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Effect of Chronic High Dose-Alcohol Consumption on the General Biochemical Parameters

[Kronik Yüksek Doz-Alkol Tüketiminin Genel Biyokimyasal Parametrelere Etkisi]

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ABSTRACT

Objectives: A chronic intake of high dose alcohol may cause oxidative stress, metabolic abnormalities and nutritional deficiencies in the body. The effect of long-term alcohol consumption on the biochemical parameters has not been explained well.

Materials and Methods: Female and male rats were maintained for 90 days as follow: I. Control (n=7), II. Alcohol-treated (2.5 gr of 50% ethanol/kg body wt administered intragastrically every other day; human equivalent is ~750 gr alcohol for 60 kg) group (n=6). At the end of treatment period; chemical, electrolyte, lipid, iron and enzymatic test analyses were measured by automated analyzer with Roche diagnostic kits in the rat serum or plasma.

Results: Albumin and iron levels were decreased in the alcohol-treated female rats as compared to the control female rats, but total iron binding capacity and sodium levels were increased in the alcohol-treated group. Lactate, sodium, total and pancreatic amylase, γ-glutamyl transferase, glucose and total cholesterol levels were elevated in the alcohol-treated male rats as compared to the control rats. Mean alcohol level was raised by 40% in the female and 26.6% in the male alcohol-treated rats compared to control rats, but there was no statistically significant difference between groups.

Conclusions: Some chemical parameters and a group of test values due to ethanol toxicity in both sexes fed chronically with high dose of alcohol may alter in the pathogenesis of alcoholism.

Key words: Chronic alcohol drinking; Toxicity; Biochemistry; Clinical chemistry tests

ÖZET

Amaç: Kronik yüksek doz alkol alımı vücutta oksidatif stres, metabolik anormallikler ve besinsel eksikliklere sebep olabilir. Uzun dönem alkol içilmesinde, biyokimyasal parametrelere alkol tüketiminin etkisi yeterince açıklanmamıştır.

Gereç ve Yöntem: Dişi ve erkek ratlar; I. Kontrol (n=7), II. Alkol (2.5 g/k %50 etanol bir gün ara ile intragastrik verildi; insanlardaki karşılığı 60 kg için ~750 g) alan grup (n=6) olarak 90 günlük periyod dahilinde bakıldı. Bu periyodik süre sonunda; rat serum veya plazmasında kimyasal, elektrolit, lipid, demir ve enzimatik test analizleri Roche kitlerin kullanıldığı otomatik analizör ile yapıldı (toplam 30 biyokimyasal parametre).

Bulgular: Albumin ve demir düzeyleri kontrol dişi ratlara kıyasla alkol alan dişi ratlarda azaldı, fakat total demir bağlama kapasitesi ve sodyum düzeyleri alkol verilen grupta arttı. Laktat, sodyum, total ve pankreatik amilaz, γ-glutamil transferaz, glukoz ve total kolesterol düzeyleri kontrol grubuna kıyasla alkol alan erkek ratlarda yüksek bulundu. Ortalama alkol düzeyi kontrol ratlara kıyasla dişi ratlarda %40, erkek ratlarda ise %26.6 yükselmiş bulundu. Ancak gruplar arasında anlamlı istatistiksel bir fark yoktu.

Sonuçlar: Alkolizm patogenezinde her iki eşeyde kronik yüksek doz etanol alımına bağlı toksisite etkisiyle bazı kimyasal parametreler ve bir grup test düzeyleri değişebilir.

Anahtar kelimeler: Kronik alkol içimi; Toksisite; Biyokimya; Klinik kimya testleri

Introduction

Alcohol is generally accepted to be a toxic compound on cells or tissues, and it is readily metabolized by alcohol dehydrogenase (ADH) to acetaldehyde (AcD), and then this primary metabolite is catabolized to CO_2 and H_2O. AcD has a cytotoxic effect within the cells or tissues and also remains capable of reacting covalently with nucleophiles including nucleic acids, proteins, peptides, amino acids, lipids, and carbohydrates in the same analogous to formaldehyde. It is much more toxic than alcohol especially in high chronic alcohol consumption as well (1,2). On the other hand; there are no specific receptors in the body for alcohol, and it permeates all tissues of the body and affects most vital functions. Besides, during alcohol metabolism there is an increment in lipid peroxidation and its toxic metabolites and in protein oxidation because of free radical production, particularly in hepatocytes. Moreover, chronic alcohol ingestion induces the cytochrome P450 2E1 system which yields additional reactive oxygen radicals during alcohol metabolism (3,4,5).

