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Hepatitis B

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Cost Analysis: Cirrhotic Patients Should Use Adefovir or Entecavir

Researchers, writing in the September 2006 issue of the *American Journal of Gastroenterology*, decided to assess which antiviral treatment strategy was the most cost effective if a patient infected with the hepatitis B virus (HBV) had cirrhosis (severe liver scarring) and was at high risk of liver cancer or failure.

Antivirals meddle with HBV's genetic material and make it difficult for the virus to reproduce.

They looked at the three antivirals approved by the U.S. Food and Drug Administration for hepatitis B treatment. Lamivudine (Epivir-HBV) is

the least expensive, but HBV quickly develops resistance to it and soon the virus rebounds. In contrast, adefovir (Hepsera) and entecavir (Baraclude), the newest antivirals, have a lower rate of viral resistance, but they are more expensive.

Researchers evaluated the cost-effectiveness of six treatment strategies, based on the cost of each year of life gained:

- No treatment: This strategy was the least effective and obviously least expensive.
- Lamivudine: While initially helpful, many patients quickly developed viral resistance to this antiviral.
- Adefovir: Using adefovir cost \$19,731 per year of life gained.
- Entecavir: This antiviral was more effective

and more expensive than adefovir, and cost \$25,626 per year gained, compared to adefovir.

- Treatment with lamivudine with a change to adefovir when HBV develops resistance to lamivudine.
- Or, lamivudine with a switch to entecavir when viral resistance develops.

Treatment with just lamivudine, and the salvage strategies that switched patients to either adefovir or entecavir after lamivudine resistance developed, were not cost-effective. However, between the two salvage strategies, adefovir salvage was more effective and less expensive than entecavir salvage.

Researchers concluded that both entecavir and adefovir are

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cost-effective in patients with cirrhosis, and choosing between adefovir and entecavir is highly dependent on the patient's health insurance coverage.

Anti-Inflammatory Colchicine May Lower Liver Cancer Risk in Hepatitis Patients

A group of Mexican physicians treated patients with viral hepatitis-related cirrhosis with colchicine, an anti-inflammatory medication that historically has been used to treat gout and scleroderma, an autoimmune skin disease.

While colchicine did not slow development of cirrhosis in the hepatitis patients, it had the surprising effect of lowering the patients' cancer risk, according to their report published in the Oct. 15, 2006, issue of *Cancer*.

The 186 patients received either a placebo or 1 mg of the anti-inflammatory agent colchicine five times a week for an unspecified period of time between 1980 and 2000, starting when their cirrhosis was diagnosed.

After three years of follow-up, cirrhosis had progressed among 56% of those taking colchicine and 60% of the other patients, indicating the drug did not decrease advancement of cirrhosis. However, in the colchicine group, 9% developed liver cancer, compared to 29% in the untreated group.

"Colchicine can prevent the development of (liver cancer), independent of other factors such as age, platelet count, alpha-fetoprotein level, and transaminase levels," researchers concluded.

Changes in Viral Load Offer No Clear Indication of Pegylated Interferon Success or Failure

Dutch researchers followed 266 patients who tested positive for the hepatitis B "e" antigen (HBeAg) and treated with pegylated interferon alone or pegylated interferon plus lamivudine to see if there were any clues offered early in treatment as to who would respond, lose HBeAg, and develop "e" antibodies (seroconversion).

Writing in the September 2006 issue of *Hepatology*, researchers reported that patients treated with both interferon and lamivudine had similar drops in viral load over the course of treatment, no matter if they lost HBeAg or not.

However, those treated with just pegylated interferon experienced a wide variety of drops in viral load. A delayed decline of at least two-fold in HBV DNA after week 4 but before week 32 was associated with the highest successful response rate (63%). In comparison, the response was 52% for patients with an early decline in viral load, and 38% for those with a late decline.

The loss of surface antigen (HBsAg) was 22% in those with delayed viral load decline, compared to 4% for those with early declines.

Researchers concluded there was no discernable or significant pattern indicating who would or would not respond based on viral load changes when taking pegylated interferon.

