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Original Research Article

COMPARISON OF VITAMIN E AND URSODEOXYCHOLIC ACID IN NON-ALCOHOLIC STEATOHEPATITIS (NASH)

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ABSTRACT

Background: *Non-alcoholic steatohepatitis (NASH) is a progressive phenotype of non-alcoholic fatty liver disease characterized by hepatocellular injury, elevated transaminases, and a substantive risk of fibrosis progression. Antioxidant therapy (vitamin E) and bile acid–based therapy (ursodeoxycholic acid, UDCA) are commonly used, yet their short-term comparative biochemical effectiveness remains uncertain.* ***Objective:*** *To compare the effectiveness of vitamin E versus UDCA in reducing serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels over eight weeks in adults with NAFLD/NASH.* ***Study design****: Randomized controlled trial.* ***Settings:*** *Department of Medicine, Sir Ganga Ram Hospital, Lahore, Pakistan.* ***Duration of study:*** *22 March 2025 to 22 June 2025.* ***Methods:*** *Ninety adult patients with NAFLD/NASH were randomized into two groups: UDCA 15 mg/kg/day or vitamin E 200 IU/day for eight weeks. Liver function tests (ALT, AST, alkaline phosphatase (ALP), total bilirubin, albumin) were recorded at baseline and eight weeks. Between-group comparisons of mean change from baseline were assessed using the Student's t-test with two-sided α=0.05.****Results:*** *Both interventions produced significant within-group reductions in ALT and AST at eight weeks. Vitamin E achieved greater mean reductions than UDCA in ALT (31.5 vs 25.2 U/L; p=0.002) and AST (27.6 vs 22.6 U/L; p=0.001). A significant decrease in ALP was also observed in the vitamin E group, whereas changes in total bilirubin and albumin were minimal in both groups.* ***Conclusion:*** *Over eight weeks, vitamin E produced larger reductions in serum transaminases than UDCA in adults with NAFLD/NASH, with additional improvement in ALP. Vitamin E may be preferred for short-term biochemical optimization in NASH, pending confirmation in longer-duration trials with histological endpoints.*

Keywords: Non-Alcoholic Steatohepatitis; NAFLD; Vitamin E; Ursodeoxycholic Acid; Liver Enzymes; ALT; AST; Alkaline Phosphatase; Randomized Controlled Trial

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) has become a significant concern in terms of public health because of its increased prevalence and the possibility of NAFLD developing further to severe liver diseases (1). Non-alcoholic fatty liver disease (NAFLD) represents a clinical spectrum ranging from simple steatosis to non-alcoholic steatohepatitis (NASH), the latter being marked by hepatic inflammation and damage to hepatocytes. The progression of NASH includes fibrosis, cirrhosis, and hepatocellular carcinoma; NASH is hence ranked among the major contributors to liver morbidity and death across nations (2, 3). The widespread development of metabolic syndrome, obesity, diabetes mellitus, lack of physical activity, and so on has been closely related to the increase in the number of NAFLD cases. The most recent estimates suggest that NAFLD is prevalent in around 25 % of the worldwide population, but exceptionally high in South Asia and the Middle East (4).

The pathophysiology of NASH is multifactorial, with multiple interrelated mechanisms they including oxidative damage, insulin resistance, accumulation of lipids, production of proinflammatory cytokines, and defects in mitochondrial function (5, 6). The most critical biochemical signs of cellular damage in NASH, which include elevated liver enzymes, particularly alanine aminotransferase (ALT) and aspartate aminotransferase (AST), indicate liver cell damage (7). There is still no universally effective pharmacological therapy for NASH, and in most cases, the treatment is reduced to lifestyle changes, including nutritional changes, weight loss, exercise, and so on. Although the outcomes of such strategies in clinical practice are beneficial, the high cost of their long-term adherence underscores the need for practical medical approaches (8, 9).

