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Research Article

Assessment of serum cyanocobalamin level and importance in patients with hematological malignancies

Hematolojik malignitesi olan hastalarda serum siyanokobalamin düzeyi ve öneminin değerlendirilmesi

Esra Zeynelgil*[1], Buğra Saglam[2], Mehmet Asil[3], Ozlem Dogan[4]

[1]Amasya University, Sabuncuoglu Serefeddin Hospital, Oncology Department, Amasya,Turkey
[2]Sanlıurfa Training and Research Hospital, Department of Hematology, Ankara, Turkey
[3]University of Necmettin Erbakan, Meram Medical Faculty, Department of Gastroenterology, Konya, Turkey
[4]Ankara Etlik City Hospital, Department of Oncology, Ankara, Turkey

ABSTRACT

Aim: In our study, we planned to investigate the effect of serum cyanocobalamin (Vitamin B12) levels at the time of diagnosis in patients with various hematological malignancies.

Material and Methods: Two hundred and one patients between 18-75 years old diagnosed with various hematological malignancies and 30 healthy controls applying to outpatient and inpatient clinics of Hematology Department in Necmettin Erbakan University Meram Faculty of Medicine between 2010-2014 years were included in the study. Demographic and clinical data and laboratory findings of the patients included in the study were recorded retrospectively.

Results: A total of 231 patients, 132 men (57.1%) and 99 women (42.9%), were included in our study, of which 201 were patients and 30 were healthy controls. The mean serum vitamin B12 concentration of all patients was found as 344.9 ± 279.0 pg/mL. When vitamin B12 levels were analyzed according to diagnostic groups, it was found to be highest in CML (596.0 ± 428.3 pg / mL) and ALL (524.5 ± 442.6 pg / mL) patients and lowest in AML patients (240.9 ± 178, 0 pg / mL); the difference was statistically significant (p <0.001). Vitamin B12 levels of diagnostic groups were found to have no significant effect on survival.

Conclusion: Cyanocobalamin levels were found to be high in patients with hematological malignancies, especially in CML patients. A high level of cyanocobalamin may be helpful in prediction of CML, however prospective studies are required to support this finding.

Keywords: cyanocobalamin, CML, ALL,AML, Vitamin B12

Corresponding Author*: Esra Zeynelgil, Amasya University, Sabuncuoglu Serefeddin Hospital, Oncology Department, Amasya,TURKEY
E-mail: esra23.05@hotmail.com
Orcid: 0000-0001-7200-9440
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ÖZ

Amaç: Çalışmamızda farklı hematolojik maligniteleri olan hasta gruplarında tanı anındaki serum siyanokobalamin (Vitamin B12) düzeylerinin tanıları ön görmede etkisini araştırmayı planladık..

Gereç ve Yöntemler: Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi Hematoloji poliklinik ve kliniğine 2010-2014 yılları arasında başvurmuş olan 18-75 yaş arası hematolojik malignite tanısı almış olan 201 hasta ve 30 sağlıklı kontrol grubu çalışma kapsamına alındı. Çalışma kapsamına dahil edilen hastaların demografik, klinik ve laboratuar verileri retrospektif olarak kayıt altına alınmıştır.

Bulgular: Çalışmamıza 132'si erkek (%57,1) ve 99'u kadın (%42,9) olmak üzere toplam 201 hasta ve 30 sağlıklı kontrol grubu olmak üzere 231 kişi dahil edildi. Tüm hastaların ortalama serum Vitamin B12 konsantrasyonu 344,9±279,0 pg/mL olarak gözlendi. Tanı gruplarına göre Vitamin B12 düzeylerinin değerlendirmesinde ise; KML (596,0±428,3 pg/mL) ve ALL (524,5±442,6 pg/mL) hastalarında en yüksek, AML (240,9±178,0 pg/mL) hastalarında ise en düşük olduğu ve bu farklılığın istatistiksel olarak anlamlı olduğu gözlendi ($p<0,001$). Hastalık gruplarının Vitamin B12 düzeylerinin sağ kalım üzerine anlamlı fark saptanmamıştır.

Sonuç: Hematolojik malignitesi olan hastalarda ve özellikle KML hastalarında siyanokobalamin düzeyi yüksek bulunmuştur. KML hastalığının tanısı için yüksek siyanokobalamin düzeyi hastalığı ön görmede yardımcı olabilir ancak bunun prospektif çalışmalarla deseklenmesi gerekmektedir.