Researchers Recommend One Year of Antivirals When HBsAg-Positive Patients Receive Chemotherapy

Chemotherapy, which weakens the immune system as it kills cancer cells, often results in a resurgence of HBV in patients who were previously asymptomatic, but had the hepatitis B surface antigen (HBsAg).

Doctors, writing in the October 2006 issue of the journal of *Alimentary Pharmacology & Therapeutics*, pointed out that while some doctors have tried using an antiviral, such as lamivudine, to prevent HBV replication during chemotherapy, there are no official guidelines recommending use of antiviral on a preventive basis for patients who test positive for HBsAg.

The team of researchers reviewed nine studies that examined the preventative use of antivirals, and found that between 0% and 24% of HBsAg-positive, asymptomatic patients receiving preventative antivirals experienced a rebound of HBV infection, compared to 29%-56% of

HBsAg-positive patients who received no antivirals.

“The available data show a four- to seven-fold decrease in the rate of hepatitis and hepatitis B virus reactivation in patients who receive lamivudine prophylaxis,” researchers noted. “It is thus recommended that all HBsAg carriers receive lamivudine, or a comparable anti-viral agent, as prophylaxis from the initiation of chemotherapy until at least one year following its completion.”

Lamivudine in Antiviral Cocktail Cuts Liver Disease Deaths Among HIV and HBV Co-infected Patients

In the recent issue of the journal of *Antiviral Therapy*, a team of Italian researchers examined the impact of the lamivudine treatment on 2,041 HBsAg- and HIV-co-infected patients, particularly those who died from liver disease or liver cancer.

Lamivudine, an antiviral used to treat both hepatitis B and HIV, has been used in com-

bination antiviral therapy to treat co-infected patients and researchers wanted to know how effective lamivudine was in preventing liver-related deaths.

In the group, 217 patients died and 57 deaths were liver-related. There was reduced death from liver disease among those treated with lamivudine, which supports the current practice of using lamivudine as part of an antiviral “cocktail” to treat HBV and HIV co-infections.

CDC: Hepatitis B-Related Cirrhosis and Cancer Killed 563,000 Worldwide in 2002

Around the world, liver disease causes about one of every 40 deaths. Researchers from the U.S. Centers for Disease Control and Prevention (CDC) calculated what percentage of these deaths from cirrhosis or liver cancer resulted from infection by either HBV or the hepatitis C virus (HCV).

In a report published in the October 2006 *Journal of Hepatology*, CDC researchers sampled causes of death in

11 World Health Organization (WHO) regions. They reported:

- 57% of cirrhosis cases were attributable to either HBV (30%) or HCV (27%).
- And 78% of liver cancer cases were attributable to either HBV (53%) or HCV (25%).
- Researchers applied the statistics to 2002 worldwide mortality estimates, and determined that these two viral infections killed 929,000 that year.
- Of 446,000 deaths from cirrhosis, 235,000 resulted from hepatitis B and 211,000 from hepatitis C.
- Of 483,000 liver cancer deaths, hepatitis B caused 328,000 deaths and hepatitis C caused 155,000 deaths.

The authors concluded that, “HBV and HCV infections account for the majority of cirrhosis and primary liver cancer throughout most of the world, highlighting the need for programs to prevent new infections and provide medical management and treatment for those already infected.”

WHO officials estimate there are 350 mil-

lion people chronically infected with HBV. Each year, an estimated 1 million to 1.5 million people die from hepatitis B-related problems, including sudden liver failure, cirrhosis, cancer and other symptoms.

Life Expectancy Longer for Female Liver Transplant Recipients than Males

Women who receive a liver transplant may live about 4.5 years longer than their male counterparts, according to a report written by British researchers and published in the Sept. 28, 2006, issue of *Gut*.

The researchers studied 2,702 patients who survived more than six months after receiving a liver transplant between 1985 and 2003. The average life expectancy of female recipients was 26.8 years compared to 18.3 years for men. Compared with the general population, this corresponds to 9.3 lost years of life for men and 4.3 years of lost life for women.

The highest life expectancy of 28.8 years was found in transplant recipients between the

ages of 17 and 34, but this group had the highest number of life years lost compared to the general population – 22.4 years.

