Vitamin E Improves Nonalcoholic Steatohepatitis

BY DIANA MAHONEY

BOSTON — The use of vitamin E supplements among patients with nonalcoholic steatohepatitis was associated with a greater improvement in nonalcoholic fatty liver disease activity scores and cytologic ballooning, compared with the use of pioglitazone or placebo, results from a randomized, controlled trial showed.

The investigation was spurred by findings suggesting that oxidative damage and insulin resistance both play a role in the chronic liver disease, Dr. Arun J. Sanyal said at the American Association for the Study of Liver Diseases. He and his colleagues at Virginia Commonwealth University, Richmond, sought to evaluate the role of vitamin E, an antioxidant, and pioglitazone, an insulin-sensitizing agent, in the treatment of nonalcoholic steatohepatitis (NASH).

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DR. SANYAL

The 247 patients were randomized to receive 800 IU of vitamin E once daily, 30 mg of pioglitazone once daily, or placebo for 96 weeks. All of the patients had biopsy-proven steatohepatitis with a nonalcoholic fatty liver disease (NAFLD) activity score of 4 or higher within 6 months prior to randomization, Dr. Sanyal said.

The study's primary end point was improvement—defined as a decrease in NAFLD activity score of 2 points or more and a decrease of at least 1 point in cytologic ballooning—and no worsening of fibrosis. Secondary end points included changes in histologic features, liver enzymes, insulin resistance, anthropometric measures, and quality of life, Dr. Sanyal explained.

Compared with placebo, both vitamin E and pioglitazone were associated with liver function improvement, decreased ballooning, and better fibrosis stabilization at 96 weeks, although only vitamin E met the prespecified level of significance for the primary end point, he said.

Of the 84 patients randomized to vitamin E, 43% showed the predefined composite improvement, compared with 34% of the pioglitazone group and 19% of the placebo group, he said.

The failure of pioglitazone to meet the end point criteria can likely be attributed to the fact that substantially fewer patients in that group had ballooning at baseline "and therefore couldn't demonstrate a reduction with treatment," Dr. Sanyal said.

Improvement in steatosis as measured by poststudy biopsy, lobular inflammation, ballooning scores, and serum alanine aminotransferase levels was observed in both treatment groups, compared with placebo, Dr. Sanyal reported.

Patients on pioglitazone had greater weight gain (mean 4.7 kg) than did those on vitamin E (0.4 kg) or placebo (0.8 kg), but they also were the only group to demonstrate an improvement in insulin resistance, said Dr. Sanyal.

Although this study suggests that both vitamin E and pioglitazone can lead to biochemical and histologic improvement in NASH, additional studies are needed to determine the sustainability of the observed outcomes and the long-term safety of the agents. "With the exception of weight gain, there were no drug-related adverse events, but the study was not powered to assess safety issues," he said.

With respect to the vitamin E findings in particular, "this should resurrect our efforts to use antioxidants [for NASH] and, more importantly, to develop very potent antioxidants that are well tolerated in these patients," Dr. Scott Friedman, AASLD president, said in a press conference. The key is to make sure the vitamin E is of sufficient quality to be effective, said Dr. Friedman, of the Mount Sinai School of Medicine, New York.

The study was sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases. Dr. Sanyal and Dr. Friedman disclosed financial relationships with several pharmaceutical companies. ■