon occurrence with pegylated interferon) and if that changed outcomes within that group.

In the two groups measured (those who were adherent to treatment and those who were not), age (47 vs 46 years old), marriage, substance-use history and employment were all similar, and therefore not considered predictive factors in adherence. Men had better adherence scores, as did Caucasians.

In discussions after the presentation, the session moderator and audience members suggested that lower adherence in women may be explained by women putting their roles as caregivers above their own health needs, and by possible gender differences in adverse events that affect treatment adherence. Both areas require further research.

Similarly, lower adherence in non-Caucasians may be a consequence of poorer early virological outcomes due to an unfavourable IL28B (non-CC) genotype, rather than a determinant of virologic response, since poor early response may act as a disincentive to subsequent adherence. Once again, further research would be useful.