Review Article

Therapeutic Effects of Tocopherol (Vitamin E) in Non-Alcoholic Fatty Liver Disease (NAFLD) and Non-Alcoholic Steato-Hepatitis (NASH) Patients - A Review.

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ABSTRACT

Around the globe, non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) pose significant health risks, with a shortage of effective therapeutic options. The potential impact of vitamin E in controlling these conditions has garnered substantial attention. This review aims to evaluate the effects of vitamin E on liver histology, biochemical indicators, and clinical outcomes, examining its influence on the progression of NAFLD and NASH.

To identify relevant research, an extensive search was conducted across multiple databases, encompassing observational studies and randomized controlled trials focusing on the impact of vitamin E on NAFLD and NASH. The findings indicate that vitamin E administration may mitigate hepatic steatosis, inflammatory processes, and scarring, demonstrating positive effects on liver histology. However, the observed heterogeneity in outcomes is attributed to variations in research designs, patient demographics, and vitamin E doses.

In conclusion, existing data support the consideration of vitamin E as a treatment approach for NAFLD and NASH, particularly in terms of enhancing liver histology. Nevertheless, to offer concrete recommendations regarding the frequency, duration, and potential long-term benefits or risks of vitamin E intake in NAFLD and NASH, more well-designed randomized controlled studies are imperative.

Keywords: Non-alcoholic fatty liver disease (NAFLD), Non-alcoholic steatohepatitis (NASH), Tocopherol (Vitamin E).

INTRODUCTION

Around 25% of the population worldwide is affected by this NAFLD (1). Non-alcoholic fatty liver disease (NAFLD) is defined as fat build up in the liver of a nonalcoholic. Simple steatosis to non-alcoholic steatohepatitis (NASH) is all disorders that fall under the umbrella of NAFLD (2). Many liver disorders and mortality associated with those disorders may develop from NASH specifically (3).

There is not much understanding on how to treat NAFLD and NASH despite their widespread incidence and propensity for significant consequences. As a first line of treatment, lifestyle changes including losing weight and increasing physical exercise are frequently

advised (4). The efficacy of pharmaceutical therapies is yet unknown, though.

Vitamin E, a lipid-soluble free radical scavenger with possible liver-protective qualities, is a viable contender in the treatment of NAFLD and NASH. Mixed results are obtained from the trials on the use of vitamin E in individuals with NAFLD and NASH with some having lowered oxidative damage and inflammatory processes (5-9).

This review aimed to assess vitamin E impacts on the histology of the liver, biochemical indicators, and clinical consequences and also looks how vitamin E use affects NAFLD and NASH progression.

MATERIALS AND METHODS

A comprehensive literature search was conducted using databases including PubMed, Embase, Cochrane Library, and Web of Science to find studies on the effects of vitamin E in individuals with NAFLD and NASH. Keywords related to clinical studies, vitamin E, NAFLD, and NASH were utilized. The inclusion criteria involved randomized controlled trials (RCTs) and observational studies published in English, from the inception of the databases to the search date. Animal studies and case reviews without relevant outcomes were excluded. Data extraction was performed independently by two reviewers using a standardized form, focusing on study design, participant demographics, treatment details, and outcomes. Disagreements were resolved through discussion or consultation with a third reviewer. The quality of RCTs was assessed using the Cochrane risk-of-bias tool, while observational studies were evaluated with the Newcastle-Ottawa Scale. Ethical approval was not required since the review was based on published data.

RESULTS

The inclusion criteria were satisfied by 15 researches in total, of which 8 randomized controlled trials and 7 observational research studies were included.

Few of the studies included investigated medical outcomes (Table.1) such as liver-related morbidity and death. According to one observational research, individuals with NASH who took vitamin E supplements had a lower incidence of liver-related incidents than those who did not. However, there was few and conflicting information about clinical results.

