Introduction

Infection with hepatitis C virus (HCV) is characterised by the high propensity of chronicity. About 50-85% of acute hepatitis C (AHC) infection will progress to chronic hepatitis C (CHC) infection, which will eventually end up in cirrhosis in 5-20% within 20 years of infection. Case fatality rate for AHC was 0.1%, higher than hepatitis A (0.01%) but lower than hepatitis B (0.4%). Nowadays, with the screening of blood products for HCV, intravenous drug users account for a significant proportion of the new cases of AHC as well as nosocomial causes such as needle stick infection in health professionals, surgery and endoscopy.

Diagnosis of acute hepatitis C infection

Most patients with AHC are asymptomatic and thus these patients are not frequently seen in general or referral practice. Moreover, there is no specific test for AHC infection. The diagnosis of AHC is most certain when there is a recognised and defined time point of exposure, absence of hepatitis C virus ribonucleic acid (HCV RNA) by reverse transcriptase polymerase chain reaction at the time of exposure, subsequent development of HCV RNA at a later time point and antibody seroconversion by enzyme immunoassay and recombinant immunoblot assay, together with clinical features of acute hepatitis and exclusion of other causes of hepatitis. Very often we are faced with diagnostic difficulty because one or more of the above features are absent on presentation. In the acute phase of the disease, the level of HCV RNA can also fluctuate over a wide range and may be intermittently undetectable.

Natural history of acute hepatitis C infection

Based on the natural history of AHC infection, spontaneous HCV clearance varies from 10-60% depending on route of transmission, underlying illness, age, viral and host factors. Most who clear will do so in the first 3 to 4 months after infection. In view of the high risk of developing chronic disease and the lack of an effective therapy for all patients once the disease is established, it is important to consider treating AHC, thus preventing its progression to the chronic state. However, we have to select the correct subgroup of AHC patients so as to avoid unnecessary treatment in those who will have spontaneous HCV clearance.

Gerlach et al showed that spontaneous HCV clearance was observed in 52% of patients with acute symptomatic hepatitis C whereas all asymptomatic patients developed chronic hepatitis C. It may be difficult to identify the symptomatic group of AHC for early treatment because the distinction between symptomatic and asymptomatic infection can be very subjective. Certainly there are other issues to consider in the treatment of AHC, when to treat, what to treat, and how long to treat. In defining the timing of treatment, we should compare time from expected exposure until start of therapy instead of time from symptoms until therapy whenever possible. The studies of acute hepatitis C are further limited by their small sample size, heterogeneity in terms of the types of patients treated, regimen of therapy, definitions of beneficial responses and monotherapy with either α or β interferon.

Therapy of acute hepatitis C infection

In a review of 17 studies, interferon therapy was shown to significantly improve the sustained biochemical and virological responses in comparison to no treatment for AHC. A recent Cochrane Database Systemic Review involving 4 randomised controlled trials of transfusion-associated AHC showed an increase in sustained virological response (SVR) rate of 29%. Interferon-treated patients had a SVR of 32% as opposed to 4%. The relatively low rate of response may be related to the suboptimal dose and duration of treatment with interferon (interferon α2b 3 MU 3 times weekly for 12 weeks). Use of high dose interferon α as exemplified in studies by Vogel (10 MU daily until transaminase normalisation), Pimstone (5MU daily for 12 weeks, then 3MU 3 times weekly for 40 weeks) and Jaeckel (5MU daily for 4 weeks, then 5MU 3 times weekly for 20 weeks) was associated with a high SVR of 83%, 100% and 98% respectively. A meta-analysis from Licata et al further supports that induction strategy and use of high dose interferon therapy improve SVR.

