Medical Xpress

Combination therapy for severe alcoholic hepatitis does not result in improved survival

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Four weeks of treatment with a combination of the drug pentoxifylline and the corticosteroid prednisolone did not improve 6-month survival compared with prednisolone alone in 270 patients with severe alcoholic hepatitis, according to a study in the September 11 issue of *JAMA*.

Treatment of severe forms of alcoholic hepatitis is extremely challenging because of the poor outcome. European and U.S. guidelines recommend the use of prednisolone or pentoxifylline in patients with severe alcoholic hepatitis. Nevertheless, a substantial proportion of patients die after 6 months regardless of first-line therapy, according to background information in the article.

Philippe Mathurin, M.D., of the Hopital Hurlez, Lille, France and colleagues compared the efficacy of a combination of prednisolone and pentoxifylline with prednisolone alone in patients with severe alcoholic hepatitis in 1 Belgian and 23 French hospitals. Duration of follow-up was 6 months. They randomly assigned 270 patients (18 to 70 years of age, who were heavy drinkers with severe biopsy-proven alcoholic hepatitis) to receive 40 mg of prednisolone once a day and 400 mg of pentoxifylline 3 times a day (n=133) for 28 days, or 40 mg of prednisolone and matching placebo (n=137) for 28 days, between December 2007 and March 2010

Eighty-two deaths occurred in the 2 groups during the 6-month follow-up, due to complications from liver failure in 67 cases (81.7 percent) and other causes including gastrointestinal bleeding in 15 cases (18.3

percent). The researchers found no difference in 6-month survival between the 2 groups (69.9 percent in the pentoxifylline-prednisolone group [40 deaths] vs. 69.2 percent [in the placebo-prednisolone group [42 deaths]). Response to treatment and the probability of being a responder were also no different between groups.

The cumulative incidence of hepatorenal syndrome (rapid deterioration in kidney function) at 6 months was also not different in the pentoxifylline-prednisolone and the placebo-prednisolone groups.

Because of the lack of difference in survival and other outcomes, "our study does not support the use of a combination of pentoxifylline and prednisolone for severe alcoholic hepatitis," the authors write, concluding that "future studies with an appropriate design are needed to provide robust data for developing new strategies to improve the outcome of patients with this life-threatening disease."

In an accompanying editorial, Dina L. Halegoua-De Marzio, M.D., and Jonathan M. Fenkel, M.D., of Thomas Jefferson University Hospital, Philadelphia, comment on the findings of this study.

"… corticosteroids and pentoxifylline are currently the only and most successful medical treatments available for severe alcoholic hepatitis despite providing only modest improvements in mortality. The results reported by Mathurin and colleagues demonstrate that the sum (corticosteroids and pentoxifylline) is no greater than the individual parts for preventing mortality in well-characterized patients with severe alcoholic hepatitis. Pentoxifylline may remain a useful option for patients who have contraindications to receiving corticosteroids; however, this group was not studied by Mathurin and colleagues. The study also emphasizes the importance of developing new treatments for severe alcoholic hepatitis. These future studies also should include well-conducted evaluations of liver transplantation for carefully selected

patients with severe alcoholic hepatitis not responding to medical management."

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