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Hepatitis B

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Antiviral and Interferon Combination Produces Longer-Lasting Results

To date, treating hepatitis B virus (HBV) infection with a combination of pegylated interferon and an antiviral, such as lamivudine (Epivir-HBV), has not produced better results than using pegylated interferon alone. While this combination works against hepatitis C virus infection (HCV), the interferon, which boosts the immune system, and the antiviral, which interferes with the viral reproductive material, hasn't worked dramatically to vanquish hepatitis B.

But a team of Greek researchers, reporting in the *Journal of Gastroenterology and Hepatology*, report that the

combination of interferon and lamivudine in hepatitis B patients who test negative for the "e" antigen (HBeAg) produces longer-lasting results.

Eighteen patients were treated for three months with lamivudine, followed by nine months of pegylated interferon alfa-2b combined with lamivudine. Meanwhile, 24 patients received just lamivudine.

At the end of the treatment period, 88.9% of the combination group and 70.8% of the lamivudine-only group had low HBV DNA levels (400 copies/mL), and 72.2% of the combination group and 70.8% of the lamivudine group had normal alanine aminotransferase (ALT) levels, which shows little difference in response. (ALT are liver enzymes that increase

when liver cells are damaged or die.)

However, 12 months after treatment ended:

- 33.3% of the combination group and 16.7% of the lamivudine group continued to have low HBV DNA levels
- 72% of the combination group and only 25% of the lamivudine group maintained normal ALT levels
- and, 25% of the lamivudine-treated patients experienced a rebounding of HBV DNA.

"Sequential combination treatment is able to improve sustained biochemical response rates and prevent the emergence of lamivudine-resistant mutants in patients with HBeAg-negative chronic hepatitis B," researchers wrote.

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Tenofovir Appears More Potent Against Lamivudine-Resistant HBV Than Adefovir

Dutch researchers examined which antiviral, adefovir (Hepsera) or tenofovir, was most effective against lamivudine-resistant HBV. In their study, published in the *Journal of Viral Hepatitis*, they report they first added tenofovir to ongoing lamivudine treatment in the resistant patients. Tenofovir was first developed as an antiviral against HIV infection, and it has been found to be highly effective against HBV. It is in its final stages of clinical trials in the United States, but has not yet been approved by the U.S. Food and Drug Administration for hepatitis B treatment.

The 78 weeks of tenofovir treatment was very successful, reducing viral load five-fold in the patients (an average decline of 5.4 log₁₀ copies/mL). Only two patients experienced a slight increase in HBV DNA during treatment.

Researchers then switched 10 patients to just adefovir and monitored changes in the patients' HBV DNA to see if adefovir was as or more effective than tenofovir.

After the switch, six of the 10 patients (60%) experienced an increase in viral load of about two-fold. The patients who did poorly on adefovir had low but detectable HBV DNA when they were switched to adefovir, and had genotype B or D. When they were retreated with tenofovir, their HBV DNA rapidly declined again.

"Switching to adefovir resulted in viral relapse in 60% of patients and retreatment with tenofovir resulted again in viral decline, which suggests that tenofovir is a more potent antiviral agent," the researchers concluded.

24-Year Study of 108 HBV-Infected Children Find Treatment Made Little Difference

Italian researchers followed 108 HBV-infected treated and untreated people for 24 years, from childhood through early adulthood, to assess the long-term impact of treatment vs. no treatment on their infection.

During the observation period, 67 children were not treated and 41 were treated with conventional interferon, which requires injections three

times a week. Currently, pegylated interferon, a time-release interferon that is believed to be more effective and requires only one injection weekly, is frequently used.

After 12 years, HBeAg loss and undetectable HBV DNA occurred in 43 untreated patients (69.3%) who were HBeAg-positive at the start of the study, and in 33 treated children (80%).

The researchers reported that of 57 children who had biopsies, 91.2% showed mild-to-moderate disease. No patient developed fatal liver disease or liver cancer.

The researchers, writing in the September 2007 issue of the journal of *Clinical Infectious Diseases*, concluded that, children with chronic HBV infection are generally symptom-free, with mild liver disease.

"Considering that the overall long-term outcomes did not differ between treated and untreated patients, the real impact of therapy on the long-term course of HBV infection remains to be established," they wrote. "Additional studies are needed to confirm our conclusions."

Low HBsAg Levels and Older Age Improve Odds of Clearing HBsAg with Lamivudine Treatment

Japanese researchers followed 486 hepatitis B patients for three years after they started lamivudine treatment to see how many would respond to treatment and clear the HBeAg and the hepatitis B surface antigen (HBsAg). They reported, in the October 2007 issue of the *Journal of Medical Virology*, that HBsAg disappeared in 17 (3.5%), who started treatment with low levels of HBsAg and were older than age 50. Neither HBV DNA (viral load or quantity of HBV in the blood) nor HBeAg status reportedly played any role in which patients cleared HBsAg.

Achieving undetectable HBsAg and developing antibodies to HBsAg indicates a person has cleared the infection.

Adefovir Equally Effective in Asian and Caucasian Patients

A team of international researchers compared the effectiveness of 48 weeks of adefovir treatment,

compared to treatment with a placebo, in 259 Asian and 242 Caucasian patients with either HBeAg-positive or HBeAg-negative hepatitis B.

According to their report in a recent issue of the journal of *Alimentary Pharmacology & Therapeutics*, improvements in liver health, declines in viral load and normalization of ALT levels were similar in both racial groups. "Adefovir was well tolerated and no resistance developed up to week 48 in either racial group," the researchers noted.

HBV DNA May Be Present in Saliva, Urine and Nasal Fluids If Viral Load Is High

A team of Swedish researchers examined whether the saliva, urine, nasal fluids or tears of HBV-infected people had enough virus in them to transmit HBV infection. According to their report in the *Journal of Hospital Infections*, the higher a person's HBV DNA level is, the more likely there will be potentially infectious HBV in their body fluids.

The team tested 25 people, who tested positive for HBV DNA in their blood, for HBV DNA in their saliva, nasal fluids, urine and tears. HBV DNA was found in two urine samples, 10 saliva samples, five nasal swabs and in tear fluid from four patients.

One person, who had an extremely high viral load, had high HBV DNA levels in both saliva and nasal fluids.

"This has particular importance for infection control programs and regulations, underlining the importance of aiming towards regular HBV DNA testing and thus infectivity assessment of chronic carriers in order to prevent transmission," researchers wrote.

Survival Hurt When Doctors Biopsy Large Liver Tumors Before Their Removal

Some doctors continue to take a biopsy of large liver tumors before surgeons completely remove the tumors. A new study by British researchers, published in the September 2007 issue of the *Journal of the*

American College of Surgeons, say this practice actually hurts the patients' long-term recovery and should be avoided.

The researchers reviewed survival and recovery data for 85 patients who had large tumors surgically removed. Survival at 1, 3, and 5 years was 76%, 54%, and 51%. Size did not influence survival, though more complex surgical techniques were required for giant tumors. Lower survival, however, was found in those whose tumors had been biopsied before their removal.

Health Officials Fear Childhood HBV Immunization Protection Waning

Eighteen years after Taiwan began universal childhood HBV immunization, researchers screened 5,875 university students to see how effective the prevention effort had been.

Each student was tested for HBsAg (indicating current infection), antibody to HBsAg (indicating a resolved infection), and antibody for the hepatitis B core antigen

(indicates past infection.)

According to an article published in the September 2007 issue of the *Journal of Viral Hepatitis*, researchers found a declining past infection rate, from 48.7% in those born in 1976 to 5.2% in those born in 1987. The prevalence of chronic or active HBV infection also declined from 14.5% to 1.9% during that time period.

However, the rate of continued immune protection against HBV from those early childhood immunizations, indicated by present HBV antibodies or titers, declined from 72% among those born in 1984 to 41.6% in those born in 1987.

While the widespread immunization decreased HBV infection, there appears to be a "waning-off" or decreasing level of antibody protection among those vaccinated during childhood, which may not provide adequate protection against HBV infection.

"A booster dose of HBV vaccine, given 18 years following HBV vaccination, perhaps even earlier, should be considered," the researchers recommended.

HBV and HCV in Surgeons Or Patients Pose Infection Risks in the Operating Room

Bloodborne infections, including HBV and HCV, are sources of occupational infection for surgeons who risk needle jabs and cuts during surgery, according to a report in the July 2007 issue of the journal of *American Surgery*.

More than 1% of the U.S. population has one or more chronic viral infections. Similarly, transmission of infection from surgeons to patients is also a concern.

Surgeons who are HBeAg-positive have been documented to pose a risk to patients in the operating room. To date, only four surgeons have been documented to transmit hepatitis C, and no surgical transmission of HIV to a patient has been identified.

Prevention of occupational infection requires the use of protective barriers, avoidance of exposure risk by modification of techniques, and a constant awareness of sharp instruments in the operating room.

People Respond Poorly to HCV Treatment When They're Also Infected with HBV

HCV-infected patients who also have "occult" HBV infection, with detectable HBV DNA but undetectable HBsAg, have poorer responses to HCV treatment than those without HBV infection, according to a report published in the *Journal of Medical Virology*.

This lack of response occurs no matter what HCV strain or genotype the patient has.

The researchers performed HBV DNA tests on 203 HCV-infected patients who tested negative for HBsAg, and found 47 patients with occult HBV infection.

A sustained and positive response to HCV combination therapy of pegylated interferon and the antiviral ribavirin was documented in 28% of HBV-positive patients, compared to 45% of patients without HBV infection.

These findings suggest that roughly one in four HCV-infected patients is also infected with HBV, which may predispose them to poor response to treatment.

When It Works, HAART Effective Against Both HBV and HIV in Coinfected Patients

French researchers report that the highly active antiretroviral therapy (HAART) that targets HIV infection in HBV-HIV coinfecting patients may also be effective against HBV infection in these patients. Many treated with HAART lose HBeAg or HBsAg antigens, according to a report in the Sept. 1, 2007, issue of *Clinical Infectious Diseases*.

Of 92 coinfecting patients, 82 received HAART. HBeAg antibodies developed in 10 of 59 HBeAg-positive patients, HBsAg clearance occurred in 3 of 10 patients, and surface antibodies developed in 2 of 3 patients. Of 23 HBeAg-negative patients, 2 cleared HBsAg and developed antibodies.

Seroconversion of HBeAg, HBsAg, or both, in combination with undetectable HBV DNA, was found primarily in those who also responded well on the HIV front. The responders experienced increased CD4+ count and had elevated ALT levels, which

indicates the immune system was attacking the HBV-infected liver cells.

The study also found that shorter courses of HAART treatment was linked to higher rates of HBeAg and HBsAg seroconversions.

HCV and HBV Spread Slows Among New Drug Users in San Francisco

Injecting drug users, always at high risk of bloodborne HBV and HCV infection due to reused and improperly sterilized needles, are becoming infected at a lower rate than in the past, according to a study published in the September 2007 issue of *Hepatology*.

To assess the effectiveness of preventive efforts, including needle exchange programs, the National Cancer Institute and the Cornell Medical College's Center for the Study of Hepatitis C researchers analyzed data from drug users in the San Francisco area and compared infection rates reported in 1987 and 2000.

Of the 2,296 drug users included in the study between 1998 and 2000, 91% had

been exposed to HCV and 80% had been exposed to HBV. However, those who had recently started injecting drugs had much lower rates, and about 5% had been vaccinated against HBV.

Among the others, 41% who had been injecting drugs for less than two years, and 57% of those who had been using for six to nine years, were infected with HBV. In contrast, HBV infection rates in the 1987 surveyed population were 45% and 80%.

Only 34% of participants surveyed during 1998-2000 said they had shared syringes in the past 30 days, compared to about 59% in 1987.

The authors concluded, "It is encouraging that the frequency of (infection) appears to have decreased markedly among new initiates to injection drug use in the San Francisco Bay area. If the reductions in the prevalence of these infections can be sustained, the risk of end stage liver disease and liver cancer should decrease in this population."

U.S. Liver Cancer Rates Double, Affecting White Men Aged 45-65

Liver cancer rates have doubled in the United States in the past 20 years, primarily affecting Caucasian men between the ages of 45 and 65 the most, according to a report in *Hepatology Research*. While it remains an affliction of the elderly (average age 65), there has been a shift toward younger cases.

Men are affected three times more frequently than women. Asian-Americans are affected two times more than African-American and Hispanic people, who are affected two times more often than Caucasians.

However, the recent increase has disproportionately affected Caucasian and Hispanic men. HCV infection acquired 20 to 40 years ago is the cause of at least half of the cancer increase and is expected to increase in the next decade.

But a significant proportion of cases (15%-50%) do not have HBV or HCV infection or heavy alcohol consumption as a source. Insulin

resistance syndrome, manifesting as obesity and diabetes, is emerging as a risk factor for liver cancer and may occur through the formation of non-alcoholic fatty liver disease (NAFLD). However, its impact on the current increase in liver cancer remains unclear, researchers noted.

Case Study Surprise: HCV-HBV Coinfected Patient Clears HBV After Hepatitis C Treatment

Currently, pegylated interferon and the antiviral ribavirin are used to treat hepatitis C. While pegylated interferon is also used to treat HBV infection, different antivirals other than ribavirin are used for hepatitis B.

A recent case study, published in the October 2007 issue of the *European Journal of Gastroenterology and Hepatology*, reported a surprising result. A woman coinfecting with HBV and HCV cleared the hepatitis B infection after her hepatitis C treatment was accompanied by vaccination against hepatitis B.

The German research-

ers reported on a 49 year-old woman with HCV genotype 2 who had undetectable HBV DNA and was negative for HBeAg. She was treated with interferon and ribavirin to address her HCV infection.

Her HCV-RNA declined, as expected, but her HBsAg levels also quickly declined and at treatment week 48, her HBsAg antigen levels were very low.

Treatment continued for another four weeks, combined with HBV immunization, and she ultimately cleared HBsAg and developed surface antibodies, indicating she had cleared the infection.

This shows that, "combination treatment of HBV-HCV-coinfected individuals cannot only induce a sustained HCV-RNA response but also HBsAg seroconversion in single patients," the researchers noted, "Monitoring of HBsAg levels can be useful in individualizing optimal treatment duration in HBV-infected patients."

