Journal of
Diabetes and Clinical Studies

REVIEW ARTICLE

The Effect of Cholestasis-related Vitamin Malabsorption on NASH Pathology

Mustafa Sahin

Department of Medical Biochemistry, Hitit University, Erol Olcok Education and Research Hospital,Corum, Turkey.

Abstract

Cholestasis can occur due to intrahepatic and extrahepatic causes. Increased free radical formation in cholestasis and the addition of the multiple hits hypothesis to it are important in vitamin malabsorption. Vitamin suplementation in NASH treatment should not be forgotten.

Introduction

Primary bile acids, cholic acid and chenodeoxycolic acid, occur in the liver by the addition of hydroxyl groups to the 7th carbon atom of cholesterol. In this reaction chain, the rate-limiting enzyme is cholesterol 7-α hydroxylase (CYP7A1). These primary bile acids are partially re-absorbed in the small intestine, and the portion that is not absorbed is deconjugated and metabolized by the bacteria that is in the large bowel to the secondary bile acids of deoxycholic acid and chenodeoxycholic acid [1]. Bile acids play an important role in the absorption of lipids and fat soluble vitamins (A, D, E, K).

Cholestasis is described as a occlusion anywhere from the production of bile acids in hepatocytes to the discharge from the duodenum. This clinical picture is evaluated in two groups as intrahepatic (genetic, hepatitis, viral and toxic hepatitis, autoimmune, alcohol, primary bilier cirrhosis, primary sclerosing cholangitis etc.) and extrahepatic cholestasis (choledocholithiasis, tumors, parasites, pancreas linked diseases). Choledocholithiasis is the most common cause of cholestasis [2].

Cholestasis-related vitamin malabsorption has been seen despite oral supplementation in all fat soluble vitamins. Especially vitamin E, is most hydrophobic fat soluble vitamin, most affected from bile acid deficiency during intraluminal absorption, approximately 50-70% deficiency. α-tochopherol is active form of vitamin E. The other fat soluble vitamins, A (active form is β-carotene), D (active form is 1,25 OH $D_{3)}$ and K (active form is phylloquinone), have been observed more less approximately 25%, 35-70%, 60% respectively, due to cholestasis related malabsorption. In addition, vitamin A absorbtion is affected from vitamin E. These vitamins effect each other during intestinal absorbtion [3, 4]. Fat soluble vitamin replacement is important an acceptable in cholestasis medical treatment. Free radical formation-antioxidant response balance is adversely affected because of deficiency fat soluble vitamins in cholestasis. DNA, protein, carbohydrate and lipid structures have been protected against to damage of reactive oxigen species (ROS) and free radikal, occur in tissues, by vitamin A and E. For this reason, vitamins A and E, fat-soluble, are evaluated as antioxidant. In chronic cholestasis, the accumulation of heavy metals such as Cu and Mn with oxidant properties in the liver might aggravate liver damage because of antioxidant response failure vitamins A and E neutralize the oxidant by turning into a weaker new molecule. This property of antioxidants is called scavenging and also vitamins A and E have [5]. Together with cholestasis-associated antioxidant response deficiency, bile salts that accumulate in hepatocytes disrupt to cell membrane integrity and suppress membrane transport proteins such as Na^+ K^+ ATPase. These pathologies chain progresses in the direction of free radical formation, inflammation and fibrosis [6]. Thus, inflammation and fibrosis occur at the result of free radical formation caused with physical barrier and vitamin malabsorption in cholestasis. This pathology can be evaluated as two hits hypothesis. However, in recent publications, multiple hits have emerged as a more advanced theory in the pathogenesis of Nonalcoholic Steatohepatitis (NASH). The two hits hypothesis is not considered sufficient to explain molecular interactions and metabolic changes in NASH development. The multiple hit hypothesis includes multiple factors which have roles in development of NASH. These are genetic and epigenetic factors, insulin resistance, metabolic syndrome, adipose tissue derived hormones, nutritional habits and gut microbiota [7].