Actually alcohol is a source of energy, a value (7.1 kcal/g) that exceeds the energy content of carbohydrates or proteins; but not lipids. Nevertheless, it can lead to a deficiency in regular nutrients, causing malnutrition; including deficiencies of some water and lipid-soluble vitamins, and also causes gastrointestinal complications, pancreatic insufficiency, and impaired hepatic metabolism of nutrients. ADH-mediated oxidation of alcohol increases the ratio of NADH to NAD^+ ratio but depleting the level of reduced glutathione in the cytosol (6). As expressed in many literatures, in the oxidation of alcohol generates an excess of NADH, which is altering redox state in the cytosol, in turn, is responsible for a variety of metabolic abnormalities such as hyperlactacidemia, hyperuricemia, the activity of the citric acid cycle is depressed, enhanced hepatic lipogenesis, decreased hepatic release of lipoproteins, lipolysis of peripheral fat, altered mitochondrial oxidative metabolism, changes in mitochondrial structure and function, protein breakdown, depending on the condition hypo/hyperglycemia, the block of hepatic gluconeogenesis by ethanol (4-9).

As mentioned above, it is thought that production of excess AcD, NADH, reactive oxygen species, lipid peroxidation and protein oxidation by alcohol metabolism may lead to metabolic chaos within the cell or tissue biochemistry in the chronic alcoholism. Toxic compounds (adducts of proteins, lipid peroxides, AcD, free radicals), which have damaging effects on cellular biomolecules, are well documented and their consequences have been implicated in the etiology of a number of human disorders (9-14).

In the light of current knowledge regarding alcoholism biochemistry, it is suggested that blood chemical test levels could be changed after acute or chronic alcohol intake. Indeed some biochemical tests like γ-glutamyl transferase (GGT), alanine transaminase, aspartate transaminase, etc. were used as a laboratory test in the evaluation of clinic alcoholism pathogenesis (18,40,42). The aim of the present study was to examine changes in certain clinical chemistry test values and to evaluate biochemical changes in the blood of female and male rats fed chronically with alcohol.

Materials and methods

Animals

A group of adult male and female Wistar rats (age of 6-7 months; Ondokuz Mayıs University Experimental Research Centre, Samsun/Turkiye) weighing 180-200 g were used in the study. The rats were housed one per cage with wood chip bedding and given standard laboratory chow. They were maintained on a 12 h light: dark cycle with a constant room temperature at 24 ± 1°C. The Animal Care and Utilisation Committee approved the procedures used in this study.

Animal treatment

After one week of acclimation, the rats were ramdomly divided into two groups of female and male animals in each (1) the control group, which received isotonic sodium chloride (isc); (2) the alcohol-treated group, which was given 2.5 gr of 50% ethanol/kg body wt every other day. Ethanol and isc were administered intragastrically and sensitively via mounth with a special injector. The animals were also fed with a standard laboratory diet, and treatments were provided for 90 days.

Biochemical analysis

The rats were fasted overnight, the next day morning blood was collected into suitable test tubes by heart puncture with injector under light ether anesthesia (inhaled 4000 ppm/h). Blood test tubes, were centrifuged at 2000*g* for 10 min at room temparature after the blood was drawn, and plasma or serum separated. Alcohol and lactate concentration in the rat plasma were determined by automated analyzer (COBAS Integra 800) and Roche diagnostic kits. Sodium, potassium and chloride values in serum were measured by ISE (ion-selective electrodes) method. Other biochemical tests in the rat serum were analysed by automated analyzer (Roche/Hitachi Modular Analytics) and Roche diagnostic kits at the Central Laboratory of the Faculty of Medicine, the Healty Practice and Research Hospital in Samsun.

Statistical analysis

Mann-Whitney U-test was used to compare differences between the two treatment groups (control and alcohol-treated group). Mean values were given with their standard deviations (mean±SD). $P < 0.05$ was accepted as statistically significant in comparisons.

Results

Biochemical parameters in the female rats

At the end of chronic alcohol consumption over a period of 90 days, albumin (in Table I) and iron (in Table V) levels were significantly decreased in rats of given ethanol (3.1 ± 0.4 g/dl, 167.3 ± 34.8 μg/dl) compared to control group (4.0 ± 0.2 g/dl, 329.6 ± 67.4 μg/dl) ($P< 0.05$), but sodium and unsaturated iron binding capacity was increased in the alcohol-treated group (140.2 ± 1.7 mmol/L, 293.9 ± 32.6 μg/dl) compared to control group (134.4 ± 1.8 mmol/L; 206.5 ± 37.5 μg/dl) ($P< 0.05$). However, as shown in Tables there were no statistically significant difference between groups in biochemical parameters ($P> 0.05$).

