

Hepatitis C

Coffee Reduces Liver Cancer Risk

Drinking coffee may reduce the risk of liver cancer, according to a meta-analysis published in the August 2007 issue of *Hepatology*. F. Bravi and colleagues searched the MEDLINE database and identified four cohort studies and five case-control studies that assessed the relationship between coffee consumption and primary liver cancer. In total, these studies included 2,260 patients with liver cancer and 239,146 control subjects without cancer. All studies found that people who drank more coffee were less likely to develop liver cancer; this association was statistically significant in six studies. Overall, coffee consumption was associated with about a 40% decrease in the risk of liver cancer, and the reduction

was even greater for heavy coffee drinkers (55%). Each additional daily cup of coffee was associated with a 23% lower risk of liver cancer – though the results do not necessarily imply that coffee caused the risk reduction. For more discussion of this study, see the September 2007 *HCV Advocate*.

Resiquimod for Hepatitis C

Due to the limited effectiveness and frequent side effects of interferon-based therapy for hepatitis C, researchers have studied other types of treatments. As reported in the August 2007 *Journal of Hepatology*, P.J. Pockros and colleagues conducted two studies to assess the safety, pharmacokinetics, and efficacy of oral resiquimod, a toll-like

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receptor (TLR) 7 and 8 agonist that stimulates production of natural interferon alpha in people with chronic hepatitis C. In a multicenter Phase IIa study, 12 patients were randomly assigned to receive 0.01 mg/kg resiquimod for four weeks, while four received placebo. In a single-center study in France, six patients received 0.01 mg/kg resiquimod, 11 received 0.02 mg/kg, and six received placebo. The 0.02 mg/kg dose demonstrated greater anti-HCV activity, with two patients in that arm experiencing HCV RNA reductions of at least 1 log, three with 2-log reductions, and one with a 3-log reduction. In most cases, viral load rose again after treatment ended. However, while the 0.01 mg/kg dose was generally well-tolerated, there were more serious adverse events with the 0.02 mg/kg dose, and two patients in this arm discontinued treatment early. Side effects were as expected with systemic cytokine induction, including fever, headache, shivering, and low lymphocyte counts. The researchers concluded that resiquimod “transiently reduced viral levels but was associated with adverse effects similar to interferon alpha.”

Mother-to-Child HCV Transmission

As reported in the August 20, 2007 issue of *AIDS*, E. Marine-Barjoan and colleagues conducted a study to identify risk factors for mother-to-child transmission of HCV, including maternal virological characteristics and mode of delivery. The analysis included 214 women with HCV and their newborn infants seen at six French hospitals. More than two-thirds of the women (69%) had detectable HCV viral load and 26% were coinfecting with HIV. In total, 12 infants had detectable HCV RNA at one year of age, for an overall perinatal transmission rate of 5.6%. All of the women whose babies were infected with HCV had detectable plasma HCV RNA. Half of the infected children were born to HIV/HCV coinfecting mothers with detectable HCV viral load, for a transmission rate of 13.6%. The other six were born to HCV monoinfected women with detectable HCV RNA, for a transmission rate of 6.5%. The risk of mother-to-child HCV transmission was three times higher for HCV/HIV coinfecting women compared to those with HCV alone. However, the effect of coinfection status was only statistically

significant among women with HCV viral load below 6 log IU/ml. The rate of HCV transmission did not differ significantly among children born by vaginal delivery, elective Caesarean section, or emergency Caesarean section after membrane rupture. The results of this study confirm previous findings that coinfecting women are more likely to transmit HCV to their babies, but emphasized the important role of viral load.

Hepatitis C in Hemophiliacs

Hemophiliacs, who have a bleeding disorder that requires the administration of clotting factor derived from donated blood, have a high rate of infection with blood-borne viruses including HCV, HBV, and HIV (such infections were common before the adoption of infection-control measures such as donor screening and treatment of blood products). Two recently published studies looked at hepatitis C in this population.

In the first study, reported in the July 31, 2007 issue of *AIDS*, L. Melendez-Morales and colleagues assessed factors associated with spontaneous HCV

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clearance among HIV positive hemophiliacs. Out of 478 HIV/HCV coinfecting hemophiliac patients, 12.8% overall experienced HCV clearance. Among the 31 participants who also had HBV, the rate of spontaneous HCV clearance was significantly higher, at 51.6%, compared with 10.1% for those without HBV. After adjusting for factors such as sex, race, and hemophilia severity, patients with chronic hepatitis B were 11 times more likely to clear HCV without treatment. Spontaneous clearance rates were lower among men, blacks and people with more severe hemophilia, but did not differ based on duration of HIV or HCV infection, age at the time of infection, HIV viral load, CD4 cell count, or use of anti-HIV therapy. The researchers concluded that, "HCV clearance is unambiguously and markedly increased with chronic HBV infection among HIV coinfecting people."

In the second study, published in the August 2007 *American Journal of Gastroenterology*, N. Assy and colleagues analyzed liver biopsies from 12 hemophiliacs and 20 non-hemophiliac control subjects with chronic hepatitis

C matched for age and sex. Most of the hemophiliacs (85%), but only 46% of the controls, had HCV genotype 1. Serum AST levels were lower and partial thromboplastin times (a measure of blood clotting efficiency) were longer in the hemophiliac patients compared with the non-hemophiliac control subjects. Biopsy results showed that histological activity and fibrosis scores were significantly lower in the hemophiliacs. None of the hemophiliacs had histological evidence of advanced liver disease (bridging fibrosis or cirrhosis), compared with 30% of the control subjects. Based on these results, the researchers concluded that, "HCV infections in hemophiliacs may be less severe than in HCV infected patients without hemophilia."

Nevirapine Hypersensitivity in Coinfecting Patients

The antiretroviral drug nevirapine (Viramune), used to treat HIV, causes liver toxicity due to a drug hypersensitivity reaction in some patients. The risk is higher for people with pre-existing liver disease, including hepatitis B or C. As reported in the July 31, 2007 issue of *AIDS*, E. Phil-

lips and colleagues assessed risks factors for and outcomes associated with nevirapine hypersensitivity in a cohort of 685 HIV positive patients in British Columbia starting HIV treatment for the first time using a three-drug regimen containing nevirapine. About 10% met the criteria for a hypersensitivity reaction. In a univariate analysis, no variables were identified as risk factors for hypersensitivity (in contrast to past studies showing that the risk is greater in women and in people with higher CD4 cell counts). HIV/HCV coinfecting patients with hypersensitivity reactions had about a seven-fold higher risk of death compared with HIV positive individuals without HCV who did not have such reactions. However, the deaths were not directly attributable to liver failure or other hypersensitivity complications, but rather were apparently due to HIV disease progression after hypersensitivity reactions led patients to interrupt their antiretroviral therapy. The researchers concluded that, "These results support the current recommendation against the use of nevirapine in HIV/HCV coinfecting patients."