

HBV JOURNAL REVIEW

Volume 6, Issue 1

January 1, 2009

Hepatitis B

Christine Kukka

Mutations in the Virus' Surface and Core Proteins Increase Risk of Liver Cancer

Certain mutations in the molecular structure of the hepatitis B virus (HBV) appear to predispose people to liver cancer, according to a report by Taiwanese researchers in the December 2008 issue of *The Journal of Infectious Diseases*.

Researchers examined the molecular structure of the hepatitis B surface antigen (HBsAg), a protein that makes up the surface or covering of the virus, and the core antigen region of the virus of 80 hepatitis B patients with liver cancer and 160 HBV-infected people without liver cancer.

Compared to the control group, liver cancer patients had higher fre-

quencies of these mutations. The researchers concluded that either mutation, or the combination of the two viral mutations, appeared to increase the risk of liver cancer.

Moderately Elevated ALT and Viral Load in HBeAg-Negative Patients May Warrant Treatment

Medical researchers are working to identify what conditions in hepatitis B patients warrant treatment with either antivirals, which prevent the virus from replicating, or interferon, which boosts the immune system to fight the infection.

A study published in the December 2008 issue of the *American Journal of Gastroenterology* found that cirrhosis (severe liver scarring)

was common in patients who tested negative for the hepatitis B "e" antigen (HBeAg), had alanine aminotransferase (ALT) levels that were moderately above normal, and who had viral loads (HBV DNA) of 10,000 copies/mL or higher. The researchers recommended that because these patients were at high risk of cirrhosis, they should be assessed for treatment.

Hong Kong researchers studied 1,197 untreated HBeAg-negative patients who had liver stiffness, 100 of whom had liver biopsies with proven cirrhosis. Possible and probable cirrhosis were present in 31% and 11% of the total patients, respectively.

The researchers found that the risk of cirrhosis was significantly increased when ALT level was 50% of the upper limit or higher, or when

HBV Journal Review

A publication of the Hepatitis C Support Project

Executive Director

Editor-in-Chief,
HCSP Publications
Alan Franciscus

Contributor

Christine Kukka

Managing Editor,

Webmaster
C.D. Mazoff, PhD

Contact Information:

The Hepatitis C Support Project

PO Box 427037
San Francisco, CA 94142

www.hbvadvocate.org

© 2009

Hepatitis C Support Project

viral load was moderately high.

Treatment Guidance Issued by Greek Researchers

All patients with elevated ALT (more than twice the upper limit of normal) and viral load above 20,000 IU/mL should be treated, according to a report by Greek researchers writing in the December 2008 issue of the *World Journal of Gastroenterology*.

They recommend a liver biopsy to guide treatment decisions when the ALT level is only moderately elevated and HBV DNA is below 20,000 IU/mL.

There are seven agents licensed for chronic hepatitis B: standard and pegylated interferon-alpha, and five antiviral medications. One-year courses with pegylated interferon induce viral clearance in 30%-32% of patients who are HBeAg-positive and in a smaller proportion of patients who are HBeAg-negative.

Oral antivirals achieve initial responses in the majority of patients, but ultimately become long-term therapy, and only works while treatment is taken.

Viral suppression has

favorable effects on patients' outcome but viral resistance is the major drawback of long-term oral antiviral therapy. The optimal first-line treatment remains unclear, the European researchers concluded.

HBsAg Levels Can Be Monitored for Treatment Success

Turkish researchers recommend monitoring HBsAg in order to identify when antiviral resistance occurs and to monitor the success of hepatitis B treatment, according to their article in the November 2008 issue of the *Journal of Digestive Diseases Sciences*.

In their study, they investigated whether HBsAg quantities correlate with viral load and might provide a more sensitive test to assess how effective a treatment it. They monitored 18 patients (13 male, 5 female, with an average age of 33) who were given pegylated interferon either with or without lamivudine. Viral load and HBsAg were monitored and compared at baseline, and at week 4, 8, 24, 48, 52, and 76. The levels were similar throughout the monitoring period and researchers concluded that

HBsAg monitoring can be a safe surrogate to use to monitor response to treatment.

