Efficacy of lamivudine in decompensated cirrhosis secondary to hepatitis B: Cautious optimism in the war not yet won

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ARTICLE

Villeneuve JP, Condreay LD, Willems B, et al. Lamivudine treatment for decompensated cirrhosis resulting from chronic hepatitis B. *Hepatology* 2000;31:207-10.

ARTICLE SUMMARY

A prospective single arm study was undertaken to determine whether lamivudine (100 mg/150 mg daily) would result in improvement biochemically (serum aspartate aminotransferase, alanine aminotransferase, albumin, total bilirubin, prothrombin time) and clinically (change in Child-Pugh score) in 35 patients with chronic hepatitis B virus (HBV) infection (serum HBV-DNA positivity) and decompensated cirrhosis (Child-Pugh score 8 or higher; 10 Child class B, 25 Child class C). Five patients died of liver disease (baseline Child-Pugh score 12 to 13), seven underwent transplantation within six months. Of the remaining 23 patients, after six months, one underwent transplantation, two died (spontaneous bacterial peritonitis and hepatocellular carcinoma). After a mean follow-up of 19 months, there was improvement in bilirubin (67 ± 13 to 30 ± 4 mmol/L, $P < 0.05$), albumin (27 ± 1 to 34 ± 1 g/L, $P < 0.05$) and Child-Pugh score (10.3 ± 0.4 to 7.5 ± 0.5 , $P < 0.05$).

COMMENTARY

The long term prognosis for patients with decompensated cirrhosis is poor. For patients with chronic HBV, the therapeutic options include liver transplantation, which is limited by the current paucity of organs; low dose interferon, which is not very effective for Child's class B/C disease (1) and may cause further deterioration (2); or antiviral agents. Lamivudine is a well tolerated antiviral agent with efficacy in suppressing HBV replication (3). In the present study, lamivudine demonstrated efficacy in improving the clinical situation of patients with decompensated cirrhosis. These encouraging findings are tempered by the fact that 34% either died of liver disease or underwent transplantation within the first six months of the study. Furthermore, another three patients died of liver disease or required transplantation after six months. Clearly lamivudine can help some patients but does not replace timely referral for transplantation.

Another concern with the long term use of lamivudine is the development of YMDD motif lamivudine-resistant HBV strains. The Asian study group has reported the emergence of these mutants in approximately 40% after two years of lamivudine use (3). Although the YMDD mutant is considered less virulent than the wild-type strain (4), progressive liver disease can still occur (5), and active viremia with HBV remains a contraindication for transplantation in

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Canada. Fortunately, there is optimism for the future with the development of additional antiviral agents such as adefovir dipivoxil (6), which has demonstrated efficacy against wild-type and YMDD mutant HBV. Combination therapy, therefore, will be the future standard as hepatologists develop their own 'highly active antiretroviral therapies' for HBV.

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