ARAŞTIRMA | RESEARCH

Complete Blood Count Parameters and Lymphocyte-Related Ratios in Patients with Alcohol Use Disorder

Alkol Kullanım Bozukluğu Olan Hastalarda Tam Kan Sayımı Parametreleri ve Lenfositle İlişkili Oranlar

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ABSTRACT

Objective: The study aimed to determine complete blood count (CBC) parameters, lymphocyte-related ratios in alcohol use disorder (AUD) patients with heavy alcohol use.

Method: The dependent group included 75 individuals with history of alcohol use for at least 10 years. CBC parameters were obtained by evaluating the required tests before alcohol detoxification was initiated. The control group included 75 healthy individuals.

Results: Alcohol use was 6.04 ± 1.45 units/day and the mean duration of alcohol use was 27.62 ± 8.68 years. There were significant differences between the groups based on white blood cell (WBC), neutrophil count, percentage, monocyte count, percentage, neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR), favoring the dependent group. There were significant differences between the groups based on lymphocyte percentage, eosinophil count, percentage, basophil percentage, RBC and eosinophil to lymphocyte ratio (ELR), favoring the control group.

Conclusion: CBC can be used as a rapid and inexpensive examination in AUD patients with heavy alcohol consumption to obtain information about inflammatory processes. and immunological systems which may be useful in AUD diagnosis treatment and follow-up.

Keywords: Alcoholism, blood cell count, lymphocytes, ınflammation

ÖZ

Amaç: Ağır alkol tüketimi olan alkol kullanım bozukluğu (AKB) hastalarında tam kan sayımı (CBC) parametreleri ve lenfosit-ilişkili oranların araştırılması planlandı.

Yöntem: En az 10 yıldır alkol kullanımı olan 75 kişiden 'bağımlı grup' oluşturuldu. CBC parametreleri, alkol detoksifikasyonuna başlanmadan önce istenen tetkiklerin değerlendirilmesiyle elde edildi. 75 sağlıklı kişiden 'kontrol grubu' oluşturuldu.

Bulgular: Alkol kullanım miktarı 6.04±1.45 birim/gün, alkol kullanım süresi ortalama 27.62±8.68 yıl idi. Beyaz küre (WBC), nötrofil sayısı, yüzdesi, monosit sayısı, yüzdesi, nötrofil-lenfosit oranı (NLO), monosit-lenfosit oranı (MLO) bağımlı grubunda daha yüksek olmak üzere, gruplar arasında anlamlı farklılık vardı. Lenfosit yüzdesi, eozinofil sayısı, yüzdesi, bazofil yüzdesi, RBC, eozinofil-lenfosit oranı (ELO) kontrol grubunda daha yüksek olmak üzere gruplar arasında anlamlı farklılık vardı.

Sonuç: CBC, kısa sürede yapılan ucuz bir tetkik olarak, ağır alkol tüketen AKB tanılı hastalarda teşhis koymada ve takipte enflamatuvar süreçler ve immünolojik sistem hakkında bilgi veren yöntem olarak kullanılabilir.

Anahtar kelimeler: Alkolizm, kan hücresi sayımı, lenfositler, inflamasyon

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INTRODUCTION

Alcohol use disorder (AUD) is one of the most common global health problems. It is a significant cause of morbidity and mortality and may lead to early onset cardiac diseases, stroke, cancer and cirrhosis. It is commonly associated with depressive disorders, anxiety disorders, suicide and other substance use disorders (1). One unit drink was accepted to contain 8-10 g alcohol (One unit drink: 33 cl beer, one glass of wine, single raki, one shot drink) (2) 0.1-9.9 g ethanol/day consumption was defined as low alcohol consumption; 10-30 g ethanol/day consumption was defined as moderate alcohol consumption and over 30 g ethanol consumption per day was defined as heavy alcohol consumption (3)..

Low-moderate alcohol consumption at social drinking level (<14 unit drinks/week) (4) stimulates behavior and reduces anxiety. However, chronic alcohol use leads to anxiety and other psychiatric disorders with a negative effect on brain functions (5). induced health problems, substance abuse and accidents causes serious economic burdens (6). Complete blood count (CBC) data can be obtained easily with a low cost. Recently, studies that analyzed CBC parameters and lymphocyte-related ratios to explain the etiology and to determine the effects of the disorder on the immune system in schizophrenia, bipolar disorders, depressive disorders and cannabinoid use disorder were conducted (7-9).

