HCV RNA detection and quantification, presence of co-infections and co-morbidity, liver biopsy to assess severity of disease and HCV genotype is recommended in patients with hepatitis C, prior to starting treatment. Transient elastography (TE) can also be used to assess cirrhosis in patients with chronic hepatitis C infection.1

There are six genotypes of hepatitis C virus (HCV). Genotype 1, with subtypes 1a and 1b is the most prevalent worldwide. In USA and Europe, genotype 1a and 1b is common respectively. Genotype 2 is found in the Mediterranean region. Genotype 3a is seen in European intravenous drug users.2,3 Genotype 4 is prevalent in the Middle East. In Pakistan, genotype 3 is the most common. However, genotype 1, 2 and 4 have also been documented.3

Chronic infection with HCV is associated with hepatic inflammation, progressive fibrosis and HCC.4 The disease process is accelerated in the presence of co-morbid conditions such as co-infection with hepatotropic viruses, HIV, diabetes mellitus etc. regardless of the genotype or viral load.5

Hence, before starting treatment in any patient, after a complete physical examination, preliminary investigations such as anti-HCV antibodies by enzyme immunoassays and HCV RNA detected by real-time polymerase chain reaction (PCR), which can quantify HCV RNA levels up to approximately 107 IU/mL HCV,6 as well as PT (prothrombin time), APTT (activated partial thromboplastin time), LFT (liver function test), complete blood picture, ultrasound abdomen (for hepatosplenomegaly), and co-morbid states such as co-existing infection with HBV and HDV need to be documented. Also, HCV genotype has to be assessed before starting treatment in order to determine the dose of ribavirin and decision regarding the treatment duration.1

To assess the grade of inflammation and stage of fibrosis (METAVIP, Scheuer, Ishak, and Knodell’s), liver biopsy is regarded as a reference method to-date.7,8 Drawbacks of liver biopsy are well-known; therefore, recent alternative methods are being used such as the TE which perform better at diagnosing cirrhosis, rather than fibrosis. However, factors such as obesity, age and biochemical necroinflammatory factors may adversely affect TE.9 The direct [ALT, AST, prothrombin time, platelets, APRI i.e. AST platelet ratio index, AST/ALT ratio [Forn's Index] and indirect biomarkers (α-2 globulin) are helpful in combination with TE for assessment of liver.10

Patients infected with HCV genotypes other than genotype 1 who failed to respond to therapy with standard IFN-α and ribavirin can be treated with pegylated interferon (PEG-IFN) and weight based ribavirin.1 The first generation protease inhibitors i.e. teleprevir and boceprevir are not effective or licensed for non-1 genotypes. Retreatment should be considered, if they have significant fibrosis, evidence of inadequate exposure to PEG-IFN and ribavirin due to dose adjustment/ or poor adherence during the first course of therapy. Longer re-treatments of 48 weeks are advisable for genotypes 2 and 3, while 72 weeks for genotype 4.11 Patients relapsing after treatment with standard IFN-based regimens respond to re-treatment with pegylated IFN-α and ribavirin in 32-53% of cases.1,12 Maintenance with low dose pegylated interferon IFN-α is not recommended.1,11

It is to be noted that studies from Europe and USA1,6,12 do not recommend using standard interferon for genotype 1 or 3, instead PEG-IFN is used with ribavirin. However, in these countries the usual genotype is 1 or 4, hence recommended therapy is PEG interferon with ribavirin. Per se standard interferon therapy is considered obsolete for any genotype in the said areas. However, in Pakistan, perhaps it is still used due to the cost constraints and the presumption that our patients are genotype 3 and will, therefore, show an excellent response with a sustained virological response (SVR) of 80%.13,14 Other than the recommendations of Pakistan Society of Gastroenterology (PSG)15, there is no literature which recommends the use of standard interferon with ribavirin, for treatment of HCV.

The article published in this issue deals with re-treatment of standard interferon and ribavirin failures. However, the genotype, and quantitative PCR were not done prior to therapy. The response rate of SVR was low in the treatment naïve patients, which could be due to the genotypes other than genotype 2 or 3. Genotype 1 has a better response with PEG-IFN than standard

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interferon and requires a longer duration of therapy. This may have been missed. Also, low response rates of standard as well as PEG-IFN may be related to inadequate storage facilities in vials dispensed from government agencies.

The PSG recommends that standard interferon be used locally. However, most RCT trials indicate that PEG-IFN should be the drug of choice regardless of the genotype when starting therapy for HCV infection. The cost of PEG-IFN is higher than standard IFN and hence its use as a first line agent in genotypes other than 1 and 4 is questionable. Also the response with standard interferon in genotype other than 1 and 4 is excellent.13,14 This contradicts international data which strongly recommends the use of PEG-IFN in all HCV infections due to better efficacy and single injection per week for all genotypes.

There are no recent local published guidelines available for the management of HCV infected patients considering the diversity of our genotypes. Also, there is no recent international published literature which recommends the use of standard IFN with ribavirin for treatment naive patients of HCV in genotypes other than genotype 1. There is a need to develop local guidelines after randomized controlled trials have been done in a scientific and ethical manner for the perusal of physicians and hepatologists.

REFERENCES