Preview

Clinical Overview of Hepatitis C Patients with Terminal Renal Disease

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Abstract | Hepatitis C virus (HCV) is a serious public health issue, and it is estimated that 3% of the world's population is infected with the virus. Patients in hemodialysis units have an increased risk for contracting HCV, and high prevalence rates have been found in hemodialysis units around the world. HCV induces chronic liver disease, which is characterized by a persistent hepatic parenchyma inflammatory process that may progress to cirrhosis and hepatocarcinoma. Viral clearance occurs in a minority of patients with viral hepatitis C, whereas chronic infection is established in 60 to 80% of all cases, 20 to 40% of which may evolve to cirrhosis and hepatocarcinoma. Genetic differences among infected hosts can determine the progression and outcome of the virus infection, causing different individuals to respond in different ways to the viral infection.

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Infection with hepatitis C virus (HCV) is a current and important global public health problem, the leading cause of chronic liver disease and the most common indication for liver transplantation in developed countries. According to the World Health Organization (WHO), about 3% of the world's population is infected with HCV. A tiny portion of the population reaches viral clearance spontaneously, whereas most people (around 85% of those infected) progress to chronic infection, which is a risk factor for the development of cirrhosis and hepatocellular carcinoma (HCC), cooperating with the increasing number of liver transplants (WHO, 2014).

In recent years, there have been major advances in the characterization of the molecular structure of HCV, the development of diagnostic tests with high sensitivity and specificity, the knowledge of pathogenic mechanisms and improved therapeutic options. The continued study about this disease allowed the characterization of its epidemiology and main routes of transmission.

Currently, HCV competes with alcoholic liver disease as the leading cause of chronic liver disease. As it is asymptomatic in most cases, the disease progresses silently to chronicity with consequent increase in cases of liver cirrhosis and HCC.

Among the known hepatotropic virus, hepatitis C virus remains a significant problem in patients with chronic renal failure undergoing dialysis treatment. The patients in hemodialysis units have been considered a risk group for infection with hepatitis C, compared to the prevalence found in groups of blood donors.

The prevalence of HCV in hemodialysis patients varies around 8.4% to 39.2% in Brazil, 3% in Holland, 22.5% in Italy and 80% in Egypt. This prevalence in-

creases with worsening socio-economic conditions in the region, but even in some developed countries, it is much higher than that observed in the general population.

Several studies have reported the frequency of blood transfusions and hemodialysis treatment time as factors associated with HCV transmission, in addition to nosocomial transmission. Sharing dialyzers and the lack of isolation of HIV-positive patients in the unit become highly significant factors in the transmission of hepatitis C.

Phylogenetic analysis showed a significant viral homogeneity in patients from the same unit, thus confirming the nosocomial transmission of hepatitis C virus. The spread can also occur during hemodialysis procedures, surface contact, medicines, gloves and materials contaminated in surgical and invasive procedures due to improper sterilization of instruments.

Factors such as biosecurity, nursing staff sharing and technical and procedural errors should also be taken into account. Regarding the group of hemodialysis patients, it is important to adapt enhanced measures of infection control and isolation of infected patients not sharing materials.

Currently, the main goal of hepatitis C treatment is to control the progression of liver disease by inhibiting viral replication, achieving sustained virological response (SVR), which is determined as viral particles undetectable in plasma six months after the end of treatment. New drugs are being used, e.g. simeprevir, sofosbuvir, daclastavir among others, all with few side effects and virological response greater than 90% (Ahn and Flamm, 2014).

HCV virus proteins are directly involved in the resistance to viral therapy and genetic susceptibility. Among the viral factors related to therapeutic response, two showed significant importance: the viral genotype and the presence of specific mutations in the viral genome. The viral genotype is a major predictive factor in the response to therapy. Genotype 1 shows high rates of resistance to therapy, whereas genotypes 2 and 3 are more susceptible. In recent years, several groups worked on identifying factors attributed to therapy resistance with interferon, focusing on the genomic region of HCV that has the ability to interfere with the antiviral properties of the immune response.

With respect to the host, many factors are involved in determining the severity of the individual disease progression and therapeutic response. There is ample evidence that genetic factors are also associated with the development of infectious disease. Studies report that mechanisms related to innate immunity have genetic variability in encoding genes, showing differences in susceptibility, severity and response to therapy of infectious and autoimmune diseases. From the elucidation of the human genome sequence, there have been great advances in relation to the structural organization and functioning of the genes involved in the innate immune response. These genes are considered highly conserved among species, though studies show inter-individual variability mainly in the form of single nucleotide polymorphisms (SNP).

It is worth highlighting that the cytokines produced in the liver are essential in the immune response against hepatitis C virus, but are also associated with liver cell injury. During viral infection, changes in the balance of stimulatory and inhibitory cytokines can enhance the inflammatory process, favoring necrosis, fibrosis and HCC. Studies have associated cytokine expression levels with the degree of liver damage and the response to antiviral therapy.

SNP in the interleukin-promoting gene, such as interleukin 10 (IL10), interleukin 28 (IL28) and (IL6), appear to be associated with successful treatment, viral clearance and liver disease progression. According to the proposed therapeutical schemes, SVR rates can reach 50 to 90% of treated people, thereby reducing the development of cirrhosis and liver cancer. However, the access to the diagnosis and treatment remains very low.

Given the complexity of factors related to HCV, it is essential to investigate the multiplicity of aspects of this infection. Knowledge about SVR predictive factors, viral clearance, progression of chronic disease and risk group are crucial information, considering the high costs of antiviral treatment. It is worth emphasizing that considering the high prevalence of HCV in patients with chronic renal failure undergoing hemodialysis treatment, molecular research presents great value to develop strategies for prevention, monitoring and treatment, thereby contributing to the interruption of HCV transmissions in this risk group.

Reference

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