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Effect of Smoking on Cirrhosis with Heavy Alcohol Consumption

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Abstract: Term and quantity of alcohol consumption is one of the most significant factors in terms of occurrence of alcoholic liver disease. In some studies, it has been found out that due to prevalence of smoking-related morbidity, reason of death of alcoholics is more probably smoking related diseases more than alcohol-related disorders. In this study, we aimed to determine characteristics of smoking in cirrhosis with heavy alcohol consumption, its effect on mortality and risk factors. 401 cirrhotic patients with heavy alcohol consumption applying to gastroenterology clinic between the years of 2008-2018 successively were assessed retrospectively. Patients used to consume alcohol minimum 40 g/day a day and for more than 10 years. Term of alcohol abuse, type of alcohol and smoking condition were questioned for the patients. Patients with GIS malignity and diseases other than liver were not included in the study. Patients were divided into 3 groups as smoker, ex-smokers and non-smokers. Rate of smoking was found as 90.3%. Age of starting alcohol and body mass index was found as significantly lower in patients who have still smoked. Quantity of daily alcohol use in smokers was significantly higher. In multi-variate analysis, age and quantity of smoking was significantly related to the mortality. Mortality was found less in persons abusing alcohol with strength of 15% above. In our study, smoking has been found as related to the mortality in cirrhosis patients with heavy alcohol consumption. For this reason, we suppose that quitting smoking will be beneficial for increasing rate of survival in in cirrhosis patients with heavy alcohol consumption.
Keywords: smoking, Alcohol, cirrhosis, alcohol abuse.

INTRODUCTION

Alcohol is an addictive substance being one of the major reasons of liver disease and consumed widespread all around the world. Every year, it is the reason of 85.000 [1] deaths in the United States of America and 2.5 million of death all over the world [2]. It is predicted that 6.5% of deaths in Europe and 5.9% in the world are related to the alcohol [3]. Half of cirrhosis induced deaths are related to the alcohol [2]. 16.6% of deaths related to the global alcohol are the deaths originating from cirrhosis [4].

Term and quantity of alcohol consumption is one of the most significant factors in terms of occurrence of alcoholic liver disease [5]. It is indicated that comorbid liver diseases, obesity and smoking increases the risk [6]. It is seen that rate of a number of addictive substance abuse mainly smoking with alcohol abuse is high. Tendency of addiction to more than one substance has been demonstrated for the addicted in the studies [7, 8].

Alcoholism is a physical and psychological addiction and alcohol affects a number of neurotransmitters mainly dopamine and also gamma aminobutiric acid, glutamate, serotonine, norepinephrine in brain [9]. It has been shown that nicotine addiction causes increase of alcohol use in the studies [10,11].

Rate of smoking has reduced in the world [12]. However, rate of smoking of alcoholics is quite high and it has been reported as rates above 80% [13, 14]. At the same time, risk of alcohol use disorder in smokers has been found as 10 times more compared to the non-smokers [15]. Nicotine addiction of alcoholic smokers is more severe and it is more difficult for them to quit smoking [14]. Synergic effects of co-use of cigarette and alcohol on occurrence of diseases such as colorectal cancer [16], esophageal cancer [17], pancreatitis [18], and hepatocellular cancer [19], cardiovascular diseases have been determined. In some studies, it has been found out that due to prevalence of smoking-related morbidity, reason of death of alcoholics is more

probably smoking related diseases more than alcohol-related disorders [21, 22]. It was determined that smoking addiction treatment in alcoholic patients reduced the mortality rates [23]. In previous studies, effect of smoking on alcoholic patients was assessed however, effect of smoking on mortality in cirrhotic patients has not been clear yet. In this study, it was aimed to determine characteristics of smoking in cirrhosis with heavy alcohol consumption, its effect on mortality and risk factors.

METHODS

401 cirrhotic patients with heavy alcohol consumption applying to gastroenterology clinic between the years of 2008-2018 successively were assessed retrospectively. Patients having the diagnosis of chronic liver disease within the last one year were included in the study. Diagnosis was established by clinic, biochemical and imaging methods. Patients used to consume alcohol minimum 40 g/day a day and for more than 10 years. Term of alcohol abuse, type of alcohol and smoking condition were questioned for the patients. Patients with GIS malignity and diseases other than liver were not included in the study. Patients were divided into 3 groups as smoker, ex-smokers and non-smokers.

Total quantity of alcohol abuse was determined as the amount of total absolute alcohol throughout the use of alcohol (daily alcohol quantity *365* term of alcohol abuse (year).

Type of alcohol was divided into two groups as drinks with low alcoholic strength (<15%) (Beer and wine) and high alcoholic strength (>15%) (Gin, vodka, whiskey, raki).

