

Management Of Hepatitis B 2006

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Hepatitis B in Children

Most children with hepatitis B in the United States have acquired the infection vertically or were adopted from countries where the infection is endemic. When hepatitis B virus (HBV) infection is vertically acquired, it nearly always becomes chronic and is often quiescent. When acquired horizontally, hepatitis B may be more active. Hepatitis B in childhood is usually asymptomatic and histologically mild. Each year, 5-10% of children spontaneously clear hepatitis Be antigen (HBeAg), at which point the disease usually becomes inactive, although a few will later reactivate. Some pediatric studies suggest that antiviral therapy hastens but does not increase the rate of HBeAg seroconversion. Severe liver disease has been reported in childhood, however, and a few percent of most pediatric biopsy series show cirrhosis. Hepatocellular carcinoma, while rare, has been reported in childhood. Prevention of severe liver disease and hepatocellular carcinoma later in life are goals of treatment of pediatric hepatitis B.

In the United States, two therapies for hepatitis B are approved for use in children. Both are recommended for use when ALT is elevated. There is some suggestion in the literature that response rate might be better in children treated at a younger age. Alpha interferon monotherapy was evaluated in a large multinational trial in children ages 1 to 17 years. At 6-month follow-up after treatment was stopped, 26% of interferon-treated patients were HBeAg and HBV DNA negative compared to 11% of controls; hepatitis B surface antigen (HBsAg) became negative in 10% of treated patients and in 1% of controls. Children tend to tolerate interferon well, although behavioral disturbances and slowing of growth during therapy may occur, in addition to the typical side-effects of interferon seen in adults. Lamivudine therapy of chronic hepatitis B in children was reported to yield a 23% virologic response rate (loss of both HBeAg and HBV DNA by hybridization assays) at the end of treatment compared to 13% in controls. Extension of therapy for 3 years was reported to increase the response rate by another 21%, although the incidence of YMDD mutations was 64%, and patients with these mutations had a lower response rate. The long-term significance of YMDD mutations in children is unclear but of great concern. Several small studies of combination interferon/lamivudine therapy in children look encouraging; one study reported a 55% rate of HBeAg seroconversion and loss of detectable HBV DNA at the end of treatment. Another pilot study of combination therapy among mostly Asian children with normal ALT levels showed a 22% rate of HBeAg seroconversion (and a remarkable 17% rate of HBsAg loss). Importantly, no YMDD mutations were detected in either study. There have been no large studies of peginterferon therapy in children with hepatitis B, although a limited experience looks encouraging. A pediatric study of adefovir dipivoxil therapy of chronic hepatitis B is ongoing.

Future research on hepatitis B should include studies of children with this infection and should focus on the relative risks and benefits of peginterferon and nucleoside combination therapy. Because even indolent infection can lead, over decades, to chronic liver disease and liver cancer, attention should be paid to management of poor-responder groups such as Asian children and

HBV-infected children with normal ALT levels. Research should focus on the optimal timing of treatment in children and both the long-term risks and benefits of therapy.

References

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