Vitamin Supplements and Chronic Alcohol Consumption

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Alcoholic drinks are extensively consumed worldwide. Drinking alcohol has negative and positive consequences. The health consequences of alcohol intake vary depending on the amount and pattern of consumption.

Keywords: alcoholic liver disease ; vitamin B1 ; vitamin C ; vitamin D ; vitamin E

1. The Pathophysiology of Alcohol Drinking

Ethanol is harmful to the human body and can cause toxicity and death when ingested in excessive amounts. Ethanol metabolism produces an alcoholic fatty liver, alcoholic hepatitis, or cirrhosis [1][2]. The major pathway of ethanol metabolism is the oxidative pathway that involves alcohol dehydrogenase (ADH) present in the cytosol of hepatocytes [3]. This ADH produces acetaldehyde, which is toxic due to its high reactivity and may form DNA or protein adducts [4][5]. Some of the alcohol that is ingested orally does not enter the systemic circulation but may be oxidized in the stomach by ADH and their isoforms. Since the Km of most ADH isozymes for ethanol is low (about 1 mM), ADH is saturated at low concentrations of alcohol, and the MEOS system is activated [6].

Another quantity of ethanol is metabolized by the cytochrome P450 2E1 (CYP2E1) in the microsomal ethanol oxidizing system (MEOS) located within the smooth endoplasmic reticulum of hepatocytes, which leads to lipid peroxidation and to the mitochondrial glutathione and S-adenosylmethionine depletion, producing increased oxidative stress and liver injury [7][8][9]. In addition, fatty acid ethyl esters (FAEE) synthase produces FAEEs via nonoxidative metabolism [10].

Through alcohol intoxication, the CYP2E1-dependent system and the microsomal respiratory chain are the principal sources of reactive oxygen species (ROS) within the hepatocytes. Because of its propensity to metabolize and activate a variety of hepatotoxic substrates in the liver, CYP2E1 is of particular interest. Ethanol, carbon tetrachloride, acetaminophen, and N-nitrosodimethylamine, as well as several hazardous compounds, are among these substrates. [11][12]. The ethanol-induced activation of cytochrome CYP2E1 appears to be one of the main mechanisms by which ethanol causes oxidative stress. Furthermore, when ethanol is oxidized by CYP2E1, it creates acetaldehyde, a highly reactive molecule that may contribute to ethanol's toxicity [13].

2. Vitamin B

It has been described that vitamin B (vitamin B1, vitamin B2 and vitamin B6) deficiency in ALD is caused by different factors, such as inadequate dietary intake, increased use of vitamin B, decreased hepatic storage, impairment of intestinal absorption by ethanol, or abnormal metabolism of the vitamins [14][15].

Due to decreased hepatic storage, vitamin B9 and vitamin B12 deficiencies can develop quickly in chronic liver illness. However, alcohol consumption affects the metabolism of homocysteine (tHcy) because the enzyme cofactor for the conversion of tHcy to methionine is vitamin B12. Decreased levels of vitamin B12 levels were shown to be adversely connected with tHcy and significantly linked with indicators of alcohol-related liver impairment in recent research [16]. Another research found that individuals with severe chronic liver disease had high vitamin B12 plasma levels but decreased vitamin B9 plasma levels [17]. Conversely, Gibson et al. [18] has shown that two weeks of moderate consumption of alcohol (i.e., red wine, or vodka) increased tHcy and reduced the statuses of both vitamin B9 and B12. In addition, other studies have studied vitamin B status as well [19][20][21]. For example, Van der Gaag et al. [19] showed that type-dependent alcohol had no effect on vitamin B12, but a fall in folate with spirits consumption and an increase in vitamin B6 with all alcohol types were observed. In contrast, Laufer et al. [20] only showed an effect of ethanol on vitamin B12, with no effect on vitamin B9. However, in another study, Beulens et al. [21] showed that beer drinking raised vitamin B6 and appeared to reduce vitamin B12 levels while having no effect on vitamin B9 levels. In this regard, Laufer et al. [20]

noted that a lack of vitamins and alcohol use may interact to deplete vitamin B9 and vitamin B12 status and that if nutritional intake matches recommended levels, a decreasing impact of alcohol on vitamin B9 may not be detected. However, further studies are required to clarify the relationship between alcohol consumption and the intake of vitamin B to be able to provide nutritional management strategies for chronic liver disease.

3. Vitamin C

One of the many risk factors for vitamin C (including the three forms of vitamin C) and E insufficiency is excessive alcohol intake [22][23]. Vitamin C and E levels are decreased in alcoholics [24]. When compared to those who do not consume alcohol, urine ascorbic acid excretion increased by 47% after acute alcohol consumption of up to 0.58 g ethanol/kg body weight [25]. In effect, pretreatment with vitamin C (doses of 5 g, 1000 mg five times daily for two weeks) significantly improved blood ethanol elimination [26] whereas pretreatment with vitamin C (doses of 2 g, 500 mg four times daily for two weeks) significantly improved alcohol elimination in plasma in the short and long term, implying that vitamin C plays a role in ethanol oxidation [27]. Furthermore, short-term intravenous vitamin C therapy (500 mg/day for five days) significantly improved serum vitamin C levels in chronic alcoholics with hypovitaminosis C [28]. Despite these findings, a previous study indicated that chronic drinkers' blood levels can take up to three months to restore to normal after taking oral vitamin C supplements [29][30].