There are studies that investigated the effects of acute and chronic alcohol use on the immune system in the literature (10-12). However, there are only a few studies that investigated the effects of alcohol with CBC analysis and lymphocyte-related ratios (13). Analysis of the functions, distribution and rate of blood cells in peripheral circulation could be used as an easy and inexpensive method to assess the inflammatory and toxic effects of AUD. Thus, the present study aimed to investigate whether easily obtained inexpensive CBC parameters and lymphocyte-related ratios in AUD patients with heavy alcohol use could be used as a method to provide information about immunological system and inflammatory processes which may be useful in AUD diagnosis, treatment and follow-up.

METHOD

Sample

This study was conducted with the cross-sectional design between March 2018-March 2019 after the ethics committee approval was obtained from Fırat University Non-Interventional Research Ethics Committee (15.02.2018/04-12). Eighty-eight inpatients or outpatients diagnosed with alcohol use disorder at Necip Fazıl Urban Hospital Alcohol and Substance Abuse Treatment and Research Center (AMATEM) outpatient clinic based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (14) were invited to participate in the study. Four patients were excluded since they declined to participate and 9 were excluded since they did not meet the study criteria because of having either physiological or psychiatric diseases or substance use history. The dependent group included 75 individuals who met the study criteria and had a history of alcohol use for at least 10 years and signed the informed consent form. Inclusion criteria were 18-65 years of age, alcohol use disorder diagnosis based on DSM-5, presence of no other accompanying DSM-5 disorder, absence of any neurological,

physiological or physical disease and medication due to any psychiatric or physiological disease. Participants with past history of above mentioned diagnoses but without symptoms or medication for last six months were included in the study. Exclusion criteria included mental retardation, any physiological, psychiatric or neurological diseases and substance use disorders. Physiological and other psychiatric diagnosis and drug use were excluded according to patients' statements and hospital data system searches (clinic applications, laboratory tests analyses).

Procedure

Psychiatric examinations were made by the specialist (ŞŞB). CBC parameters were obtained by routine assessment of the examinations conducted during outpatient examination or hospitalization and before the initiation of alcohol detoxification.

Venous blood samples of 2 ml, taken from the patients at the admission for one time, were placed in anticoagulant EDTA-containing tubes, WBC, RBC, CBC were completed via the fully automated hematology analyzer (XT5000; Sysmex, Japan) directly and lymphocytes, monocytes, basophiles, eosinophils and PLT, HGB, mean erythrocyte volume (MCV) and lymphocyte-related ratios were recorded. The examination of the blood test results of patients were obtained by the psychiatry specialist on the basis of the laboratory registration system and were noted via assigning a number for each name. Ratio calculations were completed based on cell counts.

The control group included 75 healthy individuals with similar age and gender as the study group, without a history of alcohol use and without any previous psychiatric or physiological disorder, and not under any medication for any reason. Sociodemographic and Clinical Data Form that queried clinical data such as age, gender, marital status, educational status, occupation, duration of the disease, daily alcohol and cigarette use was applied to all participants. All procedures implemented in the study were conducted in accordance with the human experiments committee ethical standards (institutional and national) and Declaration of Helsinki 2000 review (15). The mean dependent group alcohol consumption was determined as 6.04 ± 1.45 units / day in the present study. This indicated a heavy consumption rate of about 60 g alcohol consumption per day.

Statistical Analysis

The study data exhibited normal distribution (Kolmogorov-Smirnov test). Chi-square test was conducted for the analysis of categorical variables including educational level and marital status, Student's t test was used for comparison of independent groups including Complete Blood Count and calculated parameters. Pearson correlation test was used to investigate the correlations between intra-group variables. Statistical analysis was conducted with SPSS software version 22. A significance level of $p<0.05$ was considered as statistically significant.

RESULTS

The mean age of the patients in the dependent group was 45.12 ± 11.51, and the mean age in the control group was 45.84 ± 9.11. There was no statistically significant difference

between the groups based on age (p = 0.672) and gender (p = 1.000).

