Hepatitis C virus infection: an evolving field of medicine

Hepatitis C virus infection is a leading cause of chronic hepatitis, cirrhosis and hepatocellular carcinoma. It is also an important indication for liver transplantation in the USA and Europe, yet it is potentially curable. It is estimated that 3% of the world population (170 million people) are infected with hepatitis C. The highest prevalence is in North Africa and the Eastern Mediterranean. The prevalence in South Africa is not known, but is estimated to be in the range of 0.1-1.7%.1-3

The hepatitis C virus is an enveloped single-stranded RNA virus and a member of the hepacivirus genus of the Flaviviridae family. There are six major genotypes with subgenotypes and quasispecies within each genotype. The most predominant genotype in South Africa is genotype 5, constituting about 40% of chronic infections,4 while in the USA, it is genotype 1. The virus infects humans and chimpanzees, the only known susceptible hosts.

The major risk factor for acquiring hepatitis C infection is exposure to blood or blood products. Risk factors include clotting factor treatment before 1987, multiple sexual partners, blood transfusions or organ transplantation prior to 1992, as well as injection drug use, mass injections, traditional practices, and birth from infected mothers. Risk factors for new infections in developed countries are mostly drug use (using injections) and sexual exposure.

Most acute infections are asymptomatic. Up to 85% of infections progress to chronic hepatitis C infection, predisposing the individual to chronic liver disease and hepatocellular carcinoma. The most important factors associated with liver disease progression are the extent of intrahepatic inflammation elicited by hepatitis C, co-infection with human immunodeficiency virus or hepatitis B virus, alcohol consumption and the presence of metabolic syndrome or insulin resistance.5,7

Chronically infected individuals are mostly asymptomatic until they develop chronic liver disease complications. Patients might present with vague symptoms of tiredness and malaise, clinical features of chronic liver disease, e.g. oedema, jaundice and elevated liver enzymes, or may present with extrahepatic manifestations, such as aplastic anaemia, porphyria cutanea tarda, glomerulonephritis, diabetes mellitus, arthritis, arthralgia and cryoglobulinaemia. It is estimated that 30% of patients with chronic hepatitis C have at least one extrahepatic manifestation of the disease.6 Most patients are diagnosed during blood donation or during screening for other reasons.

The screening test for hepatitis C is the anti-hepatitis C virus antibody serological assay, while polymerase chain reaction (PCR) can identify patients with chronic hepatitis C. Hepatitis C virus genotyping and viral load are mandatory in patients who are being evaluated for therapy.

The current standard of care for hepatitis C virus patients is combination treatment with pegylated interferon (Peg-IFN) and ribavirin, aiming for sustained virological response (SVR) 24 weeks after completion of treatment. Generally, the duration of treatment is 24 weeks (genotypes 2 and 3) to 48 weeks (genotypes 1, 4 and 5).8 Newer guidelines emphasise individualising treatment duration depending on several prognostic factors, including baseline viral load and response to treatment at week 4.9

Patients on peg-IFN and ribavirin should be monitored closely for side-effects from therapy. Side-effects of peginterferon include neutropenia, thrombocytopenia, thyroid dysfunction and depression. Adverse effects of ribavirin include anaemia that sometimes requires erythropoietin or blood transfusion. Severe anaemia is an indication for discontinuation of treatment.

General treatment measures include loss of weight if body mass index is more than 25 kg/m², complete abstention from alcohol, management of iron overload by venesection, hepatitis A and B vaccination and monitoring of patients with hepatitis C virus-related cirrhosis every 6-12 months for hepatocellular carcinoma.2

Predictors of a favourable response to treatment include both host and virus factors. Favourable host factors for response include female gender, white race, age less than 40 years, body mass less than 85 kg, absence of liver fibrosis and host genes (IL-28B polymorphism). Favourable viral factors include hepatitis C virus genotype other than 1 and low baseline viral load (< 600 000 IU/ml/ < 800 000 IU/ml). Rapid virological response, that is undetectable hepatitis C virus at week 4, is one of the most important predictors of SVR.

In May 2011, the US Food and Drug Administration approved the use of directly acting antivirals for the treatment of
hepatitis C virus genotype 1 infection. This increased SVR rates from 40-50% to 70-80% in patients infected with this genotype. Today, treatment for genotype 1 involves the use of directly acting antivirals such as the protease inhibitors, telaprevir or boceprevir, in combination with peginterferon and ribavirin, modulating duration according to response at week 4 and 12 of therapy (response-guided therapy). For other genotypes, the standard of care is peginterferon and ribavirin.

It is foreseen that in the near future, more novel therapies will become available. Such therapeutic strategies might provide well tolerated oral combinations with less side-effects and 100% cure rates.

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References