Editorial

HEPATITIS C VIRUS: CONCERNS AND CONTROVERSIES

FADHEELA AL MAHROOS, MD, FAAP*

Hepatitis C virus (HCV) is a major public health problem world-wide. WHO estimates that 3 % of the world population are infected with HCV. There may be more than 170 million chronic carriers world-wide[1]. The prevalence of HCV infection in Bahraini children with chronic hemolytic anaemia is estimated to be 40% (27% of those with sickle cell syndromes and 71 % of those with beta-thalassaemia major)[2]. While the prevalence of HCV infection among blood donors in Bahrain has been estimated to be 1.8%[3]. If we extrapolate this data to the general population, it means that there is at least ten thousand chronically HCV infected individuals who are at risk of developing cirrhosis, hepatic failure and hepatocellular carcinoma within the next 1-2 decades, with all the entailed human suffering, shortened life expectancy and phenomenal health care costs.

Hepatitis C is an enveloped single stranded RNA virus and is a member of the flavivirus family. HCV results in acute disease which tends to be mild and insidious in onset with fatigue and jaundice as the most common symptoms. However, most patients (up to 75%) are asymptomatic. This makes disease monitoring difficult. Another challenge is the propensity of HCV infection to progress to chronic hepatitis in about 80% of the cases. About 20% of these chronically infected will develop cirrhosis, and 1-5% of cirrhotic patients will develop hepatocellular carcinoma within the following 1-2 decades. With the estimated 170 million individuals infected world-wide, this is a time bomb awaiting explosion.

Transmission of HCV is primarily by parenteral exposure to blood and blood products from HCV infected patients, the use of inadequately sterilized equipments or through needle sharing among drug abusers. However, in over 40% of the cases the mode of transmission cannot be identified. This represents a major challenge for disease control.

Is the transfusion of screened blood safe ? With the exclusion of high risk individuals from donating blood and the use of first and second generation assays for HCV antibody, the risk of HCV infection following blood transfusion is drastically reduced[4]. However, it is estimated that there is still a risk of HCV infection of 0.1% per receipient of screened blood. This is due to the fact that the current serological assays do not detect HCV antibody in approximately 5% of infected individuals and because of the rare case of donation in the early stage of infection before HCV antibody can be detected. Thus screened blood is not safe yet, and the indications for transfusion should be scrutinized carefully.

What is the risk of sexual and vertical transmission ? HCV is less infectious than hepatitis B virus (HBV) and human immunodeficiency virus (HIV). Infected blood appears to be the most efficient method of HCV transmission. Sexual transmission is uncommon. It is estimated that 8% of HCV positive patient's spouses are also HCV positive. Likewise maternal - fetal transmission is only 5% which is far less than the risk with HBV vertical transmission[5].

What about breast feeding ? HCV antibody and HCV RNA have been detected in the colostrum, but HCV transmission by breast feeding to infants has not been documented yet. The rate of transmission among breast-fed infants has been the same among bottle-fed infants. Thus, breast feeding is not contraindicated in maternal HCV infection. However, the final decision to breast feed should be based on honest and correct information given to the mother.

Treatment of HCV: Randomised clinical trials with interferon alpha - 2B have shown that about 20% of the patients with chronic hepatitis achieved a sustained response[6]. Several regimes are used but the best benefit is achieved with 3 million units subcutaneously three times weekly for 12 months. The most common side effects are flu-like syndrome, alopecia and depression.

Predictors of response: genotype, viral load, and cirrhosis

Hepatitis C virus is clustered in six genotypes with at least 3 viral subtypes for each genotype. Response to interferon is influenced by the genotype. Genotype 1b seems to be the most resistant to treatment, the rate of sustained response regardless of other factors is 0-20%[7], while genotype 3 has the most favourable sustained response of 35-40%. Genotype 1 b is common in south Italy. Genotype 4 in Egypt, and genotype 3 among drug abusers. Can we use this data to decide who should receive treatment and who should not ? The answer is no ! because, although the response of those who are non-genotype 1 is clearly better, many patients infected with genotype 1 did respond to interferon. These patients may need more aggressive treatment such as longer duration and/or combination therapy[8]. Similarly patients with higher viral load (more than 1 million/ml) and cirrhosis responded less favourably to interferon. Here again

* Consutlant Paediatrician
Salmaniya Medical Complex
Assistant Professor
College of Medicine & Medical Sciences
Arabian Gulf University
Editor
Bahrain Medical Bulletin

we cannot, based on such information exclude patients from treatment since some patients with high viral load and early cirrhosis did show sustained response. Current consensus is to treat all patients with chemical and histological evidence of active disease, (these are the ones who are at greatest risk for progression to cirrhosis), re-evaluate them at 3 months and continue therapy only for those who showed response to treatment (lower ALT and HCV RNA)[6].

Some experts advocate altering the endpoint expectation based on disease severity. In a patient with mild disease the goal is to eradicate infection, while in a patient with fibrosis and cirrhosis, the goal is to reduce histologic damage to the liver and prevent further deterioration. Some studies have shown that extended treatment to 18 months resulted in histologic improvement in non-responders. However, the question is, can we reduce the longterm complications of cirrhosis, hepatic failure and hepatocellular carcinoma by such an approach ? Finding the answer to this question is the only way to justify prolonged treatment of such patients.

Combination therapy - Interferon and Ribavirin: Recently, few studies have shown that adding Ribavirin to interferon therapy has improved response rate[9]. When the combination therapy was used in patients who received no treatment before, the sustained response was raised from 20% to 46%.

Acute HCV infection: Twenty five percent of acute hepatitis C may present with clinical hepatitis. Studies showed that high dose interferon treatment for 3-4 months starting in the early stages of symptomatic disease resulted in a response rate of 70% in the treatment group versus 20-30% in the control group[10]. Thus the treatment of acute hepatitis with interferon might be the most effective way to prevent chronic hepatitis C in these patients.

What about the patient who is HCV RNA positive, ALT normal and histologically shows mild inflammation without fibrosis and piece-meal necrosis ? There is evidence that interferon may in fact activate the disease by stimulating cytotoxic T cells, which can worsen hepatic damage. Thus, current recommendation is to follow these patients and treat only when there is chemical and histological evidence of active inflammation.

What to do when a health care worker gets stuck with a needle contaminated with blood from an infected patient ? First establish baseline status of the health worker and the patient by having ALT and HCV-RNA. Then repeat these tests every 3 months for 12 months. The use of immunoglobulins for post exposure prophylaxis against hepatitis C is not recommended, because there is no evidence of clinical efficacy[5]. If the health worker seroconverts, the current recommendation is to treat with interferon alpha - 2B for 2-3 weeks with the end point of treatment is serum clearance 0f HCV RNA.

Prevention of HCV infection: Currently, interferon therapy (and probably combination therapy with ribavirin) is the only effective therapy. However, world-wide 90% of patients who need therapy cannot afford the high cost. For the remaining 10%, 80% of them do not respond to treatment with interferon. Until we find a more effective and affordable treatment, our efforts should be directed to prevention.

What about vaccination against hepatitis C ? An important feature of the virus is the high mutation rate of its several genomic types. This is one of the reasons that makes it difficult to clear HCV by the immune system and the other being the high propencity of the virus to induce chronic infection. In addition, it hinders the efforts for developing a vaccine. Thus vaccination is not an immediate issue, and without vaccination emphasis must be placed on other means of prevention namely preventing exposure of those at high risk through standard precautions and education about transmission.

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