Biochemical parameters of male rats

Lactate (in Table I) and total cholesterol levels (in Table IV) were significantly increased in the alcohol-treated group (68.9 ± 15.5 mg/dl, 63.7 ± 11.6 mg/dl) compared to control group (48.5 ± 14.9 mg/dl, 44.6 ± 9.4 mg/dl, respectively) ($P< 0.05$). In adddition to glucose (in Table I), sodium (in Table II), γ-glutamyl transferase, total amylase and pancreatic amylase levels (in Table III) were also significantly elevated in the alcohol-treated group (195.5 ± 22.5 mg/dl, 143.5 ± 1.9 mmol/L, 2.1 ± 0.6 U/L, 2383.8 ± 218.3 U/L, 2128.0 ± 228.8 U/L) as compared to control group (115.7 ± 17.9 mg/dl, 136.9 ± 2.9 mmol/L, 1.4 ± 0.9 U/L, 1281.7 ± 258.8 U/L, 1193.9 ± 348.3 U/L, respectively) ($P< 0.01$). As seen in Tables there were no statistically significant differences between groups when other parameters were compared ($P> 0.05$).

Meanwhile, mean plasma alcohol level was raised by 40% in the female and 26.6% in the male alcohol-treated rats compared to control rats (in Tablo I).

Discussion

The results of the present study show that many biochemical test values differ (are altered) in the serum or plasma of female and male rats at the end of the 90 days of maintenance.

Previous studies showed that excess NADH, acetaldehyde, lipid peroxides, protein damage, oxidative stress and the other toxic effects of alcohol are possible key reasons in the pathogenesis of alcohol associated injury and biochemistry in tissues (7,15,16). It is generally accepted that oxidative stress plays an important role in the pathogenesis of ethanol toxicity when consumed in excess (17, 18). Once ethanol has been absorbed, it is distributed to all tissues and fluids of the body in direct proportion to the water content. Nevertheless, alcohol is metabolized more slowly than its absorption. Because the metabolism of alcohol is slow, consumption must be controlled to prevent accumulation and intoxication in the body (19). In the present study, no statisticaly significant differences were found between the blood alcohol concentration of female and male rat groups. However, as is shown in Table I, mean plasma alcohol level was raised by 40% in the female and 26.6% in the male alcohol-treated rats compared to the control rats. The actual cause of this difference in the ethanol elimination in women and men or experimental animals has been the subject of only few studies. Gender differences in body composition, estrogen levels and ethanol metabolism might also contribute to differences in ethanol elimination rates in the chronic alcoholism. How the faster or slower alcohol elimination rates of women are related to their vulnerability to ethanol toxicity is still a mystery (41). The higher alcohol levels compared to the controls may be due to an intoxication in ethanol-treated rats by the end of 90 days. Because the toxic effects of alcohol are directly related to blood levels attained after alcohol intake (9).

As expressed in earlier studies, in alcohol metabolism NADH is produced which may be be used directly in the electron transport chain to synthesize ATP as a source of energy. This reaction has the direct effect of inhibiting the normal oxidation of fats and citric acid cycle (3,4,10), therefore large quantities of NADH resulting from heavy drinking or chronic high dose alcohol intake can lead to excess lactate production, acetylCoA or triglyceride accumulation (fatty liver). Accumulation of fat in the liver can be alleviated by secreting lipids into the blood stream. The higher lipid levels in the blood may be responsible for atherosclerosis or heart attacks (20,21). In this study; total cholesterol, triglyceride, LDL-C (low density lipoprotein cholesterol) and HDL-C (high density lipoprotein cholesterol) levels were not significantly changed in female rats, but these test levels were elevated slightly by a mean of level, except for HDL-C. However, Garban-Daranyi et al. noted that the serum concentrations of total lipids and cholesterol significantly increased in chronic alcohol-treated female rats for 50 days (23). Nevertheless total cholesterol level in male rats chronically treated with ethanol was significantly increased and LDL-C in this group was raised by a mean of 30%, although HDL-C was elevated in alcohol-treated rats by a mean of 31.7% as seen in Table IV. These findings in alcoholism pathogenesis may be important for coronary artery diseases. It is often implicated that chronic heavy intake of alcohol is associated with increases in both overall mortality and cardiovascular mortality, but light to moderate intake is consistently associated with decreased coronary heart disease (22). The resulting increase of serum cholesterol may be explained by enhanced synthesis of cholesterol or impairing of cholesterol metabolism in the body owing to alcohol-induced toxicity in liver . As the activity of GGT, which is an indicator of liver toxicity induced by alcohol, was raised significantly in ethanol-treated male rats' serum compared to the controls (Table III). Similar to other metabolic abnormalities due to the increased NADH/NAD+ ratio, large amounts of lactate is produced in chronic alcoholism (2,4). Thus, plasma lactate concentration was elevated significantly in chronic

