Study finds anti-microbials a common cause of drug-induced liver injury and failure

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New research shows that anti-microbial medications are a common cause of drug-induced liver injury (DILI) leading to acute liver failure (ALF), with women and minorities disproportionately affected. While ALF evolves slowly, once it does occur a spontaneous recovery is unlikely; however liver transplantation offers an excellent survival rate. Full findings of this ten-year prospective study are published in the December issue of *Hepatology*, a journal of the American Association for the Study of Liver Diseases.

Patients with liver failure resulting from DILI may experience deep jaundice, fluid retention, advanced coagulopathy and coma. More than 1100 drugs, herbal remedies, natural products, vitamins, minerals, dietary supplements, and recreational and illicit compounds are known to cause liver injury, which reportedly affect 1 in 100,000 to 1 in 10,000 patients. Prior research shows DILI is a frequent cause of hepatitis, and accounts for 5%-10% of hospitalizations for jaundice and 12% of all cases of ALF (excluding acetaminophen).

In the current study, researchers investigated liver injury and failure caused by drugs other than acetaminophen. Detailed case reports were collected from 1,198 subjects with ALF enrolled at 23 sites participating in the National Institutes of Health-funded Acute Liver Failure Study Group, led by Principal Investigator, William M. Lee, M.D., from the University of Texas Southwestern Medical Center in Dallas, TX. Researchers identified 133 patients with DILI with 71% of those cases in women.

"Our findings confirm prior medical evidence that found a high female predominance in DILI ALF, suggesting that women may be more susceptible to liver injury or use more prescription drugs than men," said Dr. Adrian Reuben, Professor of Medicine at the Medical University of South Carolina and lead study author.

Furthermore, the research team documented a disproportionately high number of minorities with DILI ALF, including African-American (16%), Hispanic (15%) and other minority groups (12%). "We observed inexplicably high numbers of minority patients with DILI ALF. This racial disparity is atypical for acetaminophen-induced ALF in the U.S. and further studies should explore this discrepancy," commented Dr. Reuben.

Researchers identified 61 different agents that, alone or in combination, could cause liver injury and failure in the study population. Anti-microbial agents were found to be the most common cause of DILI ALF cases and included anti-tuberculosis drugs (25), sulphur-containing drugs (12), nitrofurantoin (12), other antibiotics (7), antifungal agents (6), and anti-retroviral drugs (4). Patients who develop ALF after taking these drugs typically do not experience a spontaneous recovery—the transplant-free survival rate in this study was 27%.

There were 56 eligible subjects who underwent liver transplantation of whom all but four survived, giving an overall survival for the entire cohort 66.2%. The authors highlight that the 23.3% of transplantation waitlist deaths attest to the urgent need for donor organs in this setting. "Liver transplantation offers excellent survival for ALF patients, however further investigation should include more detail on drug use duration, and the impact of alcohol use and diabetes, to provide additional understanding of idiosyncratic drug-induced liver injury and failure," Dr. Reuben concluded.

More information: "Drug-Induced Acute Liver Failure: Results of a United States Multicenter, Prospective Study." Adrian Reuben, David G. Koch, William M. Lee and the Acute Liver Failure Study Group. Hepatology; Published Online: October 14, 2010 (DOI:10.1002/hep.23937); Print Issue Date: December 2010.