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ORIGINAL ARTICLE

Hepatocytes Protection by Vitamin E in Alcoholic Liver Injury: A Light Microscopic Study

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ABSTRACT

Background: Alcohol induces histomorphological changes in the liver and vitamin E has a protective role against these changes.

Objective: To observe changes in hepatocytes of rabbits exposed to intragastric administration of alcohol and the protective role of vitamin E against these changes.

Study Design: Analytical experimental study

Place and Duration of Study: Department of Anatomy, Pathology and Pharmacology of Peshawar Medical College, Peshawar, Pakistan from 1st January 2016 to 30th June 2016.

Methodology: Eighteen male rabbits domestic type (Oryctolaguscuniculus) were included. Experimental duration for category E8 animals was 8 weeks while for category E4 animals it was 4 weeks. The groups were, control group A in which animals were given proper food and normal saline as drinking water, experimental group B in which animals were fed on proper diet and 30% ethanol solution (30 ml/kg/day) orally daily with normal saline and experimental group C in which animals were treated with proper diet, 30% ethanol solution (30 ml/kg/day), vitamin E (50 mg/kg/day) orally daily and normal saline as drinking water.

Results: The difference in the ALT, hepatocyte count and size and hepatocyte nuclear count and size of control and experimental groups and experimental group B-II and C-II from both category E4 and E8 showed a highly significant P values.

Conclusion: Alcohol causes histomorphological changes in the liver even in the short period of 4-8 weeks and these changes can be minimized by the antioxidant action of vitamin E.

Keywords: Alcohol, Liver, Histomorphology, Vitamin E, Hepatocyte, ALT

INTRODUCTION

Metabolism of alcohol produces toxic metabolites in the body which produce oxidative stress and injury in different body tissues. The liver is greatly affected by an intake of alcohol. Alcoholic fatty liver (steatosis), alcoholic hepatitis, and alcoholic cirrhosis are some of the morphological characteristics.[1]

As an antioxidant, vitamin E acts as a peroxyl radical scavenger, preventing the action of free radicals in tissues. Besides antioxidant activity, vitamin E decreases the production of tumor necrosis factor (TNF) in alcoholic hepatitis and prevents hepatic stellate cell (HSC) activation in chronic hepatitis C.[2, 3] Morphological changes both gross and microscopic in the liver due to alcohol toxicity can be minimized by the anti-oxidant effect of oral administration of vitamin E $_1$. Different molecules are formed from the metabolism of alcohol in different body tissues.[4]

Alcohol also promotes the activity of an enzyme called cytochrome P450s, which is also an important factor for the increase in ROS production.[4] Stimulation of cytochrome P4502E1 (CYP2E1) activity by ethanol is one basic pathway for inducing alcoholic injury in body tissues by reactive oxygen species which build oxidative stress in cells.[5] Another mechanism by which alcohol initiates damage in body tissues is the enhancement of the production of endotoxins by gut bacteria.[6] Ethanol promotes the entry of endotoxins produced by the gut microflora by increasing the gut permeability. These endotoxins activate Kupffer cells in the liver to stimulate nitric oxide, superoxide, and cytokines such as tumor necrosis factor-α (TNF-α), and this finally leading to liver damage.[7]

The most important enzymes that are involved in the metabolism of ethanol in the body are aldehyde dehydrogenase (ALDH), alcohol dehydrogenase (ADH), cytochrome P450 (CYP2E1), and catalase.[8] Alcohol dehydrogenase (present in the fluid of the cell i.e. cytosol), an enzyme with many distinct forms, is involved in the main route of oxidative metabolism of ethanol in the liver. When ethanol is broken down by ADH, acetaldehyde is produced a highly reactive and toxic by product that may lead to tissue damage and addiction.[9] Tocopherols (alpha, beta, gamma, and delta) and tocotrienols (chemically similar to tocopherols) are the two sets of four distinct molecules that make up vitamin E (alpha, beta, gamma, and delta). Even though all of these may be absorbed, only alpha-tocopherol has vitamin E action in the human body. Other tocopherols cannot be converted to alpha-tocopherol and do not have the same metabolic activities in the body.[10,11]