Table I. Effects of chronic ethanol administration on the biochemical parameters in rat serum or plasma.

	Biochemical test	Control group (n=7)	Alcohol-treated group (n=6)	P
Female	Alcohol (mg/dl)	1.2 ± 0.6	2.0 ±1.1	NS
	Lactate (mg/dl)	59.3± 21.4	73.2 ± 24.3	NS
	Urea (mg/dl)	15.9 ± 8.4	23.6 ± 7.3	NS
	Total Protein (g/dl)	6.4 ± 1.1	5.6 ± 0.7	NS
	Albumin (g/dl)	4.0 ± 0.2	3.1 ± 0.4	**<0.05**
	Uric Acid (mg/dl)	1.4 ± 0.8	1.3 ± 0.4	NS
	Glucose (mg/dl)	114.8 ±13.3	143.7 ± 18.0	NS
	Creatinine (mg/dl)	0.5 ± 0.2	0.3 ± 0.1	NS
	Total Bilirubin (mg/dl)	0.05 ± 0.03	0.09 ± 0.004	NS
	Indirect Bilirubin (mg/dl)	nd	nd	-
Male	Alcohol (mg/dl)	1.1 ± 0.9	1.5 ± 0.6	NS
	Lactate (mg/dl)	48.5 ± 14.9	68.9 ± 15.5	**<0.05**
	Urea (mg/dl)	23.1 ± 6.8	26.5 ± 3.6	NS
	Total Protein (gr/dl)	6.4 ± 0.5	6.7 ± 0.4	NS
	Albumin (mg/dl)	3.5 ± 0.3	3.2 ± 0.1	NS
	Uric Acid (mg/dl)	1.2 ± 0.2	1.6 ± 0.2	NS
	Glucose (mg/dl)	115.7 ± 17.9	195.5 ± 22.5	**<0.01**
	Creatinine (mg/dl)	0.3 ± 0.01	0.4 ± 0.01	NS
	Total Bilirubin (mg/dl)	0.05 ± 0.02	0.07 ± 0.03	NS
	Indirect Bilirubin (mg/dl)	nd	nd	-

Values are mean ± S.D. NS, statistically no significant difference; nd, not determined

Table II. Effects of chronic ethanol administration on electrolytes in rat serum.

	Electrolytes	Conrol group (n=7)	Alcohol-treated group (n=6)	P
Female	Sodium (mmol/L)	134.4 ± 1.8	140.2 ± 1.7	**<0.05**
	Potassium (mmol/L)	6.0 ± 0.9	5.1 ± 0.5	NS
	Chloride (mmol/L)	101.2 ± 1.8	103.0 ± 2.2	NS
	Calcium (mg/dl)	10.4 ± 0.7	9.9 ± 0.5	NS
	Magnesium (mmol/L)	0.96 ± 0.10	0.93 ± 0.01	NS
	Phosphorus (mg/dl)	7.4 ± 1.2	5.6 ± 1.3	NS
Male	Sodium (mmol/L)	136.9 ± 2.9	143.5 ± 1.9	**<0,01**
	Potassium (mmol/L)	5.8 ± 0.7	5.3 ± 0.3	NS
	Chloride (mmol/L)	98.0 ± 7.5	104.2 ± 1.9	NS
	Calcium (mg/dl)	9.2 ± 0.9	10.1 ± 1.2	NS
	Magnesium (mmol/L)	0.90 ± 0.01	0.91 ± 0.01	NS
	Phosphorus (mg/dl)	6.5 ± 0.5	5.8 ± 2.1	NS

Values are mean ± S.D.

Table III. Effects of chronic ethanol administration on selected serum enzymes in the rat.