Table 1. Alcohol use disorder group sociodemographic data

Variables	N (%)
Gender (*n*):	
Male	75 (100%)
Highest educational level (*n*):	
Illiterate	2 (2.7%)
Elementary school	7 (9.3%)
Middle school	39 (52.0%)
High school	25 (33.3%)
University	2 (2.7%)
Marital status (*n*):	
Married	38 (50.7%)
Single	19 (25.3%)
Widowed	15 (20.0%)
Live apart	3 (4.0%)

Alcohol consumption was 6.04 ± 1.45 units/day and the mean alcohol consumption duration was 27.62 ± 8.68 years. The group of AUD sociodemographic data are presented in Table 1. While all subjects in the dependent group (n = 75) were smokers (100%), 20 subjects (26.7%) were smokers in the control group (p < 0.001). Cigarette consumption was 20 ± 3 /day in the dependent group, while it was was 18 ± 5 /day in the control group (p < 0.05).

Table 2. Comparison of complete blood count (CBC) and other parameters.

	Alcohol Use Disorder (n=75)		Control (n=75)		p
	Mean	Std. Deviation	Mean	Std. Deviation	
WBC	8.78	2.09	7.43	1.91	0.000
NEU	5.63	1.92	4.14	1.46	0.000
NEU%	62.71	9.80	55.16	8.14	0.000
LYM	2.23	0.79	2.45	0.71	0.080
LYM%	26.12	8.66	33.52	7.30	0.000
MON	0.80	0.33	0.54	0.20	0.000
MON%	9.30	3.77	7.42	2.12	0.000
EOS	0.14	0.13	0.22	0.14	0.001
EOS%	1.72	1.61	2.95	1.65	0.000
BAS	0.04	0.04	0.04	0.02	0.437
BAS%	0.46	0.38	0.60	0.28	0.011
RBC	4.99	0.63	5.30	0.49	0.001
HGB	15.51	2.09	15.40	1.49	0.713
PLT	257.25	74.50	244.40	59.76	0.245
MPV	9.77	0.85	9.77	1.54	0.991
NLR	3.19	3.57	1.81	0.85	0.001
MLR	0.42	0.27	0.23	0.08	0.000
ELR	0.07	0.06	0.09	0.05	0.005
BLR	0.02	0.03	0.02	0.01	0.334
PLR	140.34	149.65	106.36	34.86	0.057

WBC: White Blood Cell; NEU: Neutrophil; LYM: Lymphocyte; MON: Monocyte; EOS: Eosinophil; BAS: Basophil; RBC: Red Blood Cell; HGB. Hemoglobin; PLT: Platelet; MPV: Mean Platelet Volume; NLR: Neutrophil to Lymphocyte Ratio; MLR: Monocyte to Lymphocyte Ratio; ELR: Eosinophil to Lymphocyte Ratio; BLR: Basophil to Lymphocyte Ratio; PLR: Platelet to Lymphocyte Ratio

There were significant differences between the groups based on WBC, neutrophil count, neutrophil percentage, monocyte count, monocyte percentage, NLR, and MLR values favoring the dependent group. There were significant differences between the groups based on lymphocyte ratio, eosinophil count, eosinophil ratio, basophil ratio, RBC and ELR favoring

the control group. Although there were no significant differences between the groups based on hemoglobin, basophil count, platelet count, MPV, BLR, and PLR, all values were higher in the dependent group, only the lymphocyte count was higher in the control group. There was no correlation between alcohol use duration and amount and the CBC parameters. The group CBC parameters are presented in Table 2.

