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Hepatitis B

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Jury Out on Milk Thistle's True Benefits

Many with chronic hepatitis B take milk thistle to decrease liver damage, but just how effective is this supplement? A review of reputable clinical trials that compared milk thistle to placebo in 915 patients with alcoholic or viral hepatitis liver disease found no evidence that milk thistle was beneficial.

Writing in the *Cochrane Database of Systematic Reviews 2005*, researchers lamented the lack of evidence to support the popular belief that this supplement was beneficial. They stressed the need for "adequately conducted and reported randomized clinical trials."

Combination of Viral Hepatitis and Raw Oysters Can Be Lethal

The most common cause of death from seafood consumption in the United States is *vibrio vulnificus* septicemia. It occurs primarily in people with chronic liver disease who eat raw oysters from warm, saltwater environments. Writing in the May 2005 issue of *The American Journal of Gastroenterology*, researchers reported that the pathogen lodges in filter feeders like oysters and causes abrupt, septic shock and death, especially in people with chronic liver diseases such as hepatitis B or C.

People with chronic liver diseases must be warned about this risk, "by signs displayed in restaurants; physicians must educate patients with chronic liver disease about the risk of raw oyster consumption; and harvesting methods which reduce contamination by *V. vulnificus*," researchers wrote.

Doctor: To Reduce HBV Drug Resistance, Think Carefully Before Prescribing

Think carefully before you treat, Dr. Stephen Locarnini, a hepatitis expert, cautioned doctors in an Expert Column on how clini-

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cians can reduce drug resistance. Today, doctors have three antiviral medications to use to lower viral load. But viral resistance to lamivudine (Epivir-HBV) develops at a rate of 20% per year of treatment, and resistance to adefovir (Hepsera) occurs at about 2% per year.

In order to not use up the available arsenal of antivirals and produce resistant hepatitis B virus (HBV), Locarnini recommends doctors:

- Avoid unnecessary drug use or treatment until it is absolutely necessary, when patients have more active or advanced liver disease.
- Make careful choices when prescribing an antiviral or a combination of antivirals. For example, HBV with mutations that can resist lamivudine's effects can also resist entecavir's antiviral effects.
- And monitor patients carefully (at least every three months) for signs of an increase in drug-resistant HBV. A surge in HBV DNA (viral load) and elevated alanine aminotransferase (ALT) levels, which rise when liver cells die, can be life-

threatening to patients with advanced liver disease.

Entecavir Bests Lamivudine and Adefovir in HBeAg-Negative and -Positive Patients

With the recent U.S. Food and Drug Administration (FDA) approval of entecavir (Baraclude), doctors now have three antivirals to treat hepatitis B patients.

An American study presented at the recent European Association for the Study of the Liver (EASL) conference in Paris reviewed studies to compare the effectiveness of the three oral medications. They found entecavir was superior to adefovir for both HBeAg-positive patients and HBeAg-negative patients. Lamivudine was superior to adefovir in HBeAg-positive patients except in preventing liver damage, and lamivudine was not as effective as adefovir in HBeAg-negative patients.

Entecavir was supe-

rior to lamivudine in all aspects except for preventing liver damage and spurring HBeAg seroconversion (causing loss of HBeAg and production of "e" antibodies.)

"For virologic endpoints, entecavir is superior to lamivudine, which is superior to adefovir," researchers wrote. Based on controlled trials and analyses of multiple studies in which lamivudine and adefovir were analyzed individually, entecavir consistently ranked highest among the three drugs for both HBeAg-positive and -negative patients, they concluded.

patients were able to sustain their response at a higher rate than patients treated with lamivudine.

At Week 48, 91% of entecavir-treated patients had undetectable HBV DNA, compared to 65% of those treated with lamivudine. ALT normalization and HBeAg loss were slightly higher in the entecavir group.

"By suppressing HBV DNA, causing loss of HBeAg, and reducing ALT levels with one year of treatment, entecavir has the potential to sustain (its response) when therapy is discontinued," researchers noted.