	Enzyme levels	Control group (n=7)	Alcohol-treated group (n=6)	P
Female	Total amylase (U/L)	1528.4 ± 192.9	1780.6 ± 247.1	NS
	Pancreatic amylase (U/L)	1388.4 ± 210.9	1553.5 ± 232.9	NS
	γ-Glutamyl transferase (U/L)	1.7 ± 1.2	1.8 ± 1.6	NS
	Alanine transaminase (U/L)	64.1 ± 23.1	67.1 ± 9.5	NS
	Aspartate transaminase (U/L)	105.1 ± 42.3	109.5 ± 40.5	NS
	Lipase (U/L)	9.3 ± 2.0	13.5 ± 1.4	NS
	Alkaline phosphatase (U/L)	548.2 ± 177.7	573.3 ± 138.9	NS
Male	Total amylase (U/L)	1281.7 ± 258.8	2383.8 ± 218.3	**<0.01**
	Pancreatic amylase (U/L)	1193.9 ± 348.3	2128.0 ± 228.8	**<0.01**
	γ-Glutamyl transferase (U/L)	1.4 ± 0.9	2.1 ± 0.6	**<0.05**
	Alanine transaminase (U/L)	60.2 ± 31.7	88.5 ± 33.3	NS
	Aspartate transaminase (U/L)	149.8 ± 75.2	132.2 ± 32.4	NS
	Lipase (U/L)	8.2 ± 2.4	9.9 ± 2.7	NS
	Alkaline phosphatase (U/L)	527.4 ± 162.1	709.8 ± 168.3	NS

Values are mean ± S.D.

Table IV. Effects of chronic ethanol administration on serum lipids in the rat.

	Serum lipid levels	Control group (n=7)	Alcohol-treated group (n=6)	P
Female	Total cholesterol (mg/dl)	54.0 ± 9.7	58.3 ± 12.2	NS
	HDL-C (mg/dl)	43.9 ± 10.7	41.6 ± 8.7	NS
	LDL-C (mg/dl)	4.8 ± 2.7	7.0 ± 2.8	NS
	Triglyceride (mg/dl)	56.8 ± 28.5	69.5 ± 22.5	NS
Male	Total cholesterol (mg/dl)	44.6 ± 9.4	63.7 ± 11.6	**<0.05**
	HDL-C (mg/dl)	29.9 ± 7.6	43.8 ± 8.4	NS
	LDL-C (mg/dl)	5.6 ± 2.7	8.0 ± 3.7	NS
	Triglyceride (mg/dl)	57.9 ± 24.1	64.0 ± 27.9	NS

Values are mean ± S.D.

Table V. Effects of chronic ethanol administration on selected iron parameters of iron metabolism in the rat.

	Iron related parameter	Control group (n=7)	Alcohol-treated group (n=6)	P
Female	Iron (μg/dl)	329.6 ± 67.4	167.3 ± 34.8	**<0.05**
	Unsaturated iron binding capacity (μg/dl)	206.5 ± 37.5	293.9 ± 32.6	**<0.05**
	Total iron binding capacity (μg/dl)	580.8 ± 64.2	461.0 ± 42.9	NS
Male	Iron (μg/dl)	189.0 ± 83.4	176.4 ± 52.6	NS
	Unsaturated iron binding capacity (μg/dl)	221.9 ± 72.2	300.4 ± 67.2	NS
	Total iron binding capacity (μg/dl)	401.1 ± 68.5	476.8 ± 49.3	NS

Values are mean ± S.D.

alcohol-treated male rats but its level was slightly increased in the plasma of female rats (Table I).

On the other hand, alcohol causes inflammation of the pancreas, stomach, and intestines which impairs the digestion of food and absorption into blood, and directly contributes to malnutrition particularly in high alcohol ingestion (3,4). Moreover, long-term heavy alcohol consumption is associated with acute and chronic pancreatitis (24). Clinically, amylase is a sensitive indicator in pancreatitis diagnosis. In the study, serum total and pancreatic amylase levels were significantly higher in male rats of alcohol-treated group but these test levels were elevated in female ethanol-fed rats by a mean of 14.1% and 11.8% compared to control group, respectively (Table III). Thus, it may be assumed that the high amylase level is a good diagnostic marker in chronic alcoholic pancreatitis, because it is still used as a marker in the clinic evaluation of pancreatitis.