Anahtar Kelimeler: siyanokobalamin, KML, ALL,AML, Vitamin B12

Introduction

The historical process of cyanocobalamin goes back to the first studies in dogs with anemia in 1925 [1]. It has been reported in the literature that vitamin B12 may be associated with malignancies in people with high levels of vitamin B12 analyzed for any reason [2, 3]. Furthermore, there are studies reporting an increase in serum cobalamin levels in patients with liver cancer, some solid tumors, and various hematological malignancies [4-9]. There is no study evaluating serum cyanocobalamin levels in hematological malignancies in our country. In this study, we wanted to evaluate the importance of serum cyanocobalamin level analysis at the time of diagnosis in patients with various hematological malignancies.

Material and Methods

Two hundred and one patients between 18-75 years old applying to outpatient and inpatient clinics of Hematology Department in Necmettin Erbakan University Meram Faculty of Medicine between 2010-2014 years and diagnosed with various hematological malignancies including Acute Lymphoblastic Leukemia (ALL), Acute Myeloblastic Leukemia (AML), Chronic Lymphocytic Leukemia (CLL), Chronic Myelocytic Leukemia (KML), Hodgkin Lymphoma (HL), Non-Hodgkin Lymphoma (NHL), Multiple Myeloma (MM), Myelodysplastic Syndrome (MDS) and Polycythemia Vera (PV), were included in this study. The data of the newly diagnosed patients with above-mentioned diagnosis groups were investigated via retrospective screening of hospital automation system and, the patients whose vitamin B12 levels were analyzed at the time of diagnosis were included in the study. Patients using cyanocobalamin preparations in the recent year or diagnosed with a disease leading to malabsorption defect (gastrectomy, inflammatory bowel disease, etc.) or having vegetarian diet habits were excluded from the study. Thirty healthy individuals with no known chronic disease or anemia or neurological complaints were included in the study as the control group. The normal range for serum cyanocobalamin level was accepted as 126.5-505 pg/mL considering the reference range used by the laboratory of our hospital.

Statistical Analysis

The numerical data of the study were shown as mean values and standard deviations. Categorical data were summarized as percentages. Numerical data comparisons between genders were performed with Mann-Whitney U test, and comparisons between diagnostic groups were performed with Kruskal-Wallis test. Mann-Whitney U test was used for pairwise comparisons in post hoc analysis in case of difference as the result of Kruskal-Wallis analysis and, Bonferroni correction was performed for significance assessment. All statistical analyzes of the study were performed bidirectionally with the assumptions of 5% Type-I error and 80% study power. SPSS 21 (IBM Inc, USA) software was used for the analyses.

Compliance with Ethical Standards:All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Approval for this cross-sectional study was granted by Necmettin Erbakan University Faculty of Medicine Ethics Committee This study was produced from the internal medicine thesis of Dr. Esra Zeynelgil.

Results

A hundred and thirty-two men (57.1%) and 99 women (42.9%) were included in our study, of which 201 were patients and 30 were healthy controls. The serum vitamin B12 levels at the time of diagnosis and numerical and demographic data of the patients are shown in the table (Table-1). Vitamin B12 levels were found as 596.0 pg/mL (± 428.3) in CML patients, 240.9 pg/mL (± 178.0) in AML patients, 280.8 pg/mL (± 262.9) in CLL patients, 216 pg/mL (± 164.3) in MDS patients.

Table-1. Demographic features and B12 levels of patients

	ALL (n:13)	AML (n:26)	HL (n:20)	KLL (n:30)	KML (n:20)	MDS (n:16)	MM (n:16)	NHL (n:43)	PV (n:17	Kontrol (n:30
Age Mean	52,1±11,5	53,5±19,5	52,1±14,5	62,2±8,8	62,2±11,2	67±11,1	67±1,1	57,1±16	52,2±14,9	40,3±14,5
Gender										
Male	8 (%62)	15 (%58)	9 (%45)	24 (%80)	8 (%40)	9 (%57)	9 (%57)	25 (%59)	15 (%89)	10 (%34)
Female	5 (%38)	11 (%42)	11 (%55)	6 (%20)	12 (%60)	7 (%43)	7 (%43)	18 (%41)	2 (%11)	20 (%66)
B12 range (pg/mL)	524,5±442,6	240,9±178,0	338,1±196,0	280,8±262,9	596,0±428,3	216±164,3	295,1±138,9	370,3±332,2	331,7±167,2	324,4±107,1
Final Situation										
Alive	3 (%23)	15 (%58)	17 (%85)	21(%70)	12 (%60)	13 (%82)	13 (%82)	26 (%60)	17 (%100)	30 (%100)
Ex	10(%77)	11 (%42)	3 (%15)	9 (%30)	8 (%40)	3 (%18)	3 (%18)	17 (%40)	0 (%0)	0 (%0)