With regard to the timing of treatment of AHC, Gerlach et al showed that there was no statistically significant difference in sustained response whether patients received immediate treatment or delayed treatment within 3 to 6 months after the onset of disease (response
rate 83% and 80% respectively). The meta-analysis from Licata et al also showed that delaying therapy by 8 to 12 weeks after the onset of disease did not affect the efficacy of treatment. Two abstracts from Kamal et al conclude that earlier treatment with Peginterferon α2b monotherapy increases SVR and this also holds true for the combination therapy with interferon α2b and ribavirin. Nomura et al reported that the SVR to 24 weeks of interferon α was 100% when therapy was initiated after 8 weeks from onset of acute hepatitis, but fell to 53% if treatment was delayed by 1 year.

Studies from Wiegand et al and Santantonio et al demonstrated that a high SVR could be achieved, 93% and 94% respectively, with the treatment of Peginterferon α2b (1.5mcg/kg/week) for 24 weeks. Comparing the use of Peginterferon α monotherapy with combination therapy with interferon α and ribavirin for 12 or 24 weeks, peginterferon was superior to interferon α and ribavirin in inducing higher rates of SVR and preventing chronicity. Peglated interferon is considered to be safe and effective for the treatment of AHC.

In a prospective study from Kamal et al involving 54 subjects, there was no difference in SVR whether or not ribavirin was added to the treatment with pegylated interferon for 24 weeks (80% in peginterferon monotherapy and 85% in combination therapy with peginterferon and ribavirin). Regardless of the treatment group, there was also no difference in SVR in terms of the genotypes 1 or 4. Therefore, the addition of ribavirin does not statistically improve the SVR.

Another controversial issue is the duration of treatment. Pimstone et al reported a SVR of 100% using daily induction dosing with interferon for 12 weeks, followed by standard dosing for 40 weeks. Several studies have shown that a 24-week course of pegylated interferon is effective and can achieve a SVR over 90%. Compared with a 6-month course, a 3-month course of pegylated interferon seems to be less effective. This was borne out by the study of Calleri et al, in which SVR was achieved in only 61% of patients, as 33% relapsed after therapy discontinuation. However, a Japanese study demonstrated that even a shorter course of daily injection with 6MU of interferon α for only 4 weeks was effective in 87% of patients.

**Recommendations**

According to the NIH Consensus 2002 in the management of hepatitis C, treatment of patients with acute hepatitis C is warranted. The minimum dose required is 3MU of interferon α given 3 times weekly for at least 12 weeks. With reference to the AASLD Practice Guideline 2004, although excellent results were achieved in reported uncontrolled studies using standard interferon monotherapy, it is appropriate to consider the use of peginterferon because of its improved ease of administration. No recommendation can be made about the addition of ribavirin, and the decision will therefore need to be considered on a case-by-case basis. In the absence of controlled study data, no definitive recommendations can be made about the timing of treatment initiation; however, it seems reasonable to delay treatment for 2 to 4 months after acute onset to allow for spontaneous resolution. No definitive recommendation can be made about the duration of treatment needed to treat acute hepatitis C; however, it seems reasonable to continue treatment for at least 6 months.

**Conclusions**

At this moment, there are certainly enough data to recommend antiviral treatment for acute hepatitis C. Treatment in the acute phase results in higher sustained response rates than treatment in the chronic phase. Data suggest that treatment with interferon-based regimens during acute infection improves the rate of SVR. However, interferon α monotherapy was used in majority of the trials. Treatment with pegylated interferon apparently improves the response rate in AHC and may be preferable because of its ease of administration. It seems reasonable to treat for at least 6 months. Treatment may be delayed for at least 12 weeks to permit spontaneous resolution and avoid unnecessary treatment. So, we are still lacking in data from larger randomised trials to give firm recommendations regarding the timing of therapy, the optimum drug regimen and duration of therapy in the treatment of acute hepatitis C infection.

**References:**

14. Pimstone NR, Powell JS, Kofilia R, Pimstone DJ, Davidson L. High dose (780 MIU/52 weeks) interferon monotherapy is highly effective...
MEETING FACILITIES

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<th>場地</th>
<th>Venue</th>
<th>面積</th>
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