More Reports Surfacing About Viral Resistance to the Antiviral Entecavir

To date, researchers have reported that viral resistance to the antiviral entecavir (Baraclude) has been very rare – even after four years of treatment—in patients who have never before been treated with an antiviral. But recently, researchers have found an increasing number of entecavir resistance cases, which is surprising because three mutations are needed in the virus in order for it to “resist” the antiviral effects of this drug and keep replicating.

Historically, patients who have been treated with lamivudine quickly developed resistance to entecavir because HBV that can resist lamivudine has already developed two of the required mutations needed to resist entecavir. As a result, nearly 40% of lamivudine-resistant patients develop entecavir resistance within four years of treatment.

Recently, Japanese researchers reported on two treatment-naïve patients

who developed entecavir resistance (signaled by at least a doubling of HBV DNA from its lowest level during treatment) after about three years of treatment. One of the patients had been receiving half of the recommended entecavir dose, which may have contributed to the ability of HBV to resist the weakened antiviral treatment.

Because of these findings, the researchers encourage doctors to carefully monitor HBV DNA during entecavir treatment to identify antiviral resistance quickly, and to always use the full, recommended dose, according to the report published in the December 2008 issue of *Hepatology International*.

Obese Patients Face Longer Waits for Liver Transplants

Obese patients face longer waits for liver transplantation, reflecting a possible “reluctance to transplant obese patients,” according to a report in the November 2008 issue of the *Annals of Surgery*.

Johns Hopkins researchers studied the association between body mass index (BMI) and access to transplantation in more than 25,000 pa-

tients. After adjusting for other factors, severely obese patients had 30% lower odds and morbidly obese patients had 38% lower odds of receiving transplants than non-obese patients with similar conditions.

Overall, after adjustments for factors related to transplantation rate, severely obese patients had 11% lower rates and morbidly obese patients 29% lower rates of being transplanted.

The findings suggest a reluctance to perform liver transplantation on obese patients, even though obesity is not an exclusion factor in the current organ allocation guidelines that doctors follow.

Patient Fares Well on Entecavir Before and After Liver Transplantation

Writing in the November 2008 issue of the *Southern Medical Journal*, U.S. researchers described the effective use of entecavir in a HBeAg-negative patient with severe cirrhosis before and after a liver transplant.

He responded to entecavir with a significant reduction in viral load after 15 weeks of treatment, however, he devel-

oped other complications and underwent a liver transplant after receiving 22 weeks of entecavir.

Doctors continued to use entecavir and added hepatitis B immunoglobulins (HBIG) following the transplant, and he showed improvements, even achieving undetectable HBV DNA. He maintained undetectable HBV DNA two years after transplantation. The researchers recommended that larger clinical trials be conducted to compare short-term and long-term use of entecavir among previously untreated patients with severe cirrhosis before and after liver transplantation.

Antibiotics Are Found to Cause Acute Liver Injury

Antibiotics are the single largest class of drugs that cause “idiosyncratic drug-induced liver injury,” (DILI), according to a report in *Gastroenterology*. It is the most common cause of death from acute liver failure and accounts for approximately 13% of cases of acute liver failure in the U.S.

It is caused by a wide variety of prescription and nonprescription medications, nutritional

supplements and herbals.

In the large study, patients with suspected DILI were enrolled and followed for at least six months. Researchers reported DILI was caused by a single prescription medication in 73% of the cases, by dietary supplements in 9% and by multiple agents in 18%. More than 100 different agents were associated with DILI; antimicrobials (45.5%) and central nervous system agents (15%) were the most common.

Of the dietary supplements causing DILI, compounds that claim to promote weight loss and muscle building accounted for nearly 60% of the cases.

Researchers found no relationship between gender and severity of DILI, but individuals with diabetes experienced more severe DILI.

Experimental Vaccine and Lamivudine Treatment Combo Generates a 24% Success Rate

Using a vaccine to spur the immune system to combat chronic HBV infection has been explored by researchers over the past several years. Recently, Turkish researchers used a special vaccine with hepatitis B

surface antigen plus the antiviral lamivudine to see if the combination would be effective in clearing chronic HBV infection.