The results of statistical analyses revealed that vitamin B12 levels showed a significant difference between diagnostic groups ($p < 0.001$). Post-hoc analysis results performed for determination of factors causing the difference revealed that vitamin B12 levels were highest in the CML and ALL groups followed by the PV and healthy control groups and, the levels were similar in the other diagnostic groups but lower than those groups. The p values obtained by comparing B12 median levels of the disease groups with the control group are presented in Table-2. It may be stated that there is a statistically significant difference between B12 levels of the control group and the diagnostic groups including AML, CLL, CML and MDS diseases.

Table-2. Comparison of the disease groups with the B12 medians and the median of the control group

No	Hastalık Grupları	Kontrol ile Karşılaştırma Sonucu p Değeri
1	ALL	0.552
2	AML	0.009
3	HL	0.394
4	KLL	0.006
5	KML	0.013
6	MDS	0.002
7	MM	0.460
8	NHL	0.166
9	PV	0.698

Discussion

Vitamin B12 is a water-soluble vitamin involved in lipid, carbohydrate and protein metabolisms [10]. Vitamin B12 has a wide reference range in the literature varying between 200-700 pg/mL, but a specified reference range has not been reported in studies. Diagnostic sensitivity and specificity of plasma cobalamin levels below 400 pg/mL is limited [11]. Therefore, B12 deficiency cannot be excluded at levels below 400 pg/mL and signs and symptoms of deficiency may be detected even in normal reference range [12]. In our study, the reference range accepted by the laboratory of our hospital, 126.5-505 pg/mL, was determined as the lower and upper limits for vitamin B12.

High serum levels of B12 were shown to be likely associated with kidney failure, carcinoma, hematological malignancies such as acute and chronic leukemias, polycythemia vera, hypereosinophilic syndrome, cirrhosis, hepatitis, hepatocellular carcinoma and metastatic liver tumors in studies conducted on clinical reflections of changes in vitamin B12 levels [13-17].

According to our results, vitamin B12 levels were in the normal range in 69.2% of patients with hematological malignancies, while 11.9% were below and 18.9% were above normal limits. The main reason of significantly lower vitamin B12 levels in patients with AML, CLL and MDS compared to the control group is the physiological role of vitamin B12 in DNA methylation and increased consumption in these patient groups. The highest vitamin B12 level was determined in CML patients. It was reported in some studies that the reference range of vitamin B12 might increase up to ten times in CML patients [18, 19]. Possible cause of this situation is the increase in leukocyte-induced haptocorrin production due to increasing number of leukocytes.

In the literature, high serum vitamin B12 levels were reported to result from various mechanisms. Elevation of serum plasma transcobalamin I/III, also called as haptocorrin, which is a carrier protein synthesized by myeloid cells, hepatic cells and other cell types in the body, may be due to increased hepatic cytolysis, decreased vitamin B12 clearance in the liver, accumulation in peripheral tissues as a result of decreased production of transcobalamin II in the liver or secondary effects resulting from therapeutic applications [20]. Besides these, circulating cobalamin-binding proteins and antibodies have also been reported to cause high plasma cobalamin levels [21, 22]. In a study conducted by Chiche et al., serum vitamin B12 levels exceeding 1275 pg/mL were reported to have a strong and statistically significant relationship with hematological malignancies and, a detailed etiology analysis was recommended especially in patients with elevated serum vitamin B12 [3].

Conclusion

In conclusion, it was determined that the serum vitamin B12 level at the time of diagnosis may be beneficial in patients likely to be diagnosed with CML. Useful results may be obtained by studies with larger patient population in other hematological malignancy groups.

Declaration of conflict of interest

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