A meta-analysis of five randomized controlled trials using vitamin E showed significant improvement in liver function and histological changes in NASH patients [8]. In a multicentre study including 149 pediatric patients, vitamin E deficiency was detected in children with NASH in all groups [9]. Vitamin

Correspondence to: Mustafa Sahin, Hitit University, Erol Olcok Education and Research Hospital, Department of Medical Biochemistry, 19020, Corum, Turkey, E-mail: mustafaistanbulx[AT]hotmail[DOT]com

Received: Feb 27, 2018; **Accepted:** Mar 02, 2018; **Published:** Mar 06, 2018

E supplementation has been shown to reduce liver steatosis and inflammation in rats [10]. In a study using wistar albino rats exposed to liver damage with carbon tetrachloride, vitamin E decreased steatosis and inflammation scores [11].

Conclusion

Experimental animal and cohort studies have shown that fat-soluble antioxidant vitamins have beneficial effects on liver steatosis, fibrosis and inflammation. Fat soluble vitamin supplementation is important and necessary against the increased free radical formation by the multiple hits hypothesis of cholestasis. Fat soluble vitamin supplementation in NASH treatment should not be forgotten. Fat soluble vitamin supplementation for free radical formation and antioxidant balance in cholestasis and NASH pathology may be evaluated in detail with experimental studies.

Conflicts of interest

There are no conflicts of interest.

References

1. Li T, Chiang JY (2013) Nuclear receptors in bile acid metabolism. Drug Metab Rev 45: 145-155. [View Article]
2. Trauner M, Meier PJ, Boyer JL (1998) Molecular pathogenesis of cholestasis. N Engl J Med 339: 1217-1227. [View Article]
3. Aydoğdu S (2006) Kolestazda medical tedavi. J Curr Pediatr 79: 125-132. [View Article]
4. Moyer V, Freese DK, Whitington PF, Olson AD, Brewer F, et al. (2004) Guideline for the evaluation of cholestatic jaundice in infants: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr 39: 115-128. [View Article]
5. Sokol RJ (2016) A New Old Treatment for Vitamin E Deficiency in Cholestasis. J Pediatr Gastroenterol Nutr 63: 577-578. [View Article]
6. Enomoto H, Bando Y, Nakamura H, Nishiguchi S, Koga M (2015) Liver fibrosis markers of nonalcoholic steatohepatitis. World J Gastroenterol 21: 7427-7435. [View Article]
7. Buzzetti E, Pinzani M, Tsochatzis EA (2016) The multiple-hit pathogenesis of non-alcoholic fatty liver disease (NAFLD). Metabolism 65: 1038-1048. [View Article]
8. Sato K, Gosho M, Yamamoto T, Kobayashi Y, Ishii N, Ohashi T, et al. (2015) Vitamin E has a beneficial effect on nonalcoholic fatty liver disease: A meta-analysis of randomized controlled trials. Nutrition 31: 923-930. [View Article]
9. Vos MB, Colvin R, Belt P, Molleston JP, Murray KF, et al. (2012) Correlation of vitamin E, uric acid, and diet composition with histologic features of pediatric NAFLD. J Pediatr Gastro Nutr 54: 90-96. [View Article]
10. Alcalá M, Sánchez-Vera , Sevillano J, Herrero L, Serra D, et al. (2015) Vitamin E reduces adipose tissue fibrosis, inflammation, and oxidative stress and improves metabolic profile in obesity. Obesity (Silver Spring) 23: 1598-1606. [View Article]
11. Eralp A, Menguc NY, Polat E, Yuncu M, Koruk M, et al. (2016) Preventative Effect Of Vitamin E On Mast Cells In Carbon Tetrachloride-Induced Acute Liver Damage. Endocr Metab Immu Disord Drug Targ 16: 205-212 [View Article]

Citation: Sahin M (2018) The Effect of Cholestasis-related Vitamin Malabsorption on NASH Pathology. J Diab Clin Stud 2: 001-002.