70% of Entecavir-Treated Patients Sustain Response 24 Weeks After Treatment

More than 70% of patients treated with entecavir for 48 weeks are able to sustain their HBeAg seroconversion, undetectable HBV DNA and reduced ALT 24 weeks after therapy ends, according to a report presented at EASL. The entecavir-treated

Telbivudine Quicker at Suppressing HBV DNA than Lamivudine

The antiviral telbivudine produced a greater drop in viral load (HBV DNA or the amount of virus in the bloodstream) and normalized ALT levels within two weeks of starting treatment, compared to lami-

vidine.

Researchers, who presented their findings at the annual EASL conference, reported that the HBV DNA decline continued for 52 weeks and produced better long-term health effects.

The trial compared telbivudine at 400 or 600 mg/day, and telbivudine at 400 or 600 mg/day plus lamivudine 100 mg/day against lamivudine 100 mg/day, in adults with HBeAg-positive hepatitis B.

the journal *Pediatrics*. Adolescents who engage in oral sex rarely use condoms or dental dams, even though chlamydia, gonorrhea, herpes, hepatitis B, HIV, and syphilis can all be orally transmitted.

77% in those treated with adefovir.

“The average cost-effectiveness ratio (cost per responding patient at year 3) was 22,571 Euros for lamivudine and 22,185 Euros for adefovir,” they wrote. “Long-term adefovir therapy has a similar cost-effectiveness than lamivudine for HBeAg-negative patients.”

week 52 and about 76% had normal ALTs, indicating no liver damage.

While the adefovir and lamivudine combination suppressed viral replication, researchers predict that continuous antiviral treatment will probably be required to maintain low viral load.

Teens Think Oral Sex Safe, and Not Really Sex

Researchers surveyed 580 ethnically diverse ninth graders and discovered that one in five had engaged in oral sex, (14 percent had had sexual intercourse), and another one-third said they intended to have oral sex within the next six months.

Previous studies have focused on intercourse, but as many as half of adolescents experience oral sex first, according to a report published in

Cost of Lamivudine and Adefovir Similar When Success Rates Compared

Doctors often prescribe the antiviral lamivudine first for hepatitis B because it is the cheapest antiviral available. But a study presented at EASL found the costs of lamivudine and the newer and more expensive antiviral adefovir were similar when success was factored in.

The total cost per patient treated with lamivudine or adefovir for three years was 7,912 and 17,088 Euros respectively, but virological response (including undetectable HBV DNA and normal ALT levels) at year 3 of lamivudine therapy was 35.1% compared to

Adding Adefovir to Lamivudine Helps, But Continued Treatment Still Required

Researchers added adefovir to the lamivudine treatment 49 patients with HBeAg-negative hepatitis B were receiving to see what impact 52 weeks of adefovir treatment would have on these patients who had developed HBV resistant to lamivudine.

Writing in the journal of *Alimentary Pharmacology & Therapeutics*, researchers reported that the addition of adefovir did cause a decline in HBV DNA, and 57% had undetectable HBV DNA at

Sequential Lamivudine and Interferon Treatment in Children Ineffective

Researchers treated children with high viral load, low ALT levels and HBeAg with a first round of lamivudine, to knock down HBV DNA, followed by interferon alpha to see if the lowered viral load might enhance the interferon’s impact on the immune system and improve viral clearance.

Eleven children received 100 mg/day of lamivudine for three months followed by interferon plus lamivudine for six months, followed by lamivudine alone for nine months.

HBV-DNA levels dropped during initial lamivudine treatment and in combination with interferon. But after interferon treatment stopped, HBV DNA levels increased to high levels in five of 11 patients who developed lamivudine-resistant HBV.

Two patients cleared HBeAg but did not produce “e” antibodies. One patient developed core-promoter and pre-core stop codon mutations.

