Is There Any Relationship Between Platelet Functions, Red Cell Distribution Width and Recurrent Pregnancy Loss?

Trombosit Fonksiyonları ve RDW İle Tekrarlayan Gebelik Kayıpları Arasında Bir İlişki Var Mıdır?

Trombosit Fonksiyonları, EDG Ve Tekrarlayan Gebelik Kaybı / Platelet Functions, RDW and Recurrent Pregnancy Loss

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Özet

Giriş: Tekrarlayan gebelik kaybı (TGK) bütün gebeliklerin %1'ini oluşturur ve etiyolojisi multifaktöriyeldir. Artmış koagülobilite tekrarlayan gebelik kaybına neden olabilmekte ve antikoagülan tedavi nedeni bilinmeyen gebelik kayıplarında canlı doğum oranını arttırmaktadır. Ortalama trombosit hacmi (OTH) ve trombosit dağılım genişliği (TDG) trombosit fonksiyonları ve agregasyonu hakkında bilgi verebilmektedir. Bu çalışmada OTH, TDG ve eritrosit dağılım genişliğinin (EDG) tekrarlayan gebelik kayıpları olan hastalar ile sağlıklı kadınlar arasında bir farkının olup olmadığı araştırıldı. Gereç ve Yöntem: Toplam TGK olan 50 hasta ve yaş olarak eşleştirilmiş 49 sağlıklı kadın çalışmaya dâhil edildi. Bütün çalışma katılanlarında hemoglobin, hemotokrit, lökosit, OTH, TDG, trombosit sayısı, EDG ve TSH bakıldı. Bulgular: TGK olan hastalar ve sağlıklı kadınlar karşılaştırıldığında OTG ve TDG arasında anlamlı bir fark bulunmadı. Ancak EDG; TGK olan gurupta anlamlı olarak daha düşüktü (p:0,023). Tartşma: Mevcut çalışma; TGK ve trombosit fonksiyonları arasında bir ilişki olmadığına dair literetürdeki ilk çalışmadır. Bu çalışma aynı zamanda TGK ile EDG arasında anlamlı bir ilişki olduğunu gösteren de ilk çalışmadır.

Anahtar Kelimeler

Tekrarlayan Gebelik Kaybı; Ortalama Trombosit Hacmi; Trombosit Dağılım Genişliği; Eritrosit Dağılım Genişliği

Abstract

Aim: Recurrent pregnancy loss (RPL) affects 1% pregnancies and its etiology is multi-factorial. Hypercoagulability might result in recurrent abortions; anticoagulant therapy could potentially increase the live-birth rate in subsequent pregnancies in women with unexplained recurrent abortions. Mean platelet volume (MPV) and platelet distribution width (PDW), are a parameter of platelet functions and may be a marker for increased platelet aggregability. In this study we aimed to determine whether MPV, PDW and red cell distribution width (RDW) values differ between patients with RPL and in healthy participants. Material and Method: A total of 50 RPL patients and 49 age matched healthy women were enrolled into the study. For all subjects following tests were performed: Hemoglobin, hematocrit, white blood cells counts (WBC), MPV, PDW, platelet count, RDW and thyroid stimulating hormone (TSH). Results: Compared with healthy controls there were no statistically differences in MPV and PDW between ($p > 0.05$, respectively) in women with RPL. However, RDW was significantly lower in patients with RPL than in group with control ($p = 0.023$,). Discussion: It was first shown in the literature that patients with RPL have no significance MPV and PDW than control subjects. However RDW levels were found that it was significantly related to recurrent pregnancy loss.

Keywords

Recurrent Pregnancy Loss; Mean Platelet Volume; Platelet Distribution Width; Red Cell Distribution Width

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Introduction

Recurrent pregnancy loss (RPL) is an important health problem, defined as the loss of two or more subsequent pregnancies, which affects 1-2% of reproductive-age women. Its etiology is blamed on genetic, endocrine, infectious, anatomic, thrombophilic and immunological reasons. In spite of the increase in our knowledge about implantation and early pregnancy, the causes of 50% of repeated pregnancy losses are unknown [1]

The haemostatic system plays an important role in the successful completion of implantation and placentation. The implantation of the fertilized egg into the uterine deciduas is linked to compatible contact between the fetus, placenta and maternal circulation. The contact between the placenta and maternal circulation is of vital importance to the success of the pregