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Hepatitis B

Sequential Interferon and Lamivudine Treatment Achieves Sustained Seroconversion

A team of Indian doctors, writing in the November 2005 issue of the *American Journal of Gastroenterology*, report that sequential treatment – administering interferon for 16 weeks during a 53-week course of lamivudine (Epivir-HBV) treatment – produced better results than using just lamivudine in patients with the hepatitis B “e” antigen (HBeAg).

The researchers from New Delhi treated 75 HBeAg-positive patients with lamivudine for 52 weeks. After eight weeks of lamivudine, they added interferon alpha treatment to the treatment regimen of 37 patients for 16 weeks.

After 52 weeks, equal numbers of patients in both groups (38%) lost HBeAg. HBeAg loss, the appearance of the “e” antibody (anti-Hbe), and undetectable HBV DNA (viral load) occurred in 26.3% of the group that also received interferon, and 13.5% of the lamivudine-only group.

However, after 76 weeks, 80% of the patients who received the sequential treatment of lamivudine and interferon sustained their loss of HBeAg, compared to 20% of the patients who received only lamivudine.

Doctors Still Can't Predict Who Will Respond to Pegylated Interferon

Despite ongoing research, doctors have found no clues – including age, viral load, or

alanine aminotransferase (ALT) levels – that indicate who will or won't respond to pegylated interferon treatment. In a recent study, doctors followed 177 patients with HBeAg-negative hepatitis up to 96 weeks after they were treated with pegylated interferon (Pegasys) for clues about what factors might indicate a successful response.

The researchers, reporting at the AASLD 2005 conference, took into consideration race, gender, age, body weight, genotype, baseline ALT and HBV DNA, and ultimately what HBV DNA was at the end of treatment.

Doctors concluded that there was no clear, predictor of sustained response to pegylated interferon. However, patients who had a high ALT level at the beginning of

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treatment, or who were infected with hepatitis B virus (HBV) genotype C had a slightly better chance of improvement. HBV DNA levels at the beginning or end of treatment did not indicate whether a patient would respond.

Interferon Helps Some HBeAg-Positive Patients Who Were Infected at Birth

A team of South Korean researchers followed 46 HBeAg-positive adult patients treated with conventional interferon to see what effect the drug would have on the patients who had all been infected at birth.

Writing in the November 2005 issue of the *Journal of Infection*, the researchers attempted to discern if interferon produced a sustained response in this group. About 35% (16 of 46) lost HBeAg and achieved normal ALT levels initially, but ultimately only 22% (10 patients) achieved a sustained response after a year.

The researchers suggest that age below 35 years old and elevated ALT levels at start of treatment may contribute to treatment success in this

group.

Viral Fluctuations Make HCV-HBV Co-infection Difficult to Diagnose and Treat

A group of Italian researchers followed 133 patients who had tested positive for infections by both hepatitis B virus (HBV) and hepatitis C virus (HCV) for one year to see how HBV and HCV viral loads varied.

In many coinfection cases, HCV may be the dominant viral infection and consequently may mask or make identification of an HBV infection difficult.

In the group, according to a report in the *Journal of Hepatitis*, active infection with both HBV and HCV was revealed in 24 cases, inactive infection by both viruses was seen in 15 cases, active HBV (with inactive HCV infection) was identified in 15 cases, and inactive HBV (active HCV) was seen in 49 cases.

However, 32 patients (31%) had dynamically fluctuating HBV and HCV levels, which made getting a correct diagnosis of HBV and HCV infections impossible, unless these patients were tested frequently.

The researchers recom-

mend more testing for both viruses in coinfecting patients in order to achieve correct diagnoses and treatment.

Viral Mutations Found to Occur in Children with Low Viral Loads

Chinese researchers compared the genetic make-up of HBV in 15 HBV-infected mothers to that of their infected children to see if viral load (the amount of HBV in their bloodstream) affected the way that HBV changes its genetic structure and mutates to evade the body's immune defenses.

Reporting in the January 2006 issue of the *Journal of Infectious Diseases*, the researchers looked carefully at the molecular sequence of the virus and the "evolutionary differences" in the "pre-S/S gene" between mother and child.

Surprisingly, they found mutations in patients with low viral loads were much more frequent than in patients with high viral loads and were not related to age.

They concluded that viral "mutations are related to virus load and HBeAg seroconversion, irrespective of age."

Overlapping Lamivudine and Interferon Achieve Limited, Long-Term Results

Researchers continue to search for the formula and sequence of interferon and antivirals treatment that may prove most effective against hepatitis B. In a recent report published in the January 2006 issue of the *Journal of Alimentary Pharmacology & Therapeutics*, a team of doctors tried overlapping treatment with lamivudine and interferon in 36 HBeAg-negative patients.

Lamivudine was administered from 1 to 12 months and conventional interferon from 7 to 18 months. A control group of 36 patients was given only interferon.

Normal ALT levels and undetectable HBV DNA was observed in 30.6% of lamivudine-interferon-treated and 8.3% of interferon-treated patients at the end of treatment. However, 12 months after treatment ended, 8.3% of the lamivudine-interferon group had sustained normal ALT and undetectable viral load, while none of the interferon-control group had sustained that result.

More Research Needed on How HBV Genotypes Respond to Treatment

Do different HBV strains or genotypes respond differently to antivirals or interferon? A report published in the December 2005 issue of *Liver International* examined published data to find the most effective treatment for each genotype.