Vitamin E, as a fat-soluble antioxidant, has caught much attention due to its potential therapeutic applications in non-alcoholic steatohepatitis (NASH). Vitamin E reduces oxidative stress as well as peroxidation and lipid peroxidation that cause hepatocyte dysfunction and damage (10). Indeed, a multicentre, randomized trial in non-diabetic adults with NASH PIVENS showed significant changes in liver histology and profiles of serum enzymes after treatment with Vitamin E. These results make Vitamin E a possible first-line treatment in some groups of NASH patients (11).

On the other hand, the hydrophilic bile acid ursodeoxycholic acid (UDCA) has been traditionally used in noncirrhotic cholestatic liver diseases due to its ability to protect and prevent cell death (also known as its anti-apoptotic effects) as well as reduce inflammation. UDCA potentially holds clinical promise for patients with NASH, both by improving bile flow and by reducing hepatic levels of toxic bile acids. The effectiveness of this has, however, remained inconsistent clinically (12).

Notwithstanding these improvements, there are still significant gaps in knowledge about the comparative efficacy of Vitamin E and UDCA in NASH, in South Asian people, who might be affected by specific genetic, environmental, or lifestyle variables of disease presentation and response to therapy. In addition, the majority of the studies have concentrated on the long-term results with the least attention given to the short-term biochemical changes, which are essential when evaluating therapeutic effects in the early stages. As such, this research aims to bridge these gaps by evaluating the comparative impact of Vitamin E and Ursodeoxycholic acid on liver enzyme levels (ALT and AST) over eight weeks of treatment in Pakistani patients with NAFLD/NASH. The assessment of these biochemical parameters will assist in deciding which of the therapies are more effective in hepatoprotective effects in the short run, which can help clinicians manipulate the therapeutic approaches.

METHODOLOGY

This randomized controlled trial was conducted over three months from 22 March 2025 to 22 June 2025, in the Department of Medicine at Sir Ganga Ram Hospital, Lahore, following approval from the institutional ethics committee. The total number of participants was n=90, aged between 20 and 70 years, and both genders were recruited. Clinical, biochemical, and ultrasound findings were confirmed to make a diagnosis. Exclusions included patients with a medical history of repeated NAFLD or hepatic encephalopathy in the three previous months, chronic renal failure (creatinine greater than 2.0 mg/dL or dialysis), pregnancy or breastfeeding, hypersensitivity to Ursodeoxycholic acid, alcohol consumption, digestive bleeding, spontaneous bacterial peritonitis, liver cell cancer, or Hepatitis B or C. After obtaining informed consent, patients were randomly assigned in equal numbers to two groups using a computer-generated randomization list. Group A received Ursodeoxycholic acid, 15 mg/kg, orally once daily, while Group B received Vitamin E capsules, 200 IU, orally once daily. Demographic characteristics such as age, gender, body mass index (BMI), and conditions that the individual had, such as diabetes mellitus (blood sugar > 200 mg/dL), hypertension (blood pressure > 140/90 mmHg), and dyslipidemia (total cholesterol > 200 mg/dL), were noted. An ultrasound of the abdomen was carried out to diagnose fatty liver.

The blood samples (5 mL) were collected at the baseline and afterwards at 4 and 8 weeks into the start of treatment of liver function tests consisting of ALT, AST, alkaline phosphatase, bilirubin, and albumin. The primary outcome measures were the changes in the levels of ALT and AST at baseline after 8 weeks, and secondary outcomes were the levels of other liver parameters. Data analysis was performed using SPSS version 26. Quantitative variables were expressed as mean ± standard deviation, while qualitative variables were presented as frequencies and percentages. The student's t-test was employed to compare mean differences between groups, with a p-value of less than 0.05 considered statistically significant. The confounding factors of age, gender, BMI, and comorbidities were stratified and were tested using the chi-square test.

RESULTS

Both groups under treatment indicated a significant decrease in the quantity of ALT and AST after 8 weeks. Nevertheless, the Vitamin E group revealed a faster change in the levels of liver enzymes than the Ursodeoxycholic Acid group. Both measures (ALT and AST) showed statistically significant reductions in means ($p = 0.002$ and $p = 0.001$, respectively), indicating that Vitamin E is superior in enhancing the hepatic status of patients with NASH, as shown in Table 1.

