EDITORIAL

Optimal Therapy for Hepatitis C

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Hepatitis C is a significant global problem with wide-ranging social and economic impacts.[1] In Iran, it seems that about 200,000 of people are infected with hepatitis C virus (HCV).[2] Multitransfused thalassemic patients are the population who are at high risk for HCV infection acquisition. Based on experience on Iranian thalassemic patients, 20-30% of them were anti-HCV Ab seropositive[3] , although the probability of virus transmission has been significantly reduced after implementation of donor screening since 1995.[4] In addition, HCV is a major cause of liver diseases among chronic renal failure patients undergoing maintenance hemodialysis and according to the latest studies 13.2% of Iranian hemodialysis patients are anti-HCV Ab seropositive.[5] Patients with hemophilia constitute another high risk group for acquisition of HCV infection. The data showed that at least 60% of Iranian hemophilic patients are anti-HCV Ab seropositive.[6]

Combination therapy with interferon plus ribavirin has been the standard treatment by now.[7] On the basis of Iranian Consensus on Management of Hepatitis C Infection, combination therapy with interferon alfa plus ribavirin is the first therapeutic choice in chronic hepatitis C, except for patients who are on hemodialysis and thalassemic patients.[8]

With the best situation, conventional interferon alfa plus ribavirin significantly improved response rates to the range of 35% to 45%.[9] The development of pegylated interferon (PEG IFN) such as PEGASYS has led to an impressive increase in virologic responses up to more than 50%. There are three large clinical trials that focused on sustained virologic response (SVR) based on intention-to-treat analysis. Manns et al., showed that the rates of SVR were higher in the group that received peginterferon alfa-2b with ribavirin (54%), compared with the group who used standard interferon combined with ribavirin (47%). Patients infected with genotype 1 and having high viral levels before treatment had the lowest rate of response, with only 30% achieving SVR, even with optimal therapy.[10] Fried et al. showed that combination therapy using peginterferon was more effective than combination therapy using standard interferon.[11] Hadziyannis et al. showed that in patients with genotypes 2 and 3, SVR rates were excellent, ranged from 73% to 78% regardless of duration of therapy (24 or 48 weeks) or ribavirin dosage (800 mg vs. 1,000 to 1,200 mg daily). These findings indicate that patients with genotype 2 or 3 are adequately treated with a 24-week course of peginterferon therapy. Moreover, the dose of ribavirin can be reduced to 800 mg in this group. On the other hand, patients with genotype 1 need to receive the full, standard dose of ribavirin as well as 48 weeks of therapy to achieve optimal response rate.[12]

There is no report regarding using peginterferon alfa in hemophilic and thalassemic patients with HCV infection in the literature as yet. In this issue there are the first reports on peginterferon alfa in these special diseases, but it is important to consider some points in interpretation of results. Unfortunately the limits of quantitative HCV RNA detection were different in reports of these different research teams. In my opinion it is very important to set up a new automated detection of HCV RNA in research centers in Iran. Second, the route of approach in analysis is very important. Intention-to-treat analysis is a concept of data analysis from clinical trials that assumes patients in analysis (each type that is appropriate) as they were at the begining of the study, not there actually went on as study progress. If some patients changed their study group during study or withdre the study, they should not excluded from intention-to-treat analysis. There are many reasons for discontinuation of the drug. They may become too ill to take the treatment, or suffer severe side-effects from it. However, it is important that article describing the study analysis the patients in treatment groups to which they were assigned, whether they actually received the treatment or not. Intention-to-treat analysis assumes that the patients who lost the study are failures. If the overall analysis shows benefit despite an intention-to-treat analysis, it will strengthen the conclusion.[13]

Overall data from several large clinical trials have shown that peginterferon is more effective than standard interferon

with or without ribavirin. For this reason, peginterferon is likely to replace standard interferon for the treatment of hepatitis C. Furthermore, all studies indicate that the addition of ribavirin to peginterferon increases the sustained response rate. Thus, only combination therapy should be used in the treatment of hepatitis C, except in situations where there are contraindications to ribavirin. Finally, choosing the ribavirin and considering the suitable duration, the Overall response rates to optimal combination therapy with peginterferon and ribavirin average 54% to 56%. Although this is an excellent response rate in comparison with previous therapeutic regimens for the treatment of hepatitis C, there is still a long way to optimum. Interferon-based therapies are also associated with various degrees of adverse effects. As clinical trials have revealed, peginterferon alfa-2a monotherapy in CHC patients was associated with statistically and clinically significant improved Quality of Life (QoL) and less fatigue compared with conventional IFN alfa. It is important to consider the best treatment with fewer adverse effects for patients. Antiviral therapy is expensive, but it will avoid later costs due to complication of HCV infection such as cirrhosis, liver failure and hepatocellular carcinoma. Considering lifetime costs, the higher sustained response rate with peginterferon and ribavirin will lead to cost savings by prevention of future liver related complications and will offset the majority of the higher antiviral costs.[14]

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