Each of HBV's eight identified genotypes has distinct geographical and ethnic distribution. Genotypes A and D occur frequently in Africa, Europe, and India, while genotypes B and C are prevalent in Asia. Genotype E is restricted to West Africa, and genotype F is found in Central and South America.

To date, it appears that patients with genotypes A and B experience a more sustained response to conventional interferon than those with genotypes C and D. However, it is not yet clear which genotype responds well to pegylated interferon.

To date, it appears that all genotypes respond equally to anti-

virals. However, no one knows what impact genotype subgroups, or infection with more than one HBV genotype, have on treatment effectiveness.

The researchers concluded, "Remarkable clinical and pathogenic differences do exist among HBV genotypes"; however additional research is urgently needed.

Older Age and Lamivudine Resistance Increase Odds of Adefovir Resistance

A team of University of Michigan researchers, writing in the November 2005 *Journal of Hepatology*, tracked 43 patients treated with adefovir (Hepsera) for an average of 18 months to determine the rate of viral resistance to the antiviral.

About 44% of the patients – most of whom had high ALT levels and were HBeAg negative – initially responded well to adefovir. Six (14%) patients were found to have adefovir-resistant mutations. After two years of treatment, on average about 22% of patients developed viral resistance to adefovir.

Patients with adefovir resistance were more likely to have been switched from lamivudine to adefovir, to be older, and to be infected with HBV genotype D.

"Our data suggest that [a] combination of lamivudine and adefovir may prevent emergence of adefovir-resistance in patients with lamivudine-resistant HBV," they concluded.

HBeAg and HBx Proteins Indicate Increased Risk of Cirrhosis

Researchers, writing in *Liver International*, reported that hepatitis B patients with high levels of HBeAg and the hepatitis B x protein are at significantly higher risk of cirrhosis.

They measured and analyzed HBV DNA levels in liver tissue, HBV antigens and liver health in 216 patients – instead of measuring HBV DNA and antigens in blood samples.

They found that the "expression" or presence of HBeAg and HBx protein was higher in patients with cirrhosis than in those without cirrhosis.

Health Officials Urge Universal HBV Vaccination of Correction Workers

Public health researchers, writing in the November issue of the *American Journal of Infection Control*, analyzed vaccination rates among health workers in three correctional centers and found protection against the bloodborne disease wanting.

They surveyed 411 workers, 64% of whom had been vaccinated. Vaccination rates varied by state and by job category. About 8.6% of clinical workers reported needle sticks while treating inmates within the past six months.

Among clinical staff, vaccination varied depending on medical degree (RN or MD) and race.

ACIP Promotes Stricter HBV Immunization for Newborns and Kids at Risk

With only half of infants born to HBV-positive women being vaccinated against hepatitis B in time to prevent infection, the Centers for Disease Control and Prevention's Advisory Com-

mittee on Immunization Practices has published stronger recommendations so every newborn at risk is immunized against the infection at birth, according to the Dec. 23, 2005 issue of the *Morbidity and Mortality Weekly Report*.

The committee also recommended that doctors and school health officials review immunization records of children and teens ages 11 to 19 who were born in countries with high rates of HBV infection, to ensure they have been vaccinated.

Some vaccine advocates say ACIP's recommendations should have included HBV immunization for all adults because the virus is easily transmitted during unsafe sex.

Without HBV Vaccination, 64.8 Million Would Become Infected Worldwide

CDC researchers, writing in the *International Journal of Epidemiology*, designed a mathematical model to calculate the impact of hepatitis B infection and immunization.

They measured the effectiveness of hepatitis B

vaccination with and without administration of the first dose of vaccine within 24 hours of birth to prevent mother-to-child infection.

During 2000, researchers estimated that 620,000 people died worldwide from HBV-related causes: 580,000 (94%) from chronic infection-related cirrhosis and liver cancer and 40,000 (6%) from acute hepatitis B.

Based on their model, researchers estimated that without vaccination, 64.8 million would become HBV-infected and 1.4 million would die from HBV-related disease. Infections acquired at birth, during early childhood (younger than 5 years old), and at 5 years of age accounted for 21%, 48% and 31% of deaths, respectively.

Vaccinating at least 90% of infants worldwide at birth would prevent 84% of global HBV-related deaths, they concluded.

Liver-Related Deaths Increase Among Hepatitis-HIV Co-infected Patients

A study of 11,000 HIV-infected patients reveals increased liver-related death rates in patients co-infected with HBV

and/or HCV since antiviral drugs were made available, according to a report in the Dec. 2, 2005 issue of *AIDS*.

The investigators reported that although the death rate from liver-related disease fell after the introduction of potent anti-HIV treatment, there was a significant increase in death rates among the hepatitis-HIV co-infected.

They found that HIV patients with hepatitis B had an almost threefold increased risk of death from liver disease, and those with HCV experienced a five-fold increased risk of liver disease-related death.

More Endorsements for Emtricitabine for HIV-HBV Coinfected

An article in the January 2006 issue of the *Journal of Clinical Infectious Diseases* endorsed the effectiveness of emtricitabine (FTC), a new antiviral, against both HIV and HBV.

The drug is very similar to lamivudine, but it performs better than lamivudine when combined with other medications.

Although emtricitabine has not been approved

for use in patients coinfected with HIV and HBV by the U.S. Food and Drug Administration, recent treatment guidelines for treatment of HIV by both the International AIDS Society and U.S. Department of Health and Human Services placed emtricitabine, in combination with tenofovir, didanosine, or zidovudine, in the "preferred category" for patients receiving antiretroviral therapy.

