

Plasma Fibronectin Levels After Chronic Ethanol Consumption: The Effect of Betaine

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Background: In this study, plasma fibronectin levels (PF) after long-term ethanol consumption were measured. The preventive effect of betaine, which is precursor of S-Adenosymethionine, were also examined.

Methods: 24 rats were divided into three groups. Control group (n=8), ethanol group (8 g/kg/day;n=8), ethanol+betaine group (0.5 % w/v;n=8). Rats were killed after 60 days and fibronectin and alanine aminotransferase (ALT) were measured in the blood samples of the rats.

Results: Plasma fibronectin levels in the ethanol (314±2 µg/ml) and ethanol+betaine group (266±2 µg/ml) were significantly higher than in the control group (146±1 µg/ml) (p<0.001;respectively). PF levels were significantly low in the betaine-given group as compared to the ethanol group (p<0.001). ALT, which is an indicator of hepatic injury, in the ethanol group were higher than in the control group (p<0.05).

Conclusion: In conclusions, PF, which have an important cellular functions, elevated with ethanol. This elevation may show ethanol-mediated hepatic tissue damage. Betaine may be effective on the liver injury after chronic ethanol consumption. Ann Med Sci 2001;10:163-165

Key words: fibronectin, ethanol, betaine

Ethanol produces toxic injury in all tissues especially liver. The liver is predominantly responsible for ethanol metabolism¹.

Fibronectin is a large glycoprotein composed of two identical or nearly identical subunits of molecular weight Mr=220.000². Plasma fibronectin (PF) is produced in vascular endothelia³. This glycoprotein is found in tissues in insoluble form and on the surface of many cells^{2,4}. PF has a role in erythrocyte and platelet adhesion to subendothelial collagen⁵, and it reduces erythrocyte deformability^{6,7}. Cell surface PF regulates intercellular effectiveness and cell adhesion to membranes. Therefore, it plays a role in microvascular structure, vascular permeability and wound healing⁶. Hepatocytes are the major source of plasma fibronectin⁸.

Betaine is the precursor of SAdenosylmethion-

ine (SAME), which is a methyl donor. Ethanol reduces SAME biosynthesis in the transmethylation pathway in liver. It has been shown that Betaine administration has the capacity to elevate hepatic SAME and to prevent the ethanol-induced fatty liver⁹.

In our study, we determined plasma fibronectin levels in the ethanol-treated rats. We also examined the effect of betaine.

Materials and Methods

Twenty four male Sprague-Dawley (150-250 body wt) rats were fed liquid diet. The pair-fed control group received an isocaloric mixture with maltose dextrin substituted for ethanol. Animal consumed approximately 60 ml diet per day during 60 days. Ethanol-given rats consumed 8 g/kg/day ethanol. Betaine was administered to the animals by dissolving it in the liquid diet at 0.5 % w/v in the ethanol plus betaine group. Rats

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were obtained from our animal research laboratory (Eskişehir-TURKEY). The research protocol was reviewed and approved by the animal care committee in our institute.

Rats were individually housed in suspended stainless steel cages in a room temperature maintained at 21 ± 1 °C. All chemicals were obtained from Sigma Chemical Co. (St. Louis, MO, USA).

All animals were fed for two months and were killed in a nonfasting state. Blood samples were obtained by intracardiac puncture. Whole blood was taken into tubes with EDTA. Samples were centrifuged at 1500 g for 5 minutes and the plasma samples were separated. Plasma Fibronectin levels were determined by an immunoturbidometric method using a kits Boehringer Mannheim (Cat No-401218, Germany). Serum ALT activities were determined using a BM Hitachi 742 autoanalyzer.

All data expressed as means $\pm$ S.E.M. The data were analyzed by one-way analysis of variance and Tukey- α test together.

Results

Plasma fibronectin levels in the control, ethanol and ethanol+betaine groups are shown in Table 1.

Plasma fibronectin levels in the ethanol (314 ± 2 µg/ml) and ethanol+betaine group (266 ± 2 µg/ml) were significantly higher than the control group (146 ± 1 µg/ml) ($p < 0.001$; respectively).

Serum ALT levels are shown in Table 1. Serum ALT levels in the ethanol given group (92 ± 4 U/L) were significantly higher than control group (74 ± 4 U/L) ($p < 0.05$).

Table 1. Plasma fibronectin levels in the control, ethanol and ethanol plus betaine given groups. (means $\pm$ SEM)

	Plasma Fibronectin (µg/ml)	Serum ALT levels (U/L)
Control group (n=8)	146.5 ± 0.5	74.5 ± 4.11
Ethanol group (n=8)	313.6 ± 2.4^a	91.9 ± 4.4^d
Ethanol+betaine group (n=8)	$266.2 \pm 2.0^{b,c}$	84.9 ± 5.6

a: $p < 0.001$ control vs. ethanol group

b: $p < 0.001$ ethanol vs. ethanol+betaine group

c: $p < 0.001$ control vs. ethanol+betaine group

d: $p < 0.05$ control vs. ethanol group

Discussion

Fibronectins are an important class of extracellular matrix. They have multiple functions, such as cellular adhesion, cellular morphology and

spreading, cytoskeletal organisation¹⁰.

PF levels change in various pathophysiological situations such as starvation, surgical operations, trauma, burns and liver insufficiency, dermatological diseases, autoimmune diseases and some kinds of cancer⁵.

Hepatocytes are the main contributors of plasma fibronectin. Therefore, alterations in liver function, such as those observed in acute and chronic liver diseases, may be accompanied by alterations in plasma fibronectin levels¹⁰.

In our study, PF levels were increased in the ethanol-treated group as compared to the control group ($p < 0.001$). PF levels in the betaine-given group were significantly lower than ethanol group ($p < 0.001$). Matsuda et al¹¹ reported decreased plasma fibronectin only for the decompensated stage of liver cirrhosis (presence of ascites), whereas elevated levels were found with acute hepatitis, fatty liver, all types of chronic hepatitis, and liver cirrhosis. Grieco et al¹² have indicated that plasma PF appears to be an index of hepatic parenchymal function. Tamkun et al⁸ have reported that fibronectin synthesized in hepatocytes and secreted into plasma. In our study, elevated PF levels after chronic ethanol consumption may be due to over secretion from hepatocytes to liver. This elevated levels of PF may show ethanol-induced hepatic injury. Because, in our study, serum ALT levels were high in ethanol-given group. Betaine prevents this over secretion.

In conclusions, our findings show that chronic ethanol consumption elevates plasma PF levels. This elevation thinks ethanol-mediated hepatic injury. Betaine have an important role on the elevated PF levels after ethanol administration.

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