ORIGINAL ARTICLE

Can serum mean platelet volume be used as an inflammatory marker in patients with celiac disease?

Ortalama eritrosit hacim değeri çölyak hastalığı olan hastalarda inflamatuvar bir belirteç olarak kullanılabilir mi?

Aylin DEMİREZER BOLAT[1], Hüseyin KÖSEOĞLU[1], Fatma Ebru AKIN[1], Öykü TAYFUR YÜREKLİ[2], Mustafa TAHTACI[2], Murat BAŞARAN[2], Osman ERSOY[2]

Department of [1]Gastroenterology, Atatürk Research and Teaching Hospital, Ankara
Department of [2]Gastroenterology, Yıldırım Beyazıt University, Faculty of Medicine, Ankara

Background and Aims: *Mean platelet volume has been studied as a simple inflammatory marker in several diseases. Some studies have reported that mean platelet volume increases in myocardial infarction and cerebrovascular disease. Contrarily, it decreases in rheumatoid arthritis, ankylosing spondylitis, and inflammatory bowel disease. The aim of this study was to evaluate whether mean platelet volume was changed in celiac disease and whether it could be used to monitor a gluten-free diet in patients.* ***Materials and Methods:*** *After excluding patients with severe comorbidities and patients who did not comply with the gluten-free diet, a total of 50 patients with celiac disease (men/women: 9/41) and 50 healthy subjects (men/women: 10/40) were included in the study. The diagnosis of celiac disease was based on standard serological, endoscopic, and histological criteria. The study enrolled patients with celiac disease who recovered clinically and serologically 1 year after gluten-free diet. Complete blood count analyses were performed within 2 h after collection with the use of the Beckman coulter analyzer.* ***Results:*** *Mean platelet volume levels were not significantly different in the celiac disease group than that of in the control group. In the celiac disease group, the mean platelet volume levels did not change after 1 year of gluten-free diet compared with the time of celiac disease diagnosis. On the contrary, a decrease in the platelet count after gluten-free diet was detected.* ***Conclusion:*** *This study demonstrates that mean platelet volume is not altered in patients with celiac disease, and it also showed that mean platelet volume cannot be used as a marker for predicting dietary compliance in patients with celiac disease.*

Key words: *Celiac disease, gluten-free diet, mean platelet volume*

Giriş ve Amaç: *Ortalama trombosit hacmi değişik hastalıklarda çalışılmış olan, basit ölçülebilen bir inflamatuvar belirteçtir. Miyokart enfarktüsü, inme gibi hastalıklarda ortalama trombosit hacminin arttığı, romatoid artrit ve ankilozan spondilit gibi inflamatuvar hastalıklarda ise ortalama trombosit hacminin azaldığı gösterilmiştir. Bu çalışmanın amacı çölyak hastalığı olan hastalarda ortalama trombosit hacmi seviyesinin değişip değişmediğinin saptanması ve glutensiz diyet tedavisi alan hastalarda tanı anındaki ortalama trombosit hacmi ile diyet sonrası ortalama trombosit hacim düzeyleri kıyaslanarak ortalama trombosit hacminin glutensiz diyete uyumun belirlenmesi için bir belirteç olarak kullanılıp kullanılamayacağının saptanmasıdır.* ***Gereç ve Yöntem:*** *Eşlik eden ciddi hastalığı olan ve glutensiz diyete yeterli şekilde uyum göstermeyen hastalar çalışmadan çıkarıldıktan sonra kalan 50 çölyak hastalığı olan hasta (erkek/kadın: 9/41) ve 50 sağlıklı gönüllü (erkek/kadın: 10/40) çalışmaya alındı ve klinik ve laboratuvar değerleri kıyaslandı. Çölyak hastalığı tanısı standart serolojik, endoskopik ve histolojik kriterlere göre konuldu. Glutensiz diyet sonrası birinci yılda klinik olarak ve serolojik olarak remisyonda olan hastaların tanı anındaki ve diyetten sonraki değerleri de karşılaştırıldı. Tam kan sayımı hastalardan kan alındıktan sonraki iki saat içinde Beckman coulter analyzer ile yapıldı.* ***Bulgular:*** *Çölyak hastalığı olanlar ile kontrol grubu arasında ortalama trombosit hacim düzeyi farklı saptanmadı. Çölyak grubunda da bir yıllık diyet sonrasında ortalama trombosit hacmi düzeyinde anlamlı bir değişiklik gözlenmedi, ancak diyet sonrasında tanı anına kıyasla hastaların ortalama trombosit sayısı daha düşük izlendi.* ***Sonuç:*** *Bu çalışma göstermiştir ki ortalama trombosit hacim düzeyinin, ne çölyak hastalığının tanısında ne de diyete uyumun bir göstergesi olarak kullanılması uygun değildir.*