MATERIALS AND METHODS

This analytical experimental study was conducted at Department of Anatomy, Pathology and Pharmacology of Peshawar Medical College, Peshawar, Pakistan from from 1st January 2016 to 30th June 2016. A total of 18 healthy adult male domestic rabbits, average 1-year-old and weighing 1-1.5 kg were selected. Female rabbits were excluded due to breeding issues because female rabbits are induced ovulators.[12] Too young (less than 6 months of age) and old (more than 2 years of age) rabbits were not

selected. These animals were kept under standard controlled conditions in specially designed iron cages with natural soil base and standardized laboratory feed and water were provided. They were divided into 3 main groups.

Control group "A" comprised of 6 rabbits, fed on a standard diet and normal saline. Permanent green color labels were used for numbering these rabbits for identification. This group was further divided into 2 subgroups based on experimental duration.

Subgroup A-I **c**omprised of 3 rabbits, fed on a standard diet and normal saline as drinking water for complete 8 weeks.

Subgroup A-II **c**omprised of 3 rabbits, fed on proper diet and normal saline as drinking water for complete 4 weeks.

Experimental Group "B" comprised of 6 rabbits, fed on a standard diet, 30% ethanol solution (30ml/kg/day) orally daily[13,14] and normal saline. Permanent red color labels were used for numbering these rabbits for identification. This group was further divided into 2 subgroups based on experimental duration.

Subgroup B-I **c**omprised of 3 rabbits, fed on the standard diet. They were treated with 30% ethanol solution (30 ml/kg/day) orally daily[13,14] and normal saline as drinking water for complete 8 weeks.

Subgroup B-II comprised of 3 rabbits, fed on the standard diet. They were treated with 30% ethanol solution (30ml/kg/day) orally daily[13,14] and normal saline as drinking water for complete 4 weeks.

Experimental Group "C": This group comprised of 6 rabbits, fed on a standard diet, 30% ethanol solution (30ml/kg/day), vitamin E (50mg/kg/day) orally daily[13-15,] and normal saline. Permanent blue color labels were used for numbering these rabbits for identification. This group was further divided into 2 subgroups based on experimental duration.

Subgroup C-I comprised of 3 rabbits, fed on a standard diet. They were treated with 30% ethanol solution (30ml/kg/day), vitamin E (50mg/kg/day) orally daily[13-14,] and normal saline as drinking water for complete 8 weeks.

Subgroup C-II comprised of 3 rabbits, fed on the standard diet. They were treated with 30% ethanol solution (30ml/kg/day), vitamin E (50mg/kg/day mixed with 2ml distilled water) orally daily[13-14,] and normal saline as drinking water for complete 4 weeks.

Based on experimental duration, the above-mentioned subgroups were divided into two main categories.

Category E4 animals: Animals whose experimental duration was 4 weeks were placed in this category which included control subgroup A-II, experimental subgroup B-II, and experimental subgroup C-II.

Category E8 animals: Animals whose experimental duration was 8 weeks were placed in this category which included control subgroup A-I, experimental subgroup B-I, and experimental subgroup C-I.

Pure (99.9% manufactured by BDH laboratories England) ethanol was purchased from an authorized chemical dealer in Peshawar, Pakistan, and then its 30% solution was prepared in distilled water according to the need. Vitamin E in powder form was purchased from Abbott Pharmaceuticals Karachi, Pakistan.

Rabbits in the experimental groups were treated with alcohol and vitamin E given through a pediatric orogastric tube daily. The presence of the stomach tube was detected every time by auscultating gurgling sound through a stethoscope in the stomach by pushing air in it and by aspirating gastric content before introducing alcohol or vitamin E into the stomach. Powder vitamin E 50mg was mixed with 2ml distilled water and this dose was given daily to each rabbit in the experimental group "**C**" through the same gastric tube.

