Pioglitazone, Vitamin E, or Placebo for Nonalcoholic Steatohepatitis

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ABSTRACT

Background Nonalcoholic steatohepatitis is a common liver disease that can progress to cirrhosis. Currently, there is no established treatment for this disease.

Methods We randomly assigned 247 adults with nonalcoholic steatohepatitis and without diabetes to receive pioglitazone at a dose of 30 mg daily (80 subjects), vitamin E at a dose of 800 IU daily (84 subjects), or placebo (83 subjects), for 96 weeks. The primary outcome was an improvement in histologic features of nonalcoholic steatohepatitis, as assessed with the use of a composite of standardized scores for steatosis, lobular inflammation, hepatocellular ballooning, and fibrosis. Given the two planned primary comparisons, P values of less than 0.025 were considered to indicate statistical significance.

Results Vitamin E therapy, as compared with placebo, was associated with a significantly higher rate of improvement in nonalcoholic steatohepatitis (43% vs. 19%, P=0.001), but the difference in the rate of improvement with pioglitazone as compared with placebo was not significant (34% and 19%, respectively; P=0.04). Serum alanine and aspartate aminotransferase levels were reduced with vitamin E and with pioglitazone, as compared with placebo (P<0.001 for both comparisons), and both agents were associated with reductions in hepatic steatosis (P=0.005 for vitamin E and P<0.001 for pioglitazone) and lobular inflammation (P=0.02 for vitamin E and P=0.004 for pioglitazone) but not with improvement in fibrosis scores (P=0.24 for vitamin E and P=0.12 for pioglitazone). Subjects who received pioglitazone gained more weight than did those who received vitamin E or placebo; the rates of other side effects were similar among the three groups.

Conclusions Vitamin E was superior to placebo for the treatment of nonalcoholic steatohepatitis in adults without diabetes. There was no benefit of pioglitazone over placebo for the primary outcome; however, significant benefits of pioglitazone were observed for some of the secondary outcomes.

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