

Treatment of hepatitis C virus infection and hemophilia

Miguel S. Contreras Jorge¹

Hemophilia is a condition in which there is a deficit of a coagulation factor. Treatment for this condition consists of administration of the missing or deficient factor by hemotransfusion. According to statistics, more than 80% of hemophiliacs in the USA are infected with the hepatitis C virus (HCV). Twenty years ago, transfusion with blood products from multiple donors constituted a major risk for persons with inherited coagulation diseases. Chronic infection with HCV is a significant cause of morbidity and mortality in hemophiliacs who undergo multiple transfusions.¹ Furthermore, 30%–50% of hemophiliacs with HCV are coinfecting with human immunodeficiency virus (HIV), which accelerates the progression of HCV infection.² In hemophiliacs, HIV–HCV coinfection is associated with an increased risk of end-stage liver disease.³ Progression of liver cirrhosis and development of hepatocarcinoma are reduced by HCV treatment.^{4–6} Increasing numbers of patients with hemophilia and viral hepatitis are dying from hepatocellular carcinoma. The incidence of hepatocarcinoma is 239 per 100,000 HCV-positive hemophiliacs per year.⁷

Treatment of hepatitis C elicits various virological response patterns. Interferon suppresses viral replication and normalizes alanine aminotransferase levels in 15%–25% of nonhemophilic patients with chronic HCV infection. The initial response of hemophiliacs to treatment with interferon alone is poor (0%–8%).⁸ Combined treatment with interferon plus ribavirin induces sustained suppression of hepatitis in one-third of hemophiliacs who are refractory to interferon monotherapy.⁹

At present, two types of therapies are based on pegylated interferon plus ribavirin. In cases of hepatitis C monoinfection, PEGASYS®, a pegylated interferon alfa-2a (40 kD), resulted in an average sustained viral response of up to 63%, and peginterferon alfa-2b (12 kD) resulted in an average sustained viral response of up to 54%.^{10,11} Combined therapy with interferon plus ribavirin is safe for hemophilic HIV patients with stable CD4 cell counts and low HIV replication, levels and results in an HCV clearance rate of 40%.

The sustained viral response in patients younger than 18 years is greater than that of adults. In a study carried out on 62 people between 2 and 17 years of age who were treated with peginterferon (1.5 mg/kg body weight per week) and oral ribavirin (15 mg/kg body weight per day) for 48 weeks, sustained viral responses were observed in 22 (47.8%) of 46 patients with genotype 1 HCV, in 13 of 13 (100%) patients with HCV genotypes 2 or 3, and in one of two (50%) patients with HCV genotype 4. When the origin of the infection was determined, it was found that 19 of 27 (70.4%) children had parenteral transmission, 12 of 25 (48%) had vertical route transmission, and 5 of 9 had an unknown route of transmission. Eighty-three percent of patients developed leucopenia, but only three required reduction of their ribavirin doses; 0.3% developed autothyroidal antibodies and thyroidal dysfunction.

In another study, the efficacy of and tolerance to treatment with pegylated interferon and ribavirin was assessed using 72 HIV-positive hemophilic patients with elevated alanine aminotransferase levels. Of the 72 patients, 72% had HCV genotype 1, 14% had HCV genotype 3, 12% had HCV genotype 2, and 3% had HCV genotype 4. Of the 65 patients who completed the study, 41 (57%) had a virological response at the end of treatment, 16 (22%) had no primary virological response, and 32 (49%) had a sustained viral response. Of these, 82% were infected with HCV genotypes 2 or 3 and 38% were infected with HCV genotypes 1 or 4. The side effects of treatment were leucopenia (40%), loss of weight (39%), and fatigue (35%). The average decrease in hemoglobin concentration was 3.1 g/dL. Treatment was discontinued in cases of diabetes, neutropenia, and persistent elevation of alanine aminotransferase levels, and a reduction of the dose was required for 30 (42%) patients.

Liver biopsies of hemophilia patients are problematic because of their coagulation anomalies. Liver biopsies are necessary to establish the extent of liver damage in hepatitis C patients and can be used to aid decision making and to measure progress during treatment. It has long been known that liver biopsies can be taken safely from hemophilic patients when concen-

¹ Clínica Corominas Restauración, Dominican Republic.

Address for correspondence:
E-mail: dcontreras@verizon.net.do

trated solutions of coagulation factors are administered and close medical supervision is maintained. Of 161 HCV–HIV coinfecting hemophilia patients, 112 (69.6%) declined biopsies because of fear and the risk associated with the procedure and 49 (30.4%) accepted biopsies (all received two doses of coagulant factor and 25 received a third dose). There was no bleeding after any of the biopsies.

In conclusion, liver biopsies of hemophilic patients (with or without coinfection with HIV) are generally safe, and in most cases, useful. Although, some patients have been successfully treated with antiviral therapies without having a biopsy, the indications for liver biopsies in patients with hemophilia are the same as those for other populations.

Recommendations of the consensus panel

What is the treatment of choice for this group of patients?

The consensus was that the treatment of choice for this group of patients is combined antiviral therapy with pegylated interferon and ribavirin in which the dose and duration is determined by the HCV genotype present.

Evidence quality: 2

References:

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