

Study examines liver transplantation after drug induced acute liver failure

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Liver transplantation offers a good chance for survival for patients with drug induced acute liver failure, however, certain pre-transplant factors are associated with worse outcomes. Patients who are on life support, who have elevated serum creatinine, and children whose liver failure was caused by antiepileptic drugs did not fare as well after transplantation. These findings are in the July issue of *Liver Transplantation*, a journal published by John Wiley & Sons.

Drug induced acute liver failure is very rare, but can be life-threatening. Acetaminophen is the most common cause, accounting for nearly half of cases in adults, but other drugs can also be responsible. For patients who are unlikely to recover spontaneously, [liver transplantation](#) is the only treatment.

Researchers, led by Ayse L. Mindikoglu, M.D., M.P.H. of the University of Maryland School of Medicine and VA Maryland Health Care System, examined the United Network for Organ Sharing (UNOS) database which contains information about outcomes of nearly all liver transplants performed in the U.S. since 1987. They planned to analyze all of the drugs associated with acute liver failure and subsequent liver transplantation, determine survival rates after transplantation, and develop a model that would predict the risk of death after transplantation for these patients.

They included 661 patients—567 adults and 94 children under age 18—who were transplanted for drug induced acute liver failure between

October 1, 1987, and December 31, 2006. For each case, they collected twenty recipient and six donor demographic and clinical variables from the database.

They found that the leading drug groups causing liver failure that required transplantation were acetaminophen (40 percent), antituberculosis drugs (8 percent), antiepileptics (7 percent) and antibiotics (6 percent). For the entire cohort of transplant recipients, median survival time was 14.4 years. One year estimated survival probabilities were 76 percent, 82 percent, 52 percent, 82 percent, and 79 percent for acetaminophen, antituberculosis, antiepileptics, antibiotics and others, respectively.

"Among the patients who had acute liver failure due to antiepileptics, one-year survival was only 27 percent in patients less than 18 years old compared to 75 percent in patients 18 years old or older," the authors report. Interestingly, these patients were least likely to be listed as status 1 and spent the most time waiting for an organ. Also, the warm and cold ischemia times were longest for this group of patients. "The relatively low survival probability persisted after controlling for these variables in multivariate analysis," the authors report. The reasons for the decreased survival in this group could not be elucidated based on the available data.

Examining the different demographic and clinical factors for each patient and donor, the researchers noted that, "elevated serum creatinine, being on life support, and drug-induced acute liver failure due to antiepileptics (at age less than 18) were found to be independent pretransplant predictors of poor survival."

Using the entire study population, the researchers developed a prognostic model which showed strong predictive ability.

An accompanying editorial by Paul B. Watkins of the Institute for Drug

Safety at the Hamner Institutes of Health Sciences, Research Triangle, NC and Paul H. Hayashi of the University of North Carolina , commends the authors for adding valuable information about acute liver failure caused by drugs. In particular, "the identification of poorer outcome for children with anti-epileptic drug induced acute liver failure is intriguing and points out the need for more focused research on drug induced liver injury in pediatric populations."

Drug induced liver injury has wide implications for all of us who take and prescribe medications, they write. And they look forward to future advances in our understanding of the issue, as researchers investigate hypotheses about preventive factors and genetic predisposition.

More information:

Article: "Outcome of Liver Transplantation for Drug Induced Acute Liver Failure in the United States. Analysis of the United Network for Organ Sharing Database." Mindikoglu, Ayse L.; Magder, Laurence S.; Regev, Arie. *Liver Transplantation*; July 2009.

Editorial: "Progress in Our Understanding of Severe Drug Induced Liver Injury." Hayashi, Paul H. Watkins, Paul B.; *Liver Transplantation*; July 2009.

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