Each group of rabbits was kept separately in a separate iron cage with a natural soil base. The dimension of each cage was 6 x 8 feet. Rabbits were provided with normal saline as drinking water through inverted bottles fixed in cages. Each bottle's capacity was up to 500 ml of water. Bottles were filled daily and cleaning of cages and bottles was carried out on regular basis. Food was provided 24 hours to rabbits because rabbits are constant eaters and they eat 30-35 times in 24 hours. The provided food contained a mixture of different fresh fruits and vegetables. Along with fruits and vegetables, dry bread made up of whole grain, dry milk, and sugar was also provided on daily basis.

The behavior and activity of all rabbits were regularly monitored before and after the administration of alcohol. All animals were weighed on the day of the beginning of the experiment and these weights were noted as pre-treatment body weights. They were then weighed on the last day of the experiment before they were sacrificed and these weights were noted as post-treatment body weights.

Blood samples were collected from each rabbit for biochemical analysis (ALT) for co-relating biochemical alterations if any with morphological changes caused by alcohol toxicity. Rabbits were given Ketarol (ketamine HCL) 1 ml/ IM/kg body weight[16], a general anesthetic for anesthetizing rabbits before slaughtering. After anesthesia, superficial neck dissection was done to expose the external jugular vein and blood samples were collected from the external jugular vein. Blood samples were collected in proper heparinized tubes and were sent immediately to the laboratory for biochemical analysis. Abdominal viscera were identified; the whole liver was removed carefully.[17] The liver was examined grossly for color and any gross lesions, weight, and size of each specimen were noted carefully.

End of experiment: Category E4 animals which included subgroup "A-II" of the control group, subgroups "B-II" and "C-II" of experimental groups were slaughtered after complete 4 weeks to observe any morphological changes in the liver due to alcohol toxicity and the protective role of vitamin E in protecting it from alcohol toxicity. Category E8 animals in subgroup "A-I" of the control group, subgroups "B-I" and "C-I" of experimental groups were slaughtered after complete 8 weeks to observe any morphological changes in the liver due to alcohol toxicity and the protective role of vitamin E in protecting it from alcohol toxicity.

Tissue processing: Specimens were fixed in 10% neutral buffered formalin for 24 hours. After 24 hours the fixative was changed and specimens were shifted to freshly

prepared 10% neutral buffered formalin. Separate containers were used for specimens of individual rabbits and these containers were labeled accordingly. Enough amount of fixative i.e., almost 5 times the bulk of specimens was put in containers to ensure proper preservation. Each container was having a capacity of 500 ml. liver was cut into small parts for better penetration of the fixative. Fixed tissues were kept at room temperature till the processing of these issues. Tissues were processed and then carefully embedded for sectioning.

The Leichardt's molds (L-shaped pieces of metal resting on a flat metal surface/plate) were used for making paraffin blocks to embed tissues. Selected tissues were cut in proper size before processing according to the size of cassettes of the processing machine.

When blocks were prepared, they were refrigerated for 1 hour before sectioning. 5 µm thin tissue section ribbons were made by microtome (American Optical rotary microtome, model # 820/ Serial # 67026- the USA) and then allowed to float on a water bath at 40-50^{0}C. After wrinkles were smoothed out, sections were picked on clean glass slides. 6 slides of each specimen were prepared in a serial order. Slides were kept in an incubator at 37^0 C overnight and then transferred to slide boxes for storage till staining.

Staining was done by the following methods: Hematoxylin and Eosin for routine microscopy, Masson's Trichrome for demonstration of collagen fibers, and Periodic Acid Schiff (PAS) to demonstrate the intracellular glycogen in hepatocytes. After staining, sections were mounted with DPX solution and carefully covered with glass coverslips for better handling, storage, and protection of the sections.