Table 1: Medical Outcomes Investigation

Medical Outcomes Investigated	Observations
Liver-related morbidity and death	Limited studies; one observational research suggested lower incidence with vitamin E supplementation
Clinical results	Varied and conflicting information
Negative Consequences of Vitamin E Intake	Alimentary issues (e.g., diarrhea, abdominal discomfort) reported, typically minor and self-limiting
Severe Complications	None reported; no substantial differences in negative events between vitamin E and control groups

A few researches revealed negative consequences linked to vitamin E intake. The most often reported negative consequences were alimentary in nature, such as diarrhea and abdominal discomfort, although they were typically minor and self-limiting. No reports of severe complications or substantial discrepancies in the frequencies of negative events among the vitamin E supplementation and control groups were made.

Randomized controlled trials done to evaluate the impact of vitamin E on the histology of the liver showed that vitamin E administration had a tendency to enhance liver histology (Table 2). The amounts and durations of vitamin E administration varied significantly between researches, though. According to subgroup evaluations based on dosage and duration, higher dosages (>800 IU/day) and more prolonged periods (>2 years) of vitamin E administration led to significant enhancements in hepatic histology.

Table 2: Consequences of Vitamin E Intake

Parameter	Observations
Overall Tendency to Enhance Liver Histology	Consistent trend observed
Variation in Vitamin E Administration (Dosage, Duration)	Substantial variability in amounts and durations across studies
Subgroup Analyses	Higher dosages (>800 IU/day) and longer durations (>2 years) associated with significant improvements

Regarding research design, patient demographics, vitamin E doses and compositions, and outcome indicators,

heterogeneity was seen across the studies that were reviewed (Table 3). These elements had played a role in the challenges encountered in evaluating the overall effect sizes and pooling data for meta-analysis.

In general, although there is some data pointing to vitamin E administration possibly improving liver histology in NAFLD and NASH patients, the findings are not totally consistent across investigations. Higher dosages and prolonged use seems to have a better potential for positive impacts on vitamin E effectiveness than shorter doses and periods. To draw more firm conclusions about the clinical advantages and long-term safety of vitamin E supplementation in NAFLD and NASH, additional well-designed randomized controlled trials are required.

Table 3: Heterogeneity across Studies

Heterogeneity Across Studies	Factors Contributing to Heterogeneity
Research Design	Varied across studies
Patient Demographics	Diverse participant characteristics
Vitamin E Doses and Compositions	Considerable variability in dosage and formulations
Outcome Indicators	Varied metrics used in different studies

DISCUSSION

The results of this analysis offer important new information on how vitamin E use affects people with NASH and NAFLD. Findings in line with earlier research that demonstrated vitamin E has anti-inflammatory and antioxidant characteristics are revealed by the analysis of the trials that were included (Table 4) (5, 6).

The results of this review provide new insights into the potential benefits of Vitamin E supplementation for individuals with nonalcoholic steatohepatitis (NASH) and nonalcoholic fatty liver disease (NAFLD). The findings align with prior studies that have shown the anti-inflammatory and anti-oxidant properties of Vitamin E, highlighting its ability to improve liver histology by reducing steatosis, inflammation, and fibrosis (5, 6. The evidence indicates that Vitamin E may have a role in mitigating lipid metabolism dysfunction and reducing fat accumulation within liver cells, which is critical in the progression of NAFLD to NASH and subsequent liver fibrosis (10). Notably, fibrosis and inflammation are key drivers of liver damage, and the reduction of these processes through Vitamin E supplementation is significant (11).

Despite these promising results, the ideal dosage and duration for Vitamin E supplementation remain uncertain. Subgroup analyses of the included studies show that higher doses (>800 IU/day) and longer treatment periods (>2 years) were associated with more pronounced improvements in liver histology. However, the variability in dosages (ranging from 400 to 1800 IU/day) and treatment durations (from 6 months to 4 years) across the studies complicates the establishment of a standardized protocol. More well-designed randomized controlled trials (RCTs) are needed to determine the optimal regimen for Vitamin E use and assess its long-term safety and efficacy.

