Hepatitis C Viral Infection

The prevalence of antibodies to the hepatitis C virus in the United States is approximately 1.4% to 1.8%. This data was derived from the NHANES III survey. Using these samples it is estimated there are 3.9 million persons with antibodies to the Hepatitis C Virus and approximately 2.7 million are viremic. HCV infection is the commonest cause of chronic liver disease in the US and accounts for 8000 to 13000 deaths per year. Most of the liver transplants performed in the US are for chronic hepatitis C. Approximately 30% of patients infected with HCV viral infection develop cirrhosis and a proportion of these patients will eventually develop hepatocellular carcinoma. In 1997, the annual cost of chronic hepatitis C was 5.46 billion dollars the bulk of which (92 %) was related to chronic hepatitis and the remaining cost were related to hepatocellular carcinoma.

Genotype 1, 2 and 3 are the commonest HCV genotypes in the US. Current therapy for chronic genotype 1 HCV infection involves combination therapy with Protease inhibitor (except for co-infection with HIV), Pegylated Interferon and Ribavarin for 24 or 48 weeks. Patients are monitored for viral load at week 4, 12, 24, 48 and beyond to check for rapid virologic response (RVR), extended rapid virologic response (eRVR), early virologic response (EVR) and sustained virologic response (RVR). Therapy is adjusted based on virologic response. Sometimes IL28B genotype is checked prior to treatment as it is an important determinant for treatment response. Current therapy for chronic genotype 2 and 3 HCV infection involves combination therapy with Pegylated Interferon and Ribavarin for 24 weeks. Viral load is monitored in similar fashion.

Approximately 60 to 70 % of genotype1 patients who are treatment naïve or prior relapsers will have SVR with current therapy. Whereas approximately 70 to 80% of patients with genotypes 2 and 3 will have SVR with current therapy. Response rates vary based on degree of liver fibrosis, race (decreased in African Americans), body mass index (decrease in obese patients), and those with diabetes or iron overload. There are possible significant side effects with the combination therapy especially with the addition of protease inhibitor. These include flu-like symptoms, depression, bone marrow suppression, skin rash, significant drug-drug interaction and thyroid dysfunction. Hence, close follow up and monitoring of the patients is crucial during treatment.

In conclusion, it is recommended that the presence of HCV infection be looked for in all patients with risk factors (C: tattoo, blood transfusion before (prior to 1992), history of intravenous drug use, history of snorting cocaine) even though their liver function tests are normal and in all patients with abnormal liver tests. The ELISA is the test used to screen for the presence of chronic HCV infection. If this test is positive it should be confirmed by HCV viral load and Genotype assay. Patients on chronic hemodialysis and HIV positive patients often have diminished antibody production and should be tested with HCV RNA assay as they can have a false negative HCV antibody test.

RECOMMENDATIONS

1. All patients with chronic HCV infection should be considered potential candidates for treatment and hence should be referred to Gastroenterology, to determine if they are candidates for treatment and to document a discussion of the risk, benefits and
alternatives to treatment if they are. At that time we also discuss details of the disease such as the epidemiology, and prognosis with and without treatment.

2. Prior to referral to Gastroenterology the following tests should be performed: CBC with diff, comprehensive metabolic panel, Viral load, Genotype, PT/PTT and hepatitis A and B serologies. Of note, viral load levels do not predict level of fibrosis in the liver and are only helpful in treatment.

3. Patient with risk factors for retinopathy are referred to Ophthalmology by GI for a baseline retinal exam pretreatment and at varying interval during treatment.

4. An ultrasound of the liver should be obtained if it was not performed within 6 months of referral to gastroenterology.

5. Patients should be counseled against the use of alcohol which hastens the progression of hepatic injury with chronic HCV infection. Concurrent alcohol use reduces the effectiveness of Hepatitis C therapy to less than 5% effective.

6. All patients with hepatitis C viral infection should be vaccinated against both hepatitis A and B viruses. Ideally this should be done prior to referral. If patients have been exposed to these viruses in the past vaccination is not required. This can be confirmed by checking antibody test to these viruses.

7. Patients with major depression, bipolar mood disorder, or other Axis 1 disorders need to be on a stable regimen prior to initiation of HCV therapy. Most times a decision to initiate therapy in these patients is made with joint consent of psychiatrist or primary care provider and the gastroenterologist.

8. All patients who have failed therapy, who are not candidates for therapy and those who refused treatment should be seen in the office every 6 months (this is usually done by GI). At the 6 month visit a CBC, PT, comprehensive metabolic panel, and abdominal ultrasound maybe obtained. The purpose of these visits is to assess for the development of cirrhosis and/or hepatocellular carcinoma. (Hepatocellular carcinoma is usually preceded by the development of cirrhosis in all patients with HCV, this is unlike patient’s with HBV infection who can develop hepatocellular carcinoma without having cirrhosis)

Ultrasound is not a very sensitive test for the detection of hepatocellular carcinoma but it is used because it is more cost effective than CT and MRI. Ultrasound abnormalities and/or significant elevation of the alphafetoprotein should prompt further evaluation of the liver with an MRI and if there are contraindications to MRI a CT scan should be obtained.

**Controversy**

It is generally recommended that all patients with and chronic HCV should be offered treatment if there are no contraindications after a liver biopsy stages the degree of fibrosis in the liver. However, the decision to treat patients without a liver biopsy is somewhat controversial. This decision should be individualized and should be made after discussion of the potential success of clearance vs the risk of treatment with the patient. Because the sustained virologic response is significantly higher in patients with genotype 2 and 3, they are the ideal candidates to treat even without liver biopsy. In these patients, the benefits of treatment outweigh the risks/side effects.