For microscopy, three slides of liver per rabbit were made in each group and each slide was examined under five fields. Following observations were made in liver sections under the light microscope. Morphology of hepatocytes included: 1) number of cells/ high power field, 2) number of nuclei/cell, 3) size of cells, and 4) size of nuclei. Statistical analysis was performed using the SPSS-25. One way ANOVA test was applied to observe an association between continuous variables, P-value of <0.05 was considered as statistically significant.

RESULTS

The mean ALT of control group A-II was 45.00±7.93 IU/L, experimental group B-II was 112.33±5.50 IU/L and experimental group C-II was 93.00±5.56 IU/L. The difference in the ALT of control and experimental groups showed a highly significant value (P=0.000). Similarly, the difference in the ALT of experimental group B-II and C-II showed significant value (P=0.013) in E4 animals category. In E8 animals, mean ALT of control group A-I was 45.33±7.09 IU/L, experimental group B-I was 140.67±7.09 IU/L and experimental group C-I was 112.33±9.60 IU/L. The difference in the ALT of control and experimental groups showed a highly significant value (P=0.000). Similarly, the difference in the ALT of experimental group B-I and C-I showed significant value (P=0.015) [Table 1). Comparison between experimental groups B-I and B-II showed a significant difference (P=0.005) and in groups C-I and C-II also showed a significant difference (P=0.05) in ALT [Table 2].

In E4 animals, mean hepatocyte count in control group A-II was 171.40±1.63, experimental group B-II was 143.86±2.61 and experimental group C-II was 161.00±1.11. The difference in the hepatocyte count in the control and experimental groups showed a highly significant value (P=0.000). Similarly, the difference in the hepatocyte count in experimental group B-II and C-II showed a highly significant value (P=0.000). Mean hepatocyte count in control group A-I was 174.66±5.55, experimental group B-I was 107.60±3.99 and experimental group C-I was 148.46±3.05.The difference in the hepatocyte count in the control and experimental groups showed a highly significant value (P=0.000). Similarly, the difference in the hepatocyte count in experimental group B-I and C-I showed a highly significant value (P=0.000) in E8 animals (Table 3). Comparison between experimental groups B-I and B-II showed a significant difference (P=0.05) abd groups C-I and C-II also showed a significant difference (P=0.05) in hepatocyte count (Table 4).

Category E4 animals showed the mean hepatocyte nuclear count in control group A-II was 191.40±3.70, experimental group B-II was 165.26±3.05 and experimental group C-II was 175.40±0.72. The difference in the hepatocyte nuclei counts in control and experimental groups showed a highly significant value (P=0.000). Similarly, the difference in the hepatocyte nuclear count in experimental group B-II and C-II showed significant value (P=0.005). While in category E8 animals, mean hepatocyte nuclear count in control group A-I was 192.73±7.15, experimental group B-I was 117.53±8.47 and experimental group C-I was 158.26±6.43 (Table 5). The difference in the hepatocyte nuclear counts in control and experimental groups showed a highly significant value (P=0.000). Similarly, in group B-I and C-I showed a highly significant value (P=0.000) in the hepatocyte nuclear count (Table 6).

In E4 animals, mean hepatocyte size in control group A-II was 11.18±0.48 µm, experimental group B-II was 17.12±0.84 µm and experimental group C-II was 19.20±0.63 µm. The difference in the hepatocyte size in the control and experimental groups showed a highly significant (P=0.000). Similarly, the difference in the hepatocyte size in experimental group B-II and C-II showed significant value (P=0.027). Mean hepatocyte size in control group A-I was 12.81±1.58 µm, experimental group B-I was 33.20±2.88 µm and experimental group C-I was 22.64±1.38 µ. The difference in the hepatocyte size in the control and experimental groups showed a highly significant value (P=0.000), the difference in the hepatocyte size in experimental group B-I and C-I showed significant value (P=0.005) in E8 animals (Table 7). The experimental groups B-I and B-II showed a significant difference (P=0.001) in hepatocyte size and groups C-I and C-II also showed a significant difference (P=0.017) in hepatocyte size (Table 8).