20 of 33 Children with HBeAg and Elevated ALTs Respond to Lamivudine and Interferon Treatment

A group of Turkish researchers achieved marked success when they treated 33 children, who had elevated alanine aminotransferase (ALT) levels and were HBeAg-positive, with a combination of lamivudine (3 mg per day) and thrice weekly interferon alpha injections (10 MU/m).

Writing in the September 2006 issue of the *European Journal of Pediatrics*, they reported that they treated 21 children with three months of lamivudine, before interferon was started. In the remaining 12 children, they began interferon and lamivudine simultaneously. After interferon treatment stopped, lamivudine treatment continued for six months in all children.

HBeAg seroconversion (loss of HBeAg and production of “e” anti-

bodies) and normalization of ALT (average decline of 143 to 31) occurred in 20 of 33 children. ALT is released by dead or injured liver cells.

Several months after treatment ended, the seroconversion was sustained in 14 of the 21 children (66.7%) who were treated first with lamivudine, and in six of 12 children (50%) who received the two drugs simultaneously.

Flu-like symptoms and anorexia were the most common complaints. Researchers proposed that interferon plus lamivudine combination therapy, “is highly successful and safe in children suffering from chronic hepatitis B.” Initially treating children with lamivudine before beginning interferon, “does not seem to be necessary,” they wrote.

The FDA has not approved this combination treatment for HBV-infected children.

HBIG and Vaccine Most Effective in Protecting Babies Born to HBV-Infected Mothers

Writing in the September 2006 issue of *Hepa-*

tology Research, published by the Japan Society of Hepatology, a group of Iranian researchers examined the effectiveness of administering both the hepatitis B immune globulin (HBIG or HBV antibodies) and the hepatitis B vaccine to babies born to HBsAg-positive mothers.

They studied 823 children born to infected mothers.

About 638 children had received neither the vaccine nor HBIG. Among this group, 481 were older than 16, and 157 were age 16 or younger.

Another 125 children had received only the vaccine, and a fourth group of 60 children received both HBV vaccine and HBIG. (The report did not specify if the vaccine and HBIG were administered immediately after birth.)

The prevalence of HBsAg was:

- 56.1% in the group older than 16 that received neither the vaccine nor the HBIG
- 40.3% in the group age 16 and younger that received neither vaccine nor HBIG.
- 12.6% in the group that received only the vaccine

- And 3.6% in the group that received both vaccine and HBIG.

“The addition of HBIG to recombinant vaccine will significantly increase the protection against HBV infection in comparison with HB vaccine alone,” they wrote.

Giving Pregnant Women HBIG Doesn't Lower Transmission of HBV to Newborns

A group of Chinese researchers treated 117 HBV-infected pregnant women with HBIG during their last three months of pregnancy to see if HBIG’s antibodies would lower the women’s viral load (HBV-DNA) and decrease transmission of HBV infection to their newborns.

This use of HBIG in pregnant women has become common in some parts of China.

The researchers, reporting in the September 2006 *Journal of Viral Hepatitis*, discovered that HBIG did not reduce the amount of HBsAg or HBV DNA in the pregnant women, and consequently did not reduce transmission of HBV infection to newborns when the

HBIG-treated group was compared to a control group of 133 infected women who gave birth.

The monthly injection of HBIG to the HBeAg-positive women during their seventh, eighth and ninth month of pregnancy conferred no immunity to the babies, the researchers concluded, because:

- HBIG, at current acceptable doses, cannot suppress the replication of HBV, especially when HBV are actively replicating in HBeAg-positive patients. HBIG's antibodies survive only for a short time and cannot overcome the rampant, replicating HBV.
- HBIG appears to work only in people with low levels of HBV-DNA and HBsAg, they noted.
- Also, in this trial, none of the babies had HBsAg antibodies at birth so the HBIG antibodies were apparently not transmitted to the fetuses.

Instead of using HBIG, researchers suggest scientists continue to explore the use of the antiviral lamivudine in women with high HBV-DNA levels dur-

ing their last one or two months of pregnancy, in addition to vaccinating newborns against hepatitis B at birth and treating them with HBIG.

Use of antivirals in HIV-infected pregnant women, for example, has greatly decreased transmission of HIV to newborns.



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