Table 4: Impact on Liver Histology and Underlying Mechanisms

Findings
- Vitamin E exhibits anti-inflammatory and anti-oxidant characteristics (5, 6)
- Significant enhancement in liver histology observed (10)
- Decreased liver steatosis suggests a potential role in lipid metabolism (11)
- Reduction in fibrosis and inflammatory processes noted
Implications
- Vitamin E administration may aid in reducing mechanisms involved in NAFLD and NASH onset and progression
- Potential contribution to mitigating serious concerns like liver fibrosis

Furthermore, the effects of Vitamin E on biochemical markers of liver damage, such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), were inconsistent across studies. While some trials reported significant reductions in these liver enzymes, others did not observe the same effect. This discrepancy may stem from variations in patient characteristics, baseline enzyme levels, and the sensitivity of these markers to changes in liver inflammation and injury. The heterogeneity in results highlights the need for more standardized approaches in future studies to better understand the biochemical effects of Vitamin E on liver health.

Clinical outcomes, particularly liver-related morbidity and mortality, were not well evaluated in the included studies. The available data are insufficient to draw strong conclusions about

whether Vitamin E supplementation leads to meaningful reductions in liver-related complications or improves long-term survival. To address this gap, future research should include longer follow-up periods and focus on assessing clinically relevant outcomes such as liver-related diseases and overall mortality.

Adverse events related to Vitamin E supplementation were generally mild and self-limiting, with gastrointestinal issues such as diarrhea and abdominal discomfort being the most commonly reported side effects. However, the long-term safety of high-dose Vitamin E supplementation remains unclear, as some studies have raised concerns about potential risks (12, 13). Further investigation is needed to thoroughly evaluate the risk-benefit profile of prolonged Vitamin E use, particularly at high doses.

Although this review highlights the potential of Vitamin E to improve liver histology in patients with NAFLD and NASH, the variability in study designs, dosages, and treatment durations limits the ability to draw definitive conclusions. Additional studies should incorporate standardized outcome measures, explore personalized treatment strategies (such as accounting for genetic factors influencing responsiveness to Vitamin E), and provide clear guidance on optimal dosing and long-term safety. A formal meta-analysis could enhance the understanding of Vitamin E's therapeutic efficacy by offering a quantitative synthesis of the available data (14, 15, 16).

Emerging research on pediatric populations, dietary intake of Vitamin E, and genetic responsiveness also suggests that Vitamin E supplementation may play a broader role in managing NAFLD and NASH. In children, a 2023 study found that the tocotrienol-rich fraction (TRF) of Vitamin E improved liver fat content and biochemical markers of liver health, suggesting that specific isomers of Vitamin E might offer additional benefits in pediatric NAFLD (17, 18, 19). Additionally, a 2024 study demonstrated that higher dietary intake of Vitamin E was inversely associated with NAFLD severity in adults, particularly in reducing liver fat and inflammation (BioMed Central, Nature). Lastly, genetic factors influencing the response to Vitamin E supplementation in NASH patients have been identified, pointing to the potential for more personalized treatment approaches (NIDDK) (20-23).

CONCLUSION

The results of this review's analysis indicate that vitamin E use may be advantageous for hepatic histology, notably in terms of lowering steatosis, inflammatory processes, and scarring in NAFLD and NASH patients. However, additional study is required to determine the most efficient regimen and evaluate long-term safety because the ideal vitamin E supplementation dosage and duration are yet unknown. Additional research is needed to better understand clinical results, possible hazards, and advantages of vitamin E administration. Overall, even though there is encouraging data, additional well planned randomized controlled studies are necessary to offer solid proof of vitamin E's effectiveness and safety in the treatment of NAFLD and NASH.

CONFLICT OF INTEREST: The authors declare no conflict of interest.

ETHIC APPROVAL: Because this work is a review, ethical clearance was exempted.

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