RESULTS

Total 401 cirrhotic patients were included in the study. Rate of smoking was found as 90.3%. Average age of the group who quit smoking was determined as significantly high. Age of starting alcohol and body mass index was found as significantly lower in patients who have still smoked. Quantity of daily alcohol use in smokers was significantly higher. A significant relationship between smoking and type of alcohol abused was not found in terms of evaluating the patients for mortality. Term of smoking, frequency (package/day) total quantity of alcohol, term of abusing alcohol, strength of alcohol being above 15% and age were found as related with mortality significantly. In multi-variate analysis, age and quantity of smoking was significantly related to the mortality. Mortality was found less in persons abusing alcohol with strength of 15% above.

Smoking (package.year) and total quantity of alcohol use ($r=0.228$, $p<0.000$) and starting age of alcohol abuse ($r=0.365$, $p<0.0001$) was found as moderately correlated.

Cut off value for smoking.package year was found as 25.5 years by ROC curve.

Table-1: Comparison of demographical data in smoker, ex-smoker and non-smoker cirrhosis patients with heavy alcohol consumption

	Smokers n=285	Ex-smokers n=77	Non-smokers n=39	p
Age	54.0±8.8	60.9±9.3	58.5±9.8	<0.0001
Age of starting alcohol consumption	26.8±8.6	29.9±9.7	30.9±7.5	0.002
Age of starting smoking	21.6±8.2	22.0±8.6		0.678
Sex (W/M)	4/281	0/77	0/39	0.439
Weight	80.9±17.4	89.8±19.8	85.5±13.5	0.009
BMI (kg/m^2)	27.2±5.4	29.8±6.2	28.1±4.1	0.021
Duration of smoking (year)	32.6±10.2	26.1±11.4	-	<0.0001
Smoking (package.year)	36.8±19.5	29.1±17.9	-	0.002
Duration of alcohol consumption	27.3±9.5	31.4±9.9	27.9±8.2	0.004
Amount of alcohol (gr/day)	151±59	129±58	133±58	0.008
Alcohol comsumption of last 10 years (gr/day)	168±81	140±70	148±79	0.014
Total quantity of alcohol consumption (lt)	1517±837	1492±920	1387±775	0.670
HBs Ag (%)	14.4	11.7	10.2	0.684
Anti HBc IgG (%)	49.4	38.6	47.1	0.284
Anti HCV (%)	3.2	2.6	2.6	0.951
Strenght of alcohol (%)	69.5	75.3	69.2	0.595
Type of alcohol				0.453
Beer (%)	22.1	19.5	28.2	
Wine (%)	8.8	5.2	2.6	
Raki /whiskey /vodka (%)	69.2	75.3	70.3	

Table-2: Relation of smoking with mortality in cirrhosis patients with heavy alcohol consumption

						95,0% CI for Exp(B)	
	B	SE	Wald	p	OR	Lower	Upper
Smoking	,412	,328	1,579	,209	1,510	,794	2,871
Duration of smoking (year)	,020	,007	8,447	,004	1,021	1,007	1,035
Smoking (package.year)	,014	,004	12,661	,000	1,014	1,006	1,022
Total quantity of alcohol (lt)	,000	,000	4,287	,038	1,000	1,000	1,000
Duration of alcohol consumption (year)	,026	,009	8,670	,003	1,026	1,009	1,044
Strenght of alcohol (>%15)	-,347	,172	4,065	,044	,707	,504	,990
Type of alcohol	-,179	,094	3,635	,057	,837	,696	1,005
Age	,032	,009	13,491	,000	1,033	1,015	1,051

Table-3: Cox regression multivariate analysis

	B	p	OR	95.0% CI for Exp(B)	
				Lower	Upper
Age	.030	.003	1.030	1.010	1.051
Duration of alcohol consumption	.007	.499	1.007	.987	1.027
Strenght of alcohol (>%15)	-.361	.036	.697	.497	.977
Smoking (package.year)	.013	.001	1.013	1.005	1.021