Category E4 animals showed the mean hepatocyte nuclear size in control group A-II was 5.80±0.65 µm, experimental group B-II was 5.40±0.20 µm and experimental group C-II was 5.60±0.13 µm. The difference in the hepatocyte nuclei size in control and experimental groups showed no significance (P=0.512). Similarly, in

experimental group B-II and C-II showed no significance (P=0.238). In E8 animals, mean hepatocyte nuclear size in control group A-I was 5.70±0.48 µm, experimental group B-I was 3.44±0.36 µm and experimental group C-I was 4.37±0.32 µm.

Table 1: ALT of animals at the end of experiment

Category	Group	Mean±SD
E4 Animals	Control Group A-II	45.00±7.93
	Experimental Group B-II	112.33±5.50
	Experimental Group C-II	93.00±5.56
E8 Animals	Control Group A-I	45.33±7.09
	Experimental Group B-I	140.67±7.09
	Experimental Group C-I	112.33±9.60

Table 3: Hepatocytes count / HPF

Category	Group	Mean±SD
E4 Animals	Control Group A-II	171.40±1.63
	Experimental Group B-II	143.86±2.61
	Experimental Group C-II	161.00±1.11
E8 Animals	Control Group A-I	174.66±5.58
	Experimental Group B-I	107.60±3.99
	Experimental Group C-I	148.46±3.05

The difference in the hepatocyte nuclei size in control and experimental groups showed a highly significant value (P=0.001) and in experimental group B-I and C-I showed significant (P=0.030) value (Table 9). The experimental groups B-I and B-II showed a significant (P=0.001) difference in hepatocyte nuclear size while in experimental groups C-I and C-II also showed also significant (P=0.004) difference in hepatocyte nuclear size (Table 10).

Table 5: Hepatocytes nuclear count/ HPF

Category	Group	Mean±SD
E4 Animals	Control Group A-II	191.40±3.70
	Experimental Group B-II	165.26±3.05
	Experimental Group C-II	175.40±0.72
E8 Animals	Control Group A-I	192.73±7.15
	Experimental Group B-I	117.53±8.47
	Experimental Group C-I	158.26±6.43

Table 7: Size of hepatocytes / HPF

Category	Group	Mean±SD
E4 Animals	Control Group A-II	11.18±0348
	Experimental Group B-II	17.12±0.84
	Experimental Group C-II	19.20±0.63
E8 Animals	Control Group A-I	12.81±1.58
	Experimental Group B-I	33.20±2.88
	Experimental Group C-I	22.64±1.38

Table 9: Hepatocyte nuclear size / HPF

Category	Group	Mean±SD
E4 Animals	Control Group A-II	5.80±0.65
	Experimental Group B-II	5.40±0.20
	Experimental Group C-II	5.60±0.13
E8 Animals	Control Group A-I	5.70±0.48
	Experimental Group B-I	3.44±0.36
	Experimental Group C-I	4.37±0.32

Table 2: ALT of control and experimental animals at the end of experiment (One way ANOVA test)

Category	Groups	Sum of Squares	Df	Mean Square	F	Sig.
E4 animals	Between	7211.556	2	3605.778	87.003	.000
	Within	248.667	6	41.444		
	Total	7460.222	8			
E8 animals	Between	14380.222	2	7190.111	111.763	.000
	Within	386.000	6	64.333		
	Total	14766.222	8			

Table 4: Hepatocyte count of control and experimental groups (One way ANOVA test)

Category	Groups	Sum of Squares	Df	Mean Square	F	Sig.
E4 animals	Between	1159.796	2	579.898	162.083	.000
	Within	21.467	6	3.578		
	Total	1181.262	8			
E8 animals	Between	6854.462	2	3427.231	182.992	.000
	Within	112.373	6	18.729		
	Total	6966.836	8			

Table 6: Hepatocytes nuclear count of control and experimental groups (One way ANOVA test)