Researchers, writing in the *Journal of Viral Hepatitis*, concluded that this three-phase treatment reduced HBV-DNA levels, but did not lead to HBeAg and HBV-DNA clearance, nor did it prevent lamivudine resistance.

Pegylated Interferon Scores Continued Success in Several Studies

In a number of reports presented at the EASL conference, doctors continued to fine-tune when pegylated interferon (peginterferon

alfa-2a) (40KD) (PEGASYS®) treatment. is most effective in treating hepatitis B. Though the FDA has not yet approved pegylated interferon, which requires one injection per week, doctors in the United States are increasingly prescribing it to patients due to its reported effectiveness.

Researchers reported the following findings at the conference in Paris:

- Patients with genotype B and C fare equally well on pegylated interferon.
- HBeAg-positive patients with high ALT, low HBV-DNA and low HBeAg levels appeared to do best on pegylated interferon. However, patients with normal or low ALT may also benefit from pegylated interferon, though their success rates were lower.
- Pegylated interferon was more effective at producing HBeAg seroconversion 24 weeks after treatment ended than was lamivudine (32% vs. 19%), even though lamivudine was better at lowering HBV DNA levels. Researchers suggest that, “more potent HBV-DNA sup-

pression does not necessarily translate into improved HBeAg seroconversion rates.”

Immune System, Not Viral Load, Key in Development of Surface Antibody

While loss of the hepatitis B surface antigen (HBsAg) and production of the surface antibody is the ultimate goal of treatment, it is a rare event.

Researchers studied 1,351 patients with HBeAg-positive and -negative hepatitis B who were treated in two randomized, partially double-blind, multinational studies with either pegylated interferon alone, pegylated interferon plus lamivudine, or lamivudine alone.

More than 75% of patients in the studies were of Asian origin, and the predominant HBV genotypes were B (27%) and C (50%).

HBsAg seroconversion only occurred in patients who achieved HBeAg seroconversion. Among those, the

rate of HBsAg seroconversion was 10% with pegylated interferon and 0% with lamivudine.

“The magnitude of HBV-DNA suppression on treatment does not seem to be the major factor leading to HBsAg response, but rather the additional immunomodulatory effect associated with (pegylated interferon),” researchers explained.

Viral Load Key Predictor of Cirrhosis Development and Liver Cancer

Two recently published looked at the impact of high viral load on the development of cirrhosis and liver cancer.

One multinational research team focused on the role of HBV DNA levels in patients with and without HBeAg who developed cirrhosis. They followed 3,774 Taiwanese patients who all received ultrasound exams. They concluded that high viral load “is a strong predictor of cirrhosis risk,” regardless of HBeAg status.

“Effective suppression of HBV DNA to very low levels, especially in HBeAg-negative patients, could reduce progression of chronic hepatitis B to cirrhosis,” they wrote.

Another research team evaluated the relationship between HBV DNA levels and liver cancer deaths over a 10-year period in 2,354 adults with chronic hepatitis B in China.

“Our results indicate that high viral load is associated with increased mortality from (liver cancer) in patients chronically-infected with HBV,” they wrote.

**Doctor:
Continue
Lamivudine 4 to
6 Months after
HBeAg
Seroconversion**

In an expert column published in *Medscape Gastroenterology*, Dr. David Bernstein, director of Hepatology at North Shore University Hospital in Manhasset, New York, addressed how long he would keep a patient with

compensated cirrhosis on lamivudine after the patient achieved HBeAg seroconversion (developed the “e” antibody) and undetectable HBV DNA.

“Patients with compensated liver disease should be treated with lamivudine for at least one year, and therapy should be continued for four to six months after HBeAg seroconversion. In the compensated cirrhotic, these same rules apply.”

HBeAg seroconversion has been reported after stopping lamivudine therapy in 70% to 90% of patients from Western countries and in 38% to 83% of patients from Southeast Asia. “If a relapse occurs after stopping lamivudine, an alternate drug should be started and the patient should be maintained on this second hepatitis B medication,” he added.



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