Editorial

Is Vitamin E or Ursodeoxycholic Acid a Valid Treatment Option for Nonalcoholic Fatty Liver Disease in 2016?

Nonalcoholic fatty liver disease (NAFLD) is a leading cause of chronic liver disease.[1] It affects 20%–40% of the general population and 20% of patients with NAFLD will progress to nonalcoholic steatohepatitis (NASH).[1,2] It is well known that NASH patients may progress to liver cirrhosis and even hepatocellular carcinoma. NASH is currently the most rapidly growing indication for liver transplantation (LT) in patients with HCC in the United States. NASH/NAFLD is predicted to soon become the leading LT indication as a result of major advances in hepatitis C therapy and the increasing prevalence of obesity and associated conditions.[3]

Metabolic abnormalities including type 2 diabetes, obesity, hypertension, and hyperlipidemia are strongly associated with NALFD.[4] Hepatic steatosis is associated not only with liver-related mortality but also with an increased incidence of chronic kidney and cardiovascular diseases.[5] NALFD is becoming a major health burden and unfortunately, to date, no optimal therapy is available. The efficacy of a number of medications, including metformin, thiazolidinediones, and omega-3 fatty acids have been evaluated but unfortunately the results were suboptimal.[6,7]

Parikh performed a prospective, single center, open-labeled, randomized trial of vitamin E or ursodeoxycholic acid (UDCA) in NAFLD patients. Diagnosis was made based on ultrasound findings and patients with high serum ALT and AST were enrolled in the study. Two hundred and fifty noncirrhotic, nondiabetic NAFLD patients were randomized to Vitamin E 400 mg twice a day or UDCA 300 mg twice a day for 52 weeks.[8] Only 42% of patients had a liver biopsy at the time of enrollment. All patients were advised lifestyle modification and were assessed by a dietician on a monthly basis to reinforce these recommendations. Seventy percent of NAFLD patients achieved the desired weight reduction (5%) by the end of the study. Normalization of transaminases (primary outcome) was achieved in 14% of NALFD patients who received vitamin E compared with 19% of patients who received UDCA. However, the percentage of ALT reduction (secondary outcome) was high in both groups (56% vs 63%, *P* value nonsignificant). At the end of the study, each group demonstrated a significant improvement in the NAFLD fibrosis score (NAS), but the result was not statistically significant between the vitamin E group and the UDCA group (44% vs 47%). Most patients tolerated both therapies with no significant side effects.[8]

Based on the study result, the authors stated that vitamin E and UDCA are equally effective in nondiabetic, noncirrhotic NAFLD patients along with life style modifications. However, such a statement should be interpreted cautiously in the light of existing evidence regarding vitamin E and UDCA in NAFLD. There is insufficient data regarding liver histology among patients who received UDCA or vitamin E in Parikh's study, and also there is a lack of evidence to assess the efficacy of both therapies by liver histology at the end of the study.

UDCA has been evaluated in multiple studies among NASH patients. There was a significant improvement in aminotransferases and steatosis in NALFD patients who were treated with UDCA.[9]

However, a large multicenter, randomized controlled trial showed that UDCA did not offer a histological benefit compared with placebo in NASH patients.[10] Therefore, it has not been recommended to treat NAFLD/NASH despite its safety profile. Likewise, UDCA in combination with vitamin E has been evaluated in a small sample size compared with UDCA alone or placebo.[11] Biochemical improvement was observed in the UDCA/vitamin E group compared with placebo or UDCA alone. Likewise, lower NAS and improvement in steotosis was observed only in the group who received combination therapy with UDCA and vitamin E. However, a larger study is required to assess the safety and efficacy of combined vitamin E and UDCA therapy, for NASH patients.

The efficacy of vitamin E has been evaluated in multiple studies among NAFLD/NASH patients. However, it is difficult to perform comparisons between these studies due to differences in vitamin E doses and utilizations of since unclear formulations. In the PIVENS study, 247 nondiabetic NASH patients were randomized to vitamin E 800 mg once daily or pioglitazone or placebo.[12] Reduction of transaminases were observed with vitamin E and pioglitazone compared with placebo. In addition, there was a significant improvement in hepatic steatosis and lobular inflammation in the vitamin E group, with no improvement in fibrosis scores.[12] Based on these results, vitamin E has been considered an option in the treatment of nondiabetic patients with biopsy-proven NASH. However, this needs to be balanced against potential risks of vitamin E including associations with increased risk of prostate cancer in men and increased all-cause mortality.[13,14]

In conclusion, there is a significant health burden from NAFLD because of increasing prevalence of obesity worldwide. Life style modifications including diet and exercise are firstline therapies; however, there has been limited success given the difficulty in achieving and sustaining weight loss.[15] Although UDCA and vitamin E may be options in selected patients, the evidence remains somewhat limited. There continues to be great interest in this field, and ongoing and future trials are anticipated to bring additional treatment options to this important patient group.

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DOI: 10.4103/1319-3767.182462