Anahtar kelimeler: *Çölyak hastalığı, glutensiz diyet, ortalama trombosit hacmi*

INTRODUCTION

Celiac disease (CD) is a genetically based chronic inflammatory disorder of the small bowel induced by the dietary gluten. Several European and American studies have shown that the true prevalence of CD may be 1:200 or higher (1,2). The cornerstone of treatment for CD is the elimination of gluten from the diet. The rapidity of the response to a gluten-free diet (GFD) is variable. Dietary compliance can be measured both noninvasively, by dietary history and measurement of serum antibodies, and invasively, by using endoscopic and histological criteria. The advantages and disadvantages of these various modalities are questionable (3). Mean platelet volume (MPV)

Correspondence: Aylin DEMİREZER BOLAT
Department of Gastroenterology, Ankara 06800, Turkey
Tel: +90 291 25 25 - 4645 • Faks: +90 312 291 27 05
E-mail: aylinz35@gmail.com

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is a parameter generated by a full blood count analyzer as a part of the routine complete blood count (CBC) test cycle (4). MPV correlates with the platelet function and activation (5). It has been studied as a simple inflammatory marker in several diseases. Some studies have reported that MPV increases in myocardial infarction and cerebrovascular disease (6,7); while in contrast, it decreases in rheumatoid arthritis and ankylosing spondylitis (8). Similarly, MPV levels have been reported to decrease in some inflammatory bowel diseases in several studies (9,10). The aim of this study was to evaluate whether MPV was changed in patients with CD and whether it could be used to monitor GFD in patients.

MATERIALS and METHODS

Eighty-one patients with CD were detected in our database. [Patients who were positive for endomysial antibody (EMA) during the etiologic evaluation of abdominal pain, diarrhea, hypothyroidism, anemia, liver test abnormalities, and constipation underwent upper gastrointestinal endoscopy, and biopsies were taken from the second part of the duodenum. GFD was introduced to patients whose diagnosis was put forward according to histology (Marsh score)]. Among these patients, 11 were excluded because of accompanying diseases that can affect MPV and 20 for non-adherence to GFD. After exclusion, the patients' records were evaluated, and the clinical and serological features in 50 patients suggested a response to GFD. [Clinical and laboratory response criteria were defined as regression of presenting complaints (diarrhea, abdominal pain, and constipation) or improvement of laboratory abnormalities (improvement in liver tests, hypothyroidism, and anemia). A serological response criterion was defined as negative EMA titer during a follow-up.] These 50 patients were included in the statistical analyses and were compared with 50 healthy individuals. The diagnosis of CD was based on standard medical, endoscopic, and histological criteria. The study included patients with CD who recovered clinically and serologically 1 year after GFD. The study was approved by the local ethics committee, and written informed consent was obtained from all the participants.

Exclusion criteria included heart failure, peripheral vascular disease, hematological disorders, acute or chronic infection, cancer, and hepatic diseases. None of the patients had received anticoagulant medications, nonsteroidal anti-inflammatory drugs (NSAIDs), and oral contraceptives.

All laboratory analyses were performed in a hematology laboratory of our hospital. Complete blood count (CBC) analyses were performed within 2 h after collection with the use of the Beckman coulter analyzer. The histopathological appearances were described according to the modified Marsh criteria (11).

The Statistical Package for Social Sciences (SPSS) v. 21.0 for Windows was used to analyze the mean±standard deviation. The dependent samples t-test was used to compare the independent samples t-test of CD patients and the control group and to evaluate the effect of GFD in the CD group. The chi-square test was used for categorical variables. P-values less than 0.05 were accepted as statistically significant.

RESULTS

A total of 50 CD patients (men/women: 9/41) and 50 healthy control subjects (men/women: 10/40) were included in the statistical analyses. The demographic and laboratory characteristics of the patients and controls are shown in Table 1. The age and gender were similar in both groups. There was no statistically significant difference in MPV and white blood count, but the hemoglobin level was lower and platelet count was higher in the CD group. In patients with CD, MPV, white blood count, and hemoglobin levels were not different before diet and 1 year after GFD. On the contrary, a decrease in platelet count was statistically significant (P = 0.026; Table2).

Table 1. The demographic and laboratory characteristics of the patients and controls

	CD (N = 50)	Healthy Group (N = 50)	*P*
Age	35.50 ± 12,54	32.50 ± 6.29	0.135
Gender M/F	9/41	10/40	0.79
White blood cell	6,116 ± 1,522	6,693 ± 1,633	0.234
Hemoglobin	12.77 ± 2.11	13.79 ± 1.08	**0.004**
Platelet count	415,840 ± 44,845	234,820 ± 41,827	**0.002**
MPV	8.60 ± 1.25	8.19 ± 0.46	0.038

CD: Celiac disease, M: Male, F: Female, MPV: Mean platelet volume.

Table 2. White blood cell count, hemoglobin, platelet, and MPV levels at the time of diagnosis and after GFD

	Diagnosis	After GFD	*P*
White blood cell	6,116±1,522	6,424±1,645	0.11
Hemoglobin	12.77±2.11	12.73±1.58	0.838
Platelet	415,840±44,845	274,920±87,761	**0.026**
MPV	8.60±1.25	8.80±1.61	0.296

GFD: Gluten-free diet, MPV: Mean platelet volume.

