Hepatitis C virus and transplantation

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HCV-related end-stage cirrhosis accounts for about 30% of liver transplantations (1,2). In most centres, this proportion is close or even higher than that of patients transplanted for alcoholic cirrhosis. In patients with chronic hepatitis C, liver transplantation is indicated for decompensated cirrhosis or hepatocellular carcinoma.

In this group of patients, the results of liver transplantation are mainly impaired by the recurrence of HCV infection on the graft. Almost all transplanted patients have ongoing viral replication, with detectable serum HCV RNA, at the time of transplantation. The recurrence of HCV infection is almost constant (2,3). Serum HCV RNA appears usually two weeks after the transplantation. HCV replication is enhanced by immunosuppressive therapy and serum HCV RNA levels are higher in this population, as compared with those in non transplanted patients (4). The reappearance of detectable HCV RNA in the serum is usually followed by acute hepatitis, occuring 2 to 6 months after transplantation. Acute hepatitis is characterized by a moderate increase of serum aminotransferases and sometimes by cholestasis with or without jaundice.

One year after transplantation, it is estimated that 50% to 75% of the patients have histologic lesions of chronic hepatitis (5). The severity of the liver disease ranges from mild chronic hepatitis to severe chronic hepatitis evolving rapidly, in less than 5 years, to cirrhosis. On the average, the progression of fibrosis is more rapid in the graft recipients that in the non transplanted population.

Despite the recurrence of HCV infection, the overall results of liver transplantation at 5 years observed in HCV related cirrhosis are not different from those observed in other types of cirrhosis (2,5,6). In particular, the survival seems to be not different from that in other populations. However, more studies are needed to confirm this observation and a significant difference in survival might appear with a longer follow-up.

Many factors might influence the outcome of HCV recurrence, including the type of immunosuppression, viral genotype and viral load. It is believed that in chronic hepatitis C, the liver lesions are not caused by a direct cytopathic effect of the virus but to immune mediated mechanisms. Therefore, the more rapid progression of chronic hepatitis C on the graft is not well understood. However, high dose immunosuppression used for the treatment of rejection has been reported to be associated with a more rapid progression of chronic hepatitis C (7). These observations justify to use, whenever it is possible, the minimal immunosuppressive schedules in graft recipients with HCV recurrence.

The role of HCV genotype has been suggested and some studies have showed that transplanted patients infected with genotype Ib had a more severe liver disease than those infected with other genotypes (8,9). The relationship between the severity of the liver disease and genotype was independent of the viral load. However, this observation was not confirmed by other studies and the role of HCV genotype remains still debated. Several studies have showed no significant influence of the viral load. Finally, the role of virological factors in the outcome of HCV recurrence need further studies.

In practical, it is usually recommended to decrease the immunosuppressive therapy as much as possible but the benefit of this strategy has not been demonstrated. Antiviral therapy is little effective. Alpha interferon therapy is associated with a transient decrease of aminotransferases in a minority of patients and has an incomplete antiviral effect with the persistence of detectable serum HCV RNA (10). Because of its immunostimulatory effects, alpha interferon administration seems to be associated with an increased risk of rejection (10,11). Combination of interferon with ribavirin is currently the best therapeutic strategy (10,12). Preliminary studies showed that this treatment induces, in some patients, a complete inhibition of viral replication with undetectable serum HCV RNA and normalization of aminotransferases. This treatment might be more effective when administered early after the transplantation. Treatment administered before the transplantation might also be baneficial. Further studies are needed to define the best treatment strategies in patients transplanted for HCV related end-stage cirrhosis.

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