Serum iron level was subsided statistically in chronic alcohol-treated female rats, despite unsaturated iron binding capacity was high with respect to control female rats as shown in Table V. Whitfield et al. have pointed out that iron stores are lower in women than men (40). If serum iron is decreased, unsaturated iron binding capacity may be elevated naturally in serum, similar to the evaluation of clinical anemia. These findings may show that serum iron status is affected by the biological effects of chronic alcohol consumption in female rats in accordance with male rats. Theoreticaly, there is a level of iron intake associated with adequate, but not large amounts of it. Iron depletion or establishing the optimal range of iron intake requires consideration of many variables, including physiologic needs and factors that enhance or inhibit absorbtion of iron from foods or alcohol consumption may lead to undernutrition (25). The amount of iron in the body is maintained by careful modulation of intestinal iron absorption. In iron deficiency, absorption is upregulated, while there is down-regulation of iron uptake when iron content is excessive. High alcohol ingestion is known to disrupt iron homeostasis and alcoholic liver disease has been reported to be associated with raised hepatic iron accumulation (26).

Pacy et al. have indicated that chronic alcoholics (> 100 g ethanol/daily for 10 years) have slightly decreased rates of all body protein synthesis and breakdown (27), likewise albumin concentration was found to be lowered by Abraham et al. in the rat plasma in the absence of hepatocellular necrosis (7). Similarly, in the current study albumin level was reduced in serum of the chronic alcohol-fed female rats with respect to control, but it was found lower in male alcohol-treated rats by a mean of 8.6% (Table I). This condition may be due to excessive albumin degradation and inhibition of synthesis in chronic alcohol ingestion in agreement with the two works above.

Other parameters, sodium and glucose, were found higher in the ethanol-fed female and male rats than in their controls (Table I and II). Electrolytes are very important for the proper functioning of cells. Alcohol-induced diuresis reduced subjects' plasma volume (22,28), as the diuretic effects of alcohol could lead to dehydration. The most likely stimulus for renin secretion is reduced plasma volume, which results from the suppression of vasopressin or gastrointestinal fluid losses, but the renin-angiotensin-aldosterone system is affected by multiple factors; however, central nervous system stimulation and electrolyte changes probably have a role as well. The role of factors such as increased cortisol and vasopressin secretion and electrolyte changes, including intracellular magnesium, calcium, potassium, chloride and sodium is unclear in chronic alcohol consumption (22).

Glucose is the main energy source for all tissues and it is derived from food intake, synthesis in the body and the breakdown of glycogen which is a form of glucose that the body stores in the liver. In addition, hormones help to maintain a constant concentration of glucose in the blood. Insulin and glucagon that are secreted by the pancreas and that ragulate blood glucose levels, and also several hormones from the adrenal glands and pituitary back up glucagon function. Insulin lowers the glucose concentration in the blood; glucagon elevates it (22). As implicated in literatures (10,29-31), acute or chronic alcohol ingestion even in well-nourished people interferes with all glucose sources and with the actions of the regulatory hormones. Acute alcohol consumption increases insulin secretion and causes temporary hypoglycemia (31), moreover in healthy subjects it has been shown that acute alcohol ingestion can impair the hormonal response to hypoglycemia (32). In contrast, the high dose chronic alcohol consumption has been associated with excessive blood glucose levels (hyperglycemia), and chronic alcohol abuse can reduce the body's responsiveness to insulin and causes glucose intolerance in both healthy individuals (33) and alcoholics with liver cirrhosis (34). In general, about 50-60% of patients with alcoholic liver disease are glucose intolerant or definitely hyperglycemic (30). Similary, in animals, chronic alcohol consumption also elevates secretion of glucagon and other hormones (35). In individuals with chronic alcoholism who have features of pseudo-cushing syndrome (36), adrenocorticotropic hormone levels might be elevated or normal. Increased serum and urinary free cortisol has been reported to raise blood glucose levels (37). Furthermore, Singh et al. and Hu et al. suggested that alcohol consumption decreases glucose transporter (Glut) gene expression (38,39). Hormones increasing blood glucose (in particularly pseudo-cushing syndrome like); decreased Glut and peripheral insulin resistance and also they may together increase the blood glucose in chronic alcohol consumption in rats.

In summary, findings of this study suggest that biochemical parameters such as lactate, glucose, sodium, total iron binding capacity, total and pancreatic amy-

lase, γ-glutamyl transferase and total cholesterol were increased in the alcohol-treated male rats. Albumin and iron levels were decreased and unsaturated iron binding capacity and sodium levels were elevated in female rats fed ethanol on a long-term basis. Therefore, it may be concluded that chronic alcohol consumption can give rise to different toxic effects in both sexes in rats and alter the normal level of many biochemical parameters in the pathogenesis of chronic alcoholism.

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