DISCUSSION

CD is a genetically based chronic inflammatory disorder of the small bowel induced by the dietary gluten (1). Treatment with a GFD should be started only after the diagnosis has been established by intestinal biopsy. In approximately 70% of symptomatic patients with CD, symptoms improved within 2 weeks after starting a GFD. In addition, tissue transglutaminase (tTG) immunoglobulin A (IgA) and EMA IgA normalize within 2 to 6 months following the initiation of the GFD. Dietary compliance can be measured both noninvasively, by dietary history and measurement of serum antibodies, and invasively, by using endoscopic and histological criteria. The advantages and disadvantages of these various modalities are questionable (3). Several researchers believe that EMA negativity reflects the absence of gluten in the diet in those who were initially positive, but it is not a predictor of mucosal damage (12-14).

Because of the false positivity of tTG and EMA with other autoimmune diseases, such as type 1 diabetes and autoimmune hepatitis, these antibodies may remain elevated in a certain subset of patients despite strict adherence to GFD (15,16). Almost 10% of CD is seronegative, and serological testing is unreliable in the very young and in people already following a gluten-reduced diet (17). A repeat small-bowel biopsy 1 to 3 years following diagnosis is often recommended to assess response to a GFD, as histological findings usually revert to normal after 3 to 12 months on a GFD (18). Despite a good clinical response, abnormal endoscopic and histopathological appearances persist in the majority of patients with CD treated with GFD (19). Therefore, the role of antibodies and duodenal histology in monitoring the course of the disease must be discussed. None of the noninvasive tests was an accurate substitute for follow-up biopsy in detecting severe mucosal damage (20).

MPV is a marker of platelet function and activation and is also influenced by inflammation. It is readily measured by clinical hematology analyzers (5). MPV has been shown to increase in several inflammatory conditions, but there is scarce literature investigating the MPV levels in CD.

Inflammatory disorders have various effects on hematopoiesis, and the most well-known clinical presentations are anemia and thrombocytosis (21). These hematopoietic presentations, particularly thrombocytosis, are presumably mediated by cytokines and growth factors, including interleukin (IL)-1, IL-3, IL-4, IL-6, IL11, and tumor necrosis factor-alpha (22,23). IL-6 is an important pro-inflammatory cytokine that can induce thrombocytosis and affect platelet volume (24,25). Patients with active CD had significantly higher levels of pro-inflammatory cytokines, such as interferon-gamma, IL-1 beta, tumor necrosis factor-alpha, IL-6, and IL-8, and also Th2 cytokines, such as IL-4 and IL-10, compared with normal controls (26). Therefore, it is reasonable to find an association between disease activity and platelet characteristics in inflammatory disorders. Increased MPV levels were determined in diseases such as myocardial infarction, acute ischemic stroke, and diabetes mellitus (6,7). In contrast, decreased MPV levels have been reported in cases with active rheumatoid arthritis and ankylosing spondylitis (8). Similarly, decreased MPV levels have been observed in inflammatory bowel diseases in several studies (9,10).

O'Grady et al. measured platelet count and MPV in 84 splenectomized subjects, 142 patients with CD, and 77 healthy subjects. An inverse, nonlinear correlation between platelet count and MPV was found in healthy subjects and in patients with CD but was not present in splenectomized subjects who had higher platelet counts (*P*=0.0001) and MPV (*P*=0.0001) than healthy subjects. Platelet counts correlated with splenic function in patients with CD and were higher in patients with severe hyposplenism than in patients with CD and normal splenic function (P=0.0001). The splenic function did not influence the MPV in CD, but normosplenic patients with CD had higher MPV than normal subjects (P=0.05). They concluded that splenic function affects platelet count and MPV in non-celiac subjects and platelet count in CD. However, other unidentified factors may influence the MPV in CD (28).

Purnak et al. investigated 60 newly diagnosed CD patients and 40 healthy subjects to detect any possible changes in MPV values after a specified period of GFD. A significantly higher MPV was observed in the CD group compared with the healthy people. After the introduction of a GFD, the MPV of the patients with CD in the diet-adherent group was significantly lower than that of in the non-adherent group. They concluded that MPV could be a promising and easily available biomarker for monitoring dietary adherence in patients with CD at a low cost in comparison with other modalities (29). In contrast to this finding, in the present study, serum MPV levels were similar in both patients with CD and the control group, and serum MPV levels did not change 1 year after GFD, so it was not related to a clinical and serologic remission. On the other hand, a decrease in platelet count was statistically significant. These results can be explained by the fact that hyposplenism is a common clinical condition in CD that fluctuates with disease activity. Splenic function improves after withdrawal of gluten from the diet (27).

Histological inflammation can persist for years in patients with CD despite a good clinical response. This can explain why the similar MPV levels in CD patients before and after GFD are distinct from other inflammatory diseases. As a result, this study shows that MPV cannot be used as an inflammatory marker for predicting dietary compliance in patients with CD. Better results can be obtained if more patients with CD are enrolled and the follow-up is longer.

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