

CORNERSTONE Critiques

Commentary by Richard A. Johnson, MD, on Current Literature

Always a Chance for Problems

Drug-Induced Liver Diseases

Larrey D. *J Hepatol Suppl.* 2000;32:77–88.

Drug-induced liver injuries make up a persisting and challenging problem for physicians, health agencies and pharmaceutical firms. The clinical expression is polymorphous, acute hepatitis being predominant. The diagnosis is frequently difficult because of the absence of specific signs in most cases and mainly relies on the exclusion of other causes. The diagnosis should be particularly evoked in patients over 50 yr who are taking many drugs, after viral infections have been ruled out. Acute hepatocellular hepatitis is particularly severe because of the risk of fulminant hepatitis or of a

more insidious course leading to cirrhosis. Cross hepatotoxicity can sometimes occur. One should avoid re-administration of not only the causative agents but also of other drugs belonging to the same family or having a related chemical structure. The prediction of the hepatotoxicity of new drugs must be improved. Investigations would be particularly useful for drugs having critical chemical structures and belonging to families with an established history of hepatotoxicity.

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COMMENTARY

This article provides an excellent review of the variety of the mechanisms of drug hepatotoxicity. It is clear that many host factors also can affect the level of toxicity. Most of the toxicity is seen within the 1-week to 3-month interval from the initiation of a drug, and rarely are there problems beyond a 1-year interval. Given that many patients are now taking multiple medications and herbal preparations, the clinician needs to keep an astute eye on liver function in polypharmacy and/or polyherbal patients.

Another Role for Vitamin E?

Vitamin E as Treatment for Chronic Hepatitis B: Results of a Randomized Controlled Pilot Trial

Andreone P, Fiorino S, Cursaro C, et al. *Antiviral Res.* 2001;49:75–81.

Background and aims: Interferon- α treatment has been the treatment of choice for chronic hepatitis with unpredictable results. Recently, lamivudine has been licensed for use against HBV infection with good results. Unfortunately, recurrence of viremia after lamivudine withdrawal is common and prolonged treatment can induce the emergence of resistant mutant strains. It has been shown that vitamin E can increase the host immune response, and this may provide protection against infectious diseases. **Methods:** We evaluated vitamin E supplementation as therapy for chronic hepatitis B in a pilot study including 32 patients. Patients were randomly allocated to receive vitamin E at the dose of 300 mg twice daily for 3 months (15 patients) or no treatment (17 patients). They were seen monthly

during the first 3 months and thereafter quarterly for additional 12 months. **Results:** The two groups were comparable at enrollment. At the end of the study period, alanine aminotransferase (ALT) normalization was observed in 7 (47%) patients in vitamin E group and only in 1 (6%) of the controls ($P = 0.011$); HBV-DNA negativization was observed in 8 (53%) patients in the vitamin E group as compared to 3 (18%) in the control group, respectively ($P = 0.039$). A complete response (normal ALT and negative HBV-DNA) was obtained in 7 (47%) patients taking vitamin E and in none of the controls ($P = 0.0019$). **Conclusion:** Vitamin E supplementation might be effective in the treatment of chronic hepatitis B.

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COMMENTARY

This small pilot study done in Italy provides encouragement that this simple approach may provide a good deal of benefit to individuals with chronic hepatitis B infections. Major improvements in markers of the level of disease were seen in ~50% of the treatment group after 6 to 12 months of therapy with vitamin E at a dose of 600 mg/d. No improvement was seen in any of the control group patients. Three of the 7 complete responders from the 15 patients in the treatment group converted their HBeAb antibody status from negative to positive, implying an immunologic mechanism for the purported benefits of vitamin E therapy in chronic hepatitis B infection.

Ecstasy with the Opposite Result

Ecstasy Ingestion and Fulminant Hepatic Failure: Liver Transplantation to be Considered as a Last Therapeutic Option

Garbino J, Henry JA, Mentha G, Romand J-A. *Vet Hum Toxicol.* 2001;43:99–102.

Severe adverse effects due to 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) are reported with increasing frequency in the medical literature. The signs of acute toxicity most often seen are fulminant hyperthermia, hyperexcitatory states, acute renal failure and hyponatraemia. In 1992, hepatotoxicity was also described with unexplained jaundice and hepatomegaly after ingestion of MDMA. We report a case of severe toxic hepatitis following ingestion of MDMA with fulminant

hepatic failure which required auxiliary liver transplantation. The diagnosis was necrotic toxic hepatitis following ecstasy ingestion. The outcome was successful, and the patient was discharged from ICU 20 d after surgery. Hepatotoxic effects of MDMA seem infrequent, but may be lethal; liver transplantation is the ultimate therapeutic option in some cases.

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COMMENTARY

This tragic case reported from Switzerland underscores the potential of drugs (illicit in this case) to cause fulminant hepatic failure. This 19-year-old man reportedly took just 1.5 tablets of Ecstasy and some alcoholic drinks. He felt poorly 5 days later, was admitted to the hospital 12 days later, continued to deteriorate, and required a liver transplant 1 month after the initial ingestion. This case report and others like it certainly have the legitimate potential to raise parental anxiety and physician concern with drug experimentation.