Category	Groups	Sum of Squares	Df	Mean Square	F	Sig.
E4 animals	Between	1041.636	2	520.818	66.281	.000
	Within	47.147	6	7.858		
	Total	1088.782	8			
E8 animals	Between	8502.196	2	4251.098	77.537	.000
	Within	328.960	6	54.827		
	Total	8831.156	8			

Table 8: Size of hepatocytes in control and experimental groups (One way ANOVA test)

Category	Groups	Sum of Squares	Df	Mean Square	F	Sig.
E4 animals	Between	103.744	2	51.872	115.465	.000
	Within	2.695	6	.449		
	Total	106.440	8			
E8 animals	Between	623.693	2	311.847	73.435	.000
	Within	25.479	6	4.247		
	Total	649.173	8			

Table 10: Hepatocyte nuclear size in control and experimental groups (One way ANOVA test)

Category	Groups	Sum of Squares	Df	Mean Square	F	Sig.
E4 animals	Between	.248	2	.124	.750	.000
	Within	.992	6	.165		
	Total	1.240	8			
E8 animals	Between	7.736	2	3.868	24.326	.000
	Within	.954	6	.159		
	Total	8.690	8			

DISCUSSION

The liver is an important organ that is greatly by alcohol abuse. The rabbits in experimental groups became violent and so aggressive that they started fighting with each other and stronger ones always tried to dominate the weaker. In this violence, some rabbits were badly injured by others. The behavioral changes in the present study are similar to the findings by Stevenson et al[18] who reported similar changes in the motor activity and social behavior in mice after 8 weeks of alcohol administration.

There was an almost equal increase in body weights of all rabbits in both categories. Our findings of the effect of alcohol on body weight were found consistent with the study conducted by Tsukamoto et al[19] which showed no significant difference in body weights of control and experimental group animals after alcohol administration to mice for sixteen weeks. The current study demonstrated that alcohol usage for a short duration does not cause an increase in body weight. Devgun and Dunbar[20] also found that alcohol does not because weight gain even for long use i.e., for 5 years. This study does not support the results of a study conducted by Wannamethee and Shaper[21] who reported that regular alcohol intake for more than 5 years in humans causes significant body weight gain.

The results of our study showed no statistically significant difference in the liver weights of control and experimental groups in category E4 animals, but there was a statistically significant difference in the liver weights of control and both experimental group in category E8 animals. In category E8 animals, there was an increase in weight of livers in experimental group B and C, but an increase in mean liver weights of group C-I was found less as compared to group B-I, which signify the effectiveness of vitamin E in minimizing alcohol-induced increase in liver weight. These findings corroborated the results of Tsukamoto et al[19] who also found an increase in liver weight, after alcohol administration to mice for sixteen weeks but they didn't use vitamin E to counter this liver weight gain due to alcohol. The present study reported that in both category E4 and E8 animals, there was a significant increase in serum ALT in the experimental groups while in control groups it was in a normal range. When comparison was done between experimental group B and C, there was less increase in ALT in experimental group C (treated with alcohol and vitamin E) as compared to experimental group B (treated only with alcohol) which meant that vitamin E has a potential role in lowering ALT, indicating the effectiveness of vitamin E in minimizing alcohol produced liver injury. These results substantiated the study conducted by Nyblom et al[22] who reported an increase in ALT of alcoholic individuals. However, our study did not align with the study conducted by Mezey et al[23] who reported no effect of vitamin E in lowering ALT in alcoholic liver disease which they attributed to the poor antioxidant activity of vitamin E against the toxic alcohol metabolites. Vitamin E treatment improves serum aminotransferase levels, and lowering ALT readings into the normal range is generally linked with histological improvement in disease activity, according to the findings (steatosis, inflammation, cell injury).[24] Khastar[25] conducted a study to see how vitamin E affects liver damage following renal ischemia-reperfusion. The ischemia reperfusion-induced rise in plasma AST and ALT was reduced when vitamin E was consumed in mice. These data revealed that vitamin E supplementation reduced IR-induced liver damage to some extent. To observe parenchymal changes in the liver, we studied different parameters including hepatocyte size, hepatocyte nuclear size, hepatocyte count, and hepatocyte nuclear counts. All these parameters showed statistically highly significant differences among all 3 groups in both category E4 and E8 animals. Mean hepatocyte size was maximum in experimental group B (treated only with alcohol) denoting ballooning of hepatocytes which is a key feature of alcoholic hepatocyte injury. Hepatocyte count and hepatocyte nuclear count in hepatocytes were at the lowest mark in experimental group B in contrast with experimental group C in both categories. This explains the worthiness of Vitamin E in preventing or minimizing alcohol-induced histomorphological changes in the liver parenchyma. A study conducted by Gao and Bataller[26] on humans showed similar changes who demonstrated ballooning of hepatocyte and necrotic nuclei in hepatocytes due to alcohol abuse. Ballooning of hepatocytes is an enlargement of hepatocytes and decreased hepatocyte nuclear size noted in our study is because of the nuclear degeneration.

