Vitamin E or metformin may not be effective for treating liver disease in children and teens

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In contrast to previous preliminary data, use of vitamin E or the diabetes drug metformin was not superior to placebo on a measured outcome for treating nonalcoholic fatty liver disease in children and adolescents, according to a study in the April 27 issue of *JAMA*.

"Coincident with the rise in prevalence of childhood and adolescent obesity over the past few decades, nonalcoholic fatty liver disease (NAFLD) has become the most common cause of chronic liver disease in children in the United States," according to background information in the article. NAFLD encompasses a range of severity, from mild to severe disease that may ultimately result in advanced fibrosis (development of excess fibrous connective tissue in an organ), cirrhosis, and liver cancer. Insulin resistance is frequently identified in both adults and children with NAFLD, and treatment approaches to NAFLD target reduction in insulin resistance and oxidative stress. Pediatric pilot data demonstrated potential efficacy of metformin or vitamin E in treating NAFLD.

Joel E. Lavine, M.D., Ph.D., of Columbia University, New York, and colleagues conducted a randomized-controlled trial evaluating vitamin E or metformin for the treatment of NAFLD in children. The study, conducted at 10 university clinical research centers between September 2005 and March 2010, included 173 patients (ages 8-17 years) with biopsy-confirmed NAFLD. Patients received daily dosing of 800 IU of

vitamin E (58 patients), 1000 mg of metformin (57 patients), or placebo (58 patients) for 96 weeks. The predefined primary outcome measure for this trial was sustained reduction in alanine aminotransferase (ALT; an enzyme which is significantly associated with NAFLD activity score and fibrosis stage in children) defined as 50 percent or less of the baseline level or 40 U/L or less at visits every 12 weeks from 48 to 96 weeks of treatment.

The researchers found that the attainment of sustained reduction in ALT level was similar to placebo (10/58; 17 percent) in both the vitamin E (15/58; 26 percent) and metformin treatment groups (9/57; 16 percent). The average change in ALT level from baseline to 96 weeks was -35.2 U/L in the placebo group vs. -48.3 U/L in the vitamin E group and -41.7 U/L in the metformin group.

Among the 121 patients who had either NASH (nonalcoholic steatohepatitis; fatty inflammation of the liver) or borderline NASH at baseline, the resolution of NASH was significantly greater in children treated with vitamin E than with placebo (58 percent vs. 28 percent). Differences between treatment groups in terms of frequency or severity of adverse events were not significant.

"In summary, this double-blind, placebo-controlled, randomized trial of metformin or vitamin E for the treatment of NAFLD in children without diabetes or cirrhosis had a negative primary outcome. The data suggest that children treated with vitamin E who had biopsy-proven NASH or borderline NASH had significant improvement in secondary histologic outcomes with vitamin E."

"However, risk of biopsy might outweigh the benefits of therapy, so development of noninvasive markers for identification and monitoring of those who may benefit is desirable. Lifestyle modification is warranted for all children with NAFLD. The role of treatment with

vitamin E in those who have a biopsy demonstrating borderline or definite NASH remains to be determined," the authors conclude.

More information: *JAMA*. 2011;305[16]1659-1668.

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