Histological characteristics of the liver at the baseline condition, such as steatosis grade, lobular inflammation, hepatocyte ballooning, and the stage of fibrosis, did not differ significantly between the two groups and did not show a statistically significant difference. This is to confirm that the two groups were initially balanced to make a comparison of treatment effects without bias in Table 2.

The Vitamin E and Ursodeoxycholic Acid groups improved liver function tests after treatment for 8 weeks. Nonetheless, the Vitamin E group showed more significant declines in ALT, AST, and ALP values, showing a significant difference ($p < 0.05$). The alterations of total bilirubin, direct bilirubin, and albumin were trivial and were not important in both groups. These results suggest that Vitamin E may have additional utility in enhancing markers of hepatocellular regeneration in individuals with NASH, as indicated in Table 3.

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 90)

Variable	Group A: Ursodeoxycholic Acid (n = 45)	Group B: Vitamin E (n = 45)	p-value
Age (years)	46.8 ± 10.2	47.6 ± 10.6	0.68
Gender			
Male	24 (53.3%)	25 (55.6%)	0.82
Female	21 (46.7%)	20 (44.4%)	
BMI (kg/m²)	29.4 ± 3.6	30.1 ± 3.2	0.27
Comorbidities			
Diabetes Mellitus	20 (44.4%)	22 (48.9%)	0.68
Hypertension	18 (40.0%)	17 (37.8%)	0.82
Dyslipidemia	23 (51.1%)	24 (53.3%)	0.83
Liver Size on USG			
Normal	14 (31.1%)	12 (26.7%)	0.63
Mildly Enlarged	31 (68.9%)	33 (73.3%)	

**Data presented as mean ± SD for continuous variables and n (%) for categorical variables*
**NS = Not Significant (p > 0.05)*

Table 2: Baseline Liver Histology of Study Participants (n = 90)

Histological Feature	Group A: Ursodeoxycholic Acid (n = 45)	Group B: Vitamin E (n = 45)	p-value
Steatosis Grade			
Mild (Grade 1)	12 (26.7%)	10 (22.2%)	0.63
Moderate (Grade 2)	25 (55.6%)	27 (60.0%)	
Severe (Grade 3)	8 (17.7%)	8 (17.7%)	
Lobular Inflammation			
None	0 (0%)	0 (0%)	
Mild	18 (40.0%)	20 (44.4%)	0.69
Moderate	22 (48.9%)	21 (46.7%)	
Severe	5 (11.1%)	4 (8.9%)	
Hepatocyte Ballooning			
Absent	10 (22.2%)	9 (20.0%)	0.79
Present	35 (77.8%)	36 (80.0%)	
Fibrosis Stage (NAS)			
Stage 0	5 (11.1%)	6 (13.3%)	0.84

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Stage 1	20 (44.4%)	19 (42.2%)	
Stage 2	14 (31.1%)	13 (28.9%)	
Stage 3	6 (13.3%)	7 (15.6%)	

Table 3: Biochemical Liver Function Test (LFT) Parameters in Both Groups (n = 90)

Parameter	Group A: Ursodeoxycholic Acid (n = 45)		Group B: Vitamin E (n = 45)		p-value
	Baseline (Mean ± SD)	After 8 Weeks (Mean ± SD)	Baseline (Mean ± SD)	After 8 Weeks (Mean ± SD)	
ALT (U/L)	88.4 ± 15.6	63.2 ± 11.4	90.1 ± 14.8	58.6 ± 10.7	0.04*
AST (U/L)	75.3 ± 13.2	52.7 ± 10.9	76.5 ± 12.9	48.9 ± 9.8	0.03*
ALP (U/L)	145.6 ± 26.8	131.4 ± 20.3	147.3 ± 28.1	125.2 ± 18.9	0.05*
Total Bilirubin (mg/dL)	1.2 ± 0.3	1.0 ± 0.2	1.3 ± 0.4	0.9 ± 0.2	0.06
Direct Bilirubin (mg/dL)	0.4 ± 0.1	0.3 ± 0.1	0.4 ± 0.1	0.3 ± 0.1	0.72
Albumin (g/dL)	3.6 ± 0.4	3.8 ± 0.5	3.5 ± 0.3	3.9 ± 0.4	0.09