Hepatocytes metabolize around 90% of ethanol, which is transformed to acetaldehyde by the enzyme ADH. Once the ADH has exhausted its ability to metabolize alcohol, cytochrome P450 isoenzymes take over and convert the molecule to acetaldehyde [31]. This has been found in tissues, including the liver and brain, that have poor ADH activity. By acting as an electron donor and, thereby, unleashing the NAD/NADH pathway, vitamin C is theorized to speed up alcohol metabolism [32]. A positive relationship between ADH activity and leukocyte ascorbic acid concentration has been discovered in people with liver disease [33]. Furthermore, the acetaldehyde produced has been associated with ethanol-induced hepatotoxicity [34][35], and when paired with hepatic CYP2E1 activation, these factors enhance oxidative stress in hepatocytes [36][37][38][39]. On the other hand, vitamin C has been demonstrated to protect against the detrimental effects of acetaldehyde in animal experiments [40]. Given the function of acetaldehyde in the brain's dopaminergic stimulation of opiate receptors, this could reduce hepatotoxicity and possibly the biochemical basis of addiction [28].

4. Vitamin D

Calcium homeostasis and bone metabolism require vitamin D to function properly [41]. It is well known for its role in immune response control as well as its anticancer activities [42][43]. Vitamin D deficiency, less than 50 nmol/L of 25-hydroxy vitamin D (25(OH)D) is increasingly being recognized as a global public health issue [44]. According to published studies, the activities and functions of important vitamins and minerals including vitamin B9 and vitamins D, C and E are impaired by chronic ethanol consumption [15][45]. In effect, chronic alcohol consumption has been demonstrated to lower vitamin D levels (inactive vitamin D (25(OH)D3) and active vitamin D (1,25(OH)2D3) as well as cathelicidin/LL-37 expression [46].

Immune system deficiency, muscle weakness, osteopenia, osteoporosis, severe upper respiratory tract infections, community-acquired pneumonia, and acute respiratory distress syndrome have all been associated with vitamin D deficiency [47][48][49][50][51]. Furthermore, epidemiologic data linking vitamin D insufficiency to autoimmune disorders, such as multiple sclerosis (MS), rheumatoid arthritis (RA), diabetes mellitus (DM), inflammatory bowel disease, and systemic lupus erythematosus (SLE), have been raised [52]. Vitamin D deficiency, in effect, has been found to hasten the course of existing autoimmune disorders [53]. Reduced immunological function and responsiveness can be caused by lower amounts of inactive vitamin D and active vitamin D. As a result, the frequency of community-acquired and bacterial pneumonia has increased among susceptible populations, such as those with alcoholism [54][55]. Furthermore, in a mouse model of alcoholic myopathy, low vitamin D levels were associated with muscle fiber atrophy [56] where changes in muscular antioxidant enzyme levels may play a key role in the alcoholic etiology.

5. Vitamin E

Antioxidants are necessary for avoiding free radical-induced cellular damage. Vitamin E is a lipid-soluble vitamin that is carried as a component of lipoprotein, and efficiently reduces peroxidation susceptibility both in in vivo and in vitro assays [57][58].

Vitamin E insufficiency has long been linked to ALD [59]. Vitamin E levels in the liver of alcoholics with cirrhosis are frequently low [60]. Vitamin E deficiency, according to earlier research, makes the liver more sensitive to alcohol [61].

Vitamin E has been demonstrated to have hepatoprotective characteristics in rat models, including membrane stability, reduced nuclear factor-kappa B activation, decreased TNF-α generation, and suppressed hepatic stellate cell activation [36][37][39][59].

There are three histological stages for ALD, and they could be classified into the following: (1) simple steatosis or fatty liver, (2) alcoholic hepatitis (AH), and (3) chronic hepatitis with hepatic fibrosis or cirrhosis [62]. The first-line treatment for severe AH is the administration of corticosteroids [63]. However, some patients with severe AH are refractory to corticosteroids. Nonetheless, Miyashima et al. [64] have reported that vitamin E, as a supplement to corticosteroids therapy, may be a new therapeutic option for these patients.

By raising ROS and lowering endogenous antioxidant levels, alcohol promotes oxidative stress [65]. In this sense, Prakash et al. [66] have demonstrated that prognostic factors, including the Child−Pugh score and the Model for End-Stage Liver Disease (MELD) score, increased significantly, demonstrating that vitamin E treatment improves short-term mortality more than long-term mortality. In addition, Kaur et al. [67] examined vitamin E supplementation in ethanol-treated mice and found that it restored redox state, decreased apoptosis, and lowered oxidative stress markers. However, as compared to the placebo, 1000 IU of vitamin E per day improved serum hyaluronic acid but had no favorable impact on liver function tests or mortality in individuals with mild to severe alcoholic hepatitis [68].

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