Previously, von Herbay et al[27] had conducted a high-performance liquid chromatography and electrochemical detection to measure the RRR alpha-tocopherol (vitamin E) concentration in plasma from 46 patients with liver disorders and 23 healthy controls. Acute or chronic ethanol intoxication with high bilirubin levels resulted in a 37% decreased lipid-standardized vitamin E level in the group with alcoholic liver disorders compared to controls. Hemochromatosis patients with hemochromatosis exhibited a 34% poorer vitamin E/lipid ratio than healthy controls. In the remaining patients with hemochromatosis, there was no significant reduction in the vitamin E/lipid ratio. Only individuals with Wilson's disease and high free serum copper showed a substantial reduction in the vitamin E/lipid ratio. The findings suggested that free radicals have a role in the development of active liver disorders.[23] However, Mezey et al[23] found that vitamin E did not result in significantly lower blood aminotransferases and serum bilirubin levels, nor did it result in significantly higher serum albumin levels. In terms of hepatic fibrogenesis indicators, vitamin E therapy reduced serum hyaluronic acid, but

neither group's serum aminoterminal peptide of type III procollagen changed. Treatment with vitamin E raises blood hyaluronic acid levels but does not affect liver function tests in patients with mild to severe alcoholic hepatitis.

Serum selenium and vitamin E levels were found to be significantly depressed in the alcoholic study groups, with serum selenium levels being even lower in those with established liver disease. Serum selenium levels were shown to be strongly associated with low nutritional status. Subjects with combined vitamin E and selenium insufficiency had significantly higher levels of liver disease activity as measured by transaminase (AST) than those with normal levels or isolated deficits. In individuals with combined deficiency, serum lipid peroxides were higher, and the levels were strongly associated with serum transaminases.[28] There is plenty of evidence that lipid peroxidation caused by free radicals plays a role in the etiology of different illnesses, that vitamin E is a powerful radical-scavenging antioxidant, and that vitamin E prevents lipid peroxidation both in vivo and in vitro. These findings imply that vitamin E may lower the risk of illnesses caused by free radicals, or may be beneficial in the prevention and treatment of such disorders.[29]

CONCLUSION

The use of Vitamin E in these animals has shown considerable recovery in alcohol-induced liver dysfunction. The alcohol intake in high doses has a great impact on the liver and causes alterations in the normal morphology of the liver by its toxic metabolites. These changes in liver morphology due to alcohol abuse range from reversible steatosis (fatty change) to irreversible fibrosis of liver parenchyma (cirrhosis) even in a short duration of 8 weeks. This can lead to the failure of this vital organ that may be fatal. The extent of alterations and damage in the liver by alcohol toxicity can be minimized by regular administration of a recommended dose of Vitamin E which acts as an antioxidant and reduces the injury caused by free radicals liberated from alcohol metabolism.

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