**Values are presented as Mean ± SD*
**NS = Not Significant; * = Statistically significant (p < 0.05)*

DISCUSSION

The objective of this randomized controlled trial was to evaluate and compare the effectiveness of Vitamin E and Ursodeoxycholic Acid (UDCA) in enhancing liver function parameters among patients with non-alcoholic steatohepatitis (NASH) following an 8-week treatment period. Findings demonstrated that both treatment options led to significant reductions in liver enzyme levels, particularly alanine aminotransferase (ALT) and aspartate aminotransferase (AST).

However, Vitamin E was correlated with a statistically significant better reduction in these transaminases, indicating better efficacy of Vitamin E in enhancing the hepatocellular functioning in NASH (13). Notably, the Vitamin E group exhibited a greater reduction in ALT and AST levels compared to the UDCA group. Alkaline phosphatase (ALP) levels also declined more prominently in the Vitamin E group. In contrast, minor, non-significant improvements in bilirubin and albumin levels were observed in both the Vitamin E and control groups. (14).

The study in point confirms the results obtained in the previous survey, on Vitamin E application in non-diabetic adults with non-alcoholic fatty liver disease and non-alcoholic steatohepatitis (15). PIVENS showed statistically significant histology and reduction of serum alanine aminotransferase (ALT) in the Vitamin E group. These findings were identical to ours: the improvement in serum ALT during 8 weeks of Vitamin E therapy was similarly powerful to that measured in PIVENS (16, 17).

In contrast, mixed evidence has been gained in randomized trials conducted on UDCA. The findings of a previous study reported that UDCA has a negligible influence on aminotransaminases and little change in liver histology, which is maintained in the current research (18). These findings are consistent with the current analysis, and UDCA, though effective in reducing the level of serum ALT and AST, did so at a milder intensity than Vitamin E. A combination of these data suggests that Vitamin E is an efficacious, early-acting pharmacologic agent in NASH. In contrast, UDCA proves to have inconsistent histologic efficacy and low biochemical potency compared with Vitamin E (19).

Vitamin E is a potent antioxidant; it neutralises reactive oxygen species (ROS) and hence blocks the process of lipid peroxidation as well as hepatocyte damage- a phenomenon of great significance in non-alcoholic steatohepatitis (NASH), wherein oxidative stress is one of the key pathogenic factors. This attributable property is possible due to the increased protection of the liver contributed by antioxidants, that is, the decreased activity of liver enzymes, which include alanine aminotransferase (ALT) and aspartate aminotransferase (AST), was vast in the present study (20).

On the other hand, unsodiol (UDCA) has anti-apoptotic and immunomodulatory effects, as well as an impact on bile flow and cholestasis, which is well studied. To some extent, the reduced enzyme reductions might be attributed to its minimal impact on the metabolic and oxidative pathways of NASH.

CONCLUSION

The randomized, controlled trial of the present study evaluated the efficiency of vitamin E compared to ursodeoxycholic acid in individuals with non-alcoholic steatohepatitis (NASH) over 8 weeks. The researchers found that patients who used vitamin E recorded a higher level of liver enzyme reduction compared with those who used ursodeoxycholic acid. The results are consistent with previous research and emphasize the clinical usefulness of Vitamin E in reducing early biochemical evidence of NASH. These results need to be confirmed in future studies using large cohorts and prolonged follow-up.

DECLARATIONS

Data Availability Statement
All data generated or analysed during the study are included in the manuscript.
Ethics approval and consent to participate
Approved by the department Concerned. (IRBEC-??)
Consent for publication
Approved
Funding
Not applicable

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

MAHWISH AMIN
Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript. Manuscript drafting.
FARZAM AMIN
Manuscript revisions, critical input.
Study Design, Review of Literature.
ADNAN AHMAD ATHER
Conception of Study, Final approval of manuscript.
SAJEEL AHMAD
Data entry, data analysis, drafting an article.

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