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Study shows steroids ineffective, possibly harmful in pediatric liver disease

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A multi-center study concludes that treating infants with high doses of steroids fails to improve medical outcomes in the end-stage pediatric liver disease biliary atresia and leads to earlier onset of serious adverse events.

Researchers say the clinical trial involving 14 sites provides new evidence on a growing controversy in the medical community – whether treating infants with steroids to augment surgery improves outcomes. Results for the study will be published May 7 in the *Journal of the American Medical Association*. The data are being released early to coincide with the Pediatric Academic Societies Annual Meeting.

"The results from this clinical trial differ from previous reports of a benefit from steroid therapy on bile drainage or survival in biliary atresia," said Jorge Bezerra, MD, a lead investigator on the study and physician in the division of Gastroenterology, Hepatology and Nutrition at Cincinnati Children's Hospital Medical Center.

"Although we cannot exclude some small potential benefit from steroid treatment, we observed no statistical differences in two-year survival between patients receiving steroid treatment after surgery and those receiving placebo," Bezerra said. "Children receiving steroids during the study also developed serious adverse events more quickly, raising a potential increase in risks associated with steroid therapy."

Biliary atresia is the leading cause of pediatric liver transplantation in the

world. The disease accounts for about 50 percent of transplants in children and 10 percent of transplants at any age. It results from inflammation and rapid accumulation of connective tissues that obstruct and restrict bile ducts from draining. The condition then manifests as cholestatic jaundice in the first few weeks after birth.

At diagnosis, the primary treatment is the hepatoportoenterostomy (HPE, the Kasai procedure) – a surgical procedure that removes the diseased bile ducts and gallbladder and connects an intestinal loop directly to the liver to restore bile drainage. Study authors point out that some clinicians suggest steroid treatment after surgery may help prevent additional fibrosis and improve bile drainage. The current study – called START (Steroids in Biliary Atresia Randomized Trial) – was designed to provide rigorous medical data to help answer that question.

The study involved 140 infants with a median age of 2.3 months. The initial study was conducted between September 2005 and February 2011, with follow up ending in January 2013.

Researchers report that in 70 children treated with steroids, bile drainage was not significantly different six months post-surgery compared to 70 children who received placebo after surgery. Of the 70 who received steroids, 41 of 70 patients (58.6 percent) had improved bile drainage. Of 70 patients who did not receive steroids, 34 of 70 (48.6 percent) had improved bile drainage.

When researchers compared survival rates between the steroid/non-steroid groups at age 24 months, 58.7 percent of children in the steroid group survived compared to 59.4 percent in the placebo group.

The percent of children who experienced serious safety events was relatively the same between the steroid group (81.4 percent) and non-steroid group (80 percent), but children who received steroids had an

earlier time to onset for those events. Serious safety events occurred with 30 days post-surgery in 37.2 percent of children who received steroid treatment, versus 19 percent in the placebo group.

Potential serious safety events the authors pointed to included complications such as immunosuppression, associated risk of infection, poor wound healing, hyperglycemia, gastrointestinal bleeding, poor growth, and inadequate response to routine immunizations.

More information: Paper: doi:10.1001/jama.2014.2623

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