DISCUSSION

Alcohol is the most abused substance in the world. It affects and disrupts the immune system (16). There are studies in the literature that investigated the correlation between alcohol use and immunological system findings and inflammatory processes. In a study by Szabo et al., it was reported that heavy alcohol use inhibited auxiliary cell functions in monocyte and myeloid dendritic cells and the study concluded that disruption of the functions of these antigen presenting cells may lead to a decrease in the immune system response (11). Heavy alcohol use was demonstrated to cause immunosuppression in pulmonary infections (17), affecting TNF, IL-1, IL-6, and inhibiting monocyte and macrophage functions (18). Nakanishi et al. reported that mild alcohol use led to a reduction in WBC by inhibiting tumor necrosis factor-α (TNF-α) production, one of the proinflammatory cytokines that increase WBC (19). In another study, cytopenia was diagnosed in patients with chronic alcohol use and 65% of patients with cytopenia were reported to use alcohol (20). In a recent retrospective cohort study conducted by Orum et al., CBC parameters and NLR, BLR, ELR and MLR values obtained from the CBC parameters of 32 AUD patients were compared to the same parameters of healthy controls, however no significant difference was observed between these two groups (13). Literature review revealed that there are only a few studies that analyzed immune system findings and inflammatory processes based on CBC parameters and the ratios obtained with these parameters in patients with AUD (13). However, there are increasing number of studies that investigated immune and inflammatory processes and etiology in psychiatric disorders using CBC parameters. In the present study, analysis of the CBC parameters and lymphocyte-related ratios in AUD patients with heavy alcohol consumption which were obtained with CBC demonstrated that lymphocyte count and ratio were decreased, and real and relative increases were observed in the count and ratios of the cells involved in inflammatory processes such as neutrophils and monocytes, increasing the inflammatory processes. The small sample size and shorter alcohol consumption duration (17.78 ± 10.33 years) in Orum et al.'s study when compared to the present study (27.62 ± 8.68) could have led to similar findings in both patient and control groups. The fact that the mean age of the patients in the present study (45.12 ± 11.51) was higher when compared to the above-mentioned study (38.50 ± 12.50) was another factor that could have affected the findings. Smoking was another factor that could have affected the CBC findings. In previous studies, it was reported that the mean leukocyte count was higher in smokers when compared to ex-smokers and non-smokers, and the lowest leukocyte count was observed in the non-smokers group. Previous studies demonstrated that the increase in the leukocyte count was associated with the amount of smoked cigarettes, smoking history and how deep the cigarette smoke was inhaled 21, 22, and it was reported that WBC levels decreased after quitting smoking (23, 24). In the present study, all patients in the dependent group were smokers (100%). In the control group, smoker ratio was 26.7%. In addition to direct effect of alcohol in the dependent group, it can be suggested that the

increase in WBC and other associated parameters could be associated with smoking cigarettes.

AUD is associated with anxiety and depressive disorders (25-27). It was demonstrated that anxiety and depression increased leukocyte and neutrophil count, leading to a decrease in lymphocyte count (28). Neutrophil / lymphocyte ratio (NLR) and platelet / lymphocyte ratio (PLR) are used as new biomarkers in the determination of systemic inflammation (29). In certain studies, it was determined that the sympathetic nervous system activation that plays a role in the etiology of anxiety and depression might increase the mean platelet volume (MPV), which is a significant marker of blood platelet activity (30). In another study, was shown that experimentally induced stress could lead to an inflammatory reaction. This was explained by the fact that exposure to acute stress could lead to a high level of inflammation in anxiety disorder (31, 32). In addition to the direct toxic effect of alcohol on peripheral circulatory system cells, concomitant anxiety and depression might lead to numerical, morphological and functional changes in these cells. It is known that the familial and occupational functionalities of the patients with AUD are severely impaired and alcohol use leads to major social problems which could lead to anxiety and depressive disorders. The study group included patients, who were diagnosed with AUD, decided to leave alcohol due to significant social, health and economic losses they experienced and exhibited symptoms of depression and anxiety. It was likely that the clinically observed depression and anxiety in these patients might have also led to changes in CBC parameters by affecting inflammatory and immune system processes (30, 33-35).

The present study has some limitations. It was conducted mostly with male patients due to the general profile of the patients that were admitted in the hospital. Thus, it may not be adequate to generalize the findings to both genders. Smoking is not an easily excluded factor in AUD patients. It may be more adequate to compare groups with similar smoking habits to minimize the effect of smoking as a confounding factor on the outcome. Prospective studies that would be conducted with a larger sample that would include subjects of both genders could contribute more to the literature.

In the present study, analysis of the CBC parameters and the lymphocyte-related ratios in AUD patients with heavy alcohol consumption demonstrated that heavy alcohol use is associated with reduced lymphocyte count and ratio and increased inflammatory processes by leading to real and relative increases in the count and ratio of cells such as neutrophils and monocytes that play role in inflammatory processes. CBC can be used as a rapid, easy and inexpensive examination in AUD patients with heavy alcohol consumption to obtain information about inflammatory processes and immunological systems which may be useful in AUD diagnosis, treatment and follow-up.

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