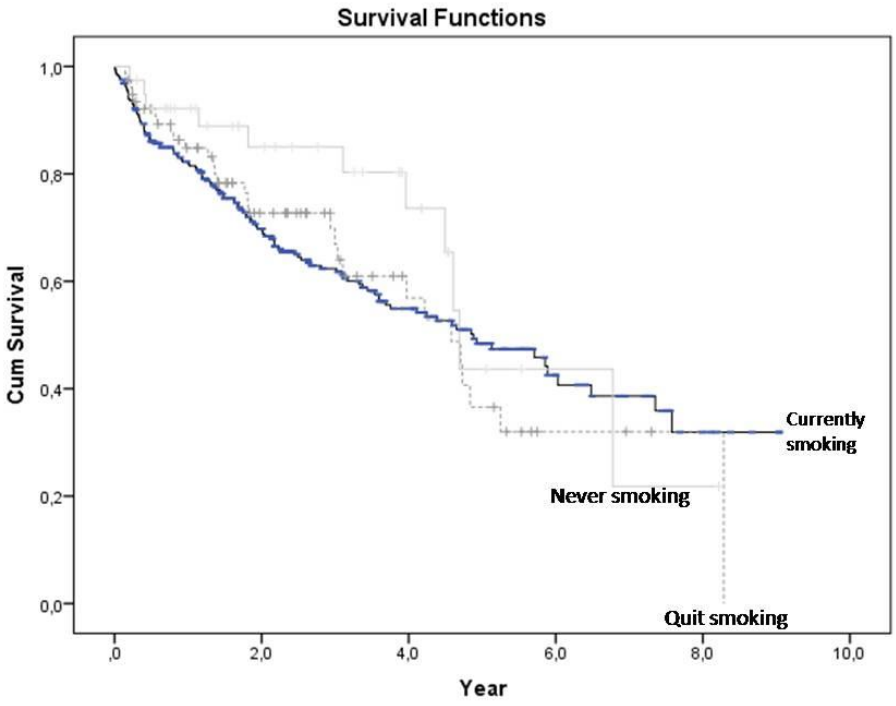

Fig-1: Relation between time and survival in smoker cirrhosis patients with heavy alcohol consumption (p=0.406)

DISCUSSION

It was shown in the literature that rate of smoking of persons abusing alcohol increased. For instance, while rate of smoking in the society in the United States of America was 23%, it was 75% for alcohol addict [24-26]. In the study performed by Batel *et al*. rate of smoking addiction was found as 88% in alcohol addict [27]. The reason of it was suggested as genotypes causing nicotine and alcohol addiction [28]. In our study, rate of smoking in alcoholic patients were found as 90.1%. In a study carried out in Turkey, rate of smoking in general population was determined as 60.3% [29].

In the study conducted by Paavola *et al*. a strong relationship was found between abusing alcohol in early-adolescent period and prevalence of smoking in adult age [30]. It was seen that age of starting to abuse alcohol in smokers was earlier in our study. Moreover, age of starting to smoke was found as earlier than age of starting to abuse alcohol in smokers. We suppose that the reason of it is that smoking encourages abusing alcohol due to common genotypes.

In the study conducted by Hurt *et al*. they analyzed the reasons of mortality in alcoholic cirrhosis patients and found reasons of mortality related to the smoking in 50.9% and they also determined reasons of mortality related to the alcohol in 34.1%. Mortality rate expected within 20 years was found as 48.1% in smokers and as 18.5% in non-smokers. It was indicated that nicotine addiction increased the risk in terms of mortality in alcoholic patient group [21]. In another study published by Hunt et.al, in 2003, they expressed those treatments for quitting smoking was necessary for alcoholics smoking due to high mortality and morbidity rates [22].

Finney *et al*. followed patients for 10 years after they had received alcohol treatment in their study and mortality was found as related to the quantity of alcohol [31]. In another study conducted by Dawson, reasons of mortality in alcohol addicts were investigated and mortality was found as higher in persons abusing alcohol for longer time and more, having heavy drinking episodes and having additional disease [32]. In the study performed by Yuan *et al*. with 18,244 Chinese males, mortality was found as related to the quantity of alcohol [33]. Similar studies were carried out with 12,321 British males and 13,285 Danish females and males and in these studies, mortality was found as related to the alcohol quantity however, a relationship between smoking and mortality was not found [34, 35]. Littleton *et al*. expressed that smoking-based mortality increased in persons abusing alcohol in the review they published in [36]. Bullock *et al*. followed 234 males quitting alcohol and they found mortality more in persons having relapse. They did not find the relationship between smoking and mortality in Cox analysis [37]. There are studies in the literature showing the relationship btween age and mortality in alcohol abusers [31, 38, 39].

John *et al*. evaluated mortality due to liver cirrhosis for 62 years in a study they performed in 2013 and found out that mortality due to cirrhosis reduced. They suggested that reduction of alcohol use and smoking were the main factors reducing the mortality in cirrhosis patients [40].

As it is seen, there are various studies in the literature investigating the effect of smoking on mortality in alcoholic patients. In these studies, alcohol addicted patients were evaluated. The property of our study is that we have investigated patients having liver dysfunction and organic symptoms together with alcohol abuse. According to our study, it was seen that mortality was related to the age and frequency of smoking in alcoholic patients. Effect of smoking on mortality was found in cirrhosis patients with heavy alcohol consumption ($p<0.001$).

Limitations of our study include being retrospective, not evaluating the patients in terms of addiction scores and number of non-smokers is low.

CONCLUSION

Rate of smoking is quite high in alcohol abusers. While there are studies showing the effect of alcohol and smoking on morbidity and mortality, there are also contrary studies. In our study, smoking has been found as related to the mortality in cirrhosis patients with heavy alcohol consumption. For this reason, we suppose that quitting smoking will be beneficial for increasing rate of survival in in cirrhosis patients with heavy alcohol consumption. Alcoholic cirrhosis patients should be encouraged to quit smoking.

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