A pre-S2-containing vaccine, which had shown success to spurring cellular immunity and suppressing HBV, was used in 48 patients (32 males, 16 females, average age 33) without cirrhosis. They were treated daily with lamivudine, and received four weekly vaccine injections over 24 weeks.

Nineteen of the patients were hepatitis B e antigen (HBeAg) positive and 29 were HBeAg-negative. HBeAg seroconversion occurred in five of the 19 patients, and 18 of 29 HBeAg-negative patients achieved normal ALTs and undetectable HBV DNA levels.

During follow-up, none of the patients who seroconverted and lost HBeAg relapsed (and regained HBeAg). Eleven of the 18 HBeAg-negative group relapsed, resulting in an overall sustained treatment response rate of 24%.

Those who succeeded from this treatment – about one in four of the patients – tended to have lower viral load and higher ALT levels at the

start of treatment.

Two-year GLOBE Trial Shows Telbivudine More Effective Than Lamivudine

The GLOBE trial, which compared the success of the antiviral telbivudine (Tyzeka) against lamivudine in 921 HBeAg-positive patients and 446 HBeAg-negative patients over a two-year period, found telbivudine to be superior to lamivudine.

Seventy-eight percent of telbivudine patients achieved undetectable HBV DNA and/or lost HBeAg (if they had it), compared to 66% of lamivudine patients.

HBeAg-positive patients receiving telbivudine also had better outcomes in achieving undetectable HBV DNA, HBeAg loss (35.2% versus 29.2%), and lower emergence of viral resistance (25.1% versus 39.5%).

Telbivudine-treated HBeAg-negative patients had higher rates of undetectable viral load compared with lamivudine (82% versus 56.7%) and less resistance at 10.8% versus 25.9% at the end of two years, according to the report published in the November 2008 issue

of *Gastroenterology*.

Research Reinforces Need for HBV Retesting in Internationally Adopted Children

Researchers studied the prevalence of HBV infection in internationally-adopted to determine if the current American Academic of Pediatric guidelines provided adequate screening for hepatitis B. Currently, the guidelines call for HBV screening upon arrival in the United States, and retesting six months later. It can take up to six months after infection for HBV to be identified by lab test.

The researchers screened 1,282 adoptees between 1999 and 2006 and found a 4% HBV infection rate, including 1.1% with acute or chronic infection and 2.9% with resolved infection. Overall, 64% of internationally adopted children had evidence of hepatitis B immunization, with protective antibodies.

The researchers also highlighted a case where HBV infection transmission occurred just before adoption, and was not identified during the initial screening, but was found during a follow-up

hepatitis B test.

“These data reinforce the American Academy of Pediatrics recommendations regarding hepatitis B virus screening and infection control measures for international adoptees,” researchers wrote in the December 2008 issue of *Pediatrics*, which include initial screening and follow-up screening after six months.

Study Shows Steep Decline in Accidental Needle-stick Injuries Among Health-care Workers

Twenty years of intense regulatory and legislative action have reduced the number of needle-stick injuries among health-care workers, according to a study by the University of Virginia International Healthcare Worker Safety Center.

Since passage of the U.S. Needlestick Safety and Prevention Act in 2000, healthcare workers have benefited from an unprecedented level of protection from occupationally transmitted diseases, according to the report published in the Dec. 8, 2008, issue of the *Journal of Infection and Public Health*.

Researchers analyzed

12 years of needle-stick injury data (1993-2004) from a large network of U.S. hospitals and found a 34% decline in needle-stick injury rates overall and a 51% decline among nurses, who handle needles most frequently. While the law wasn't passed until 2000, it was preceded by a lengthy worker education campaign and other design changes in how sharps were handled.

The study also found that the largest reductions in injury rates were for the high-risk phlebotomy needles and intravenous catheter needles, which declined 59% and 53% respectively.

The U.S. Centers for Disease Control and Prevention estimates that U.S. healthcare workers sustain an estimated 384,000 needle-stick injuries each year. The World Health Organization estimates that nearly 3 million healthcare workers worldwide are exposed to bloodborne diseases every year, resulting in an estimated 15,000 hepatitis C infections, 70,000 HBV infections, and 500 HIV infections annually. More than 90 percent of these occupational infections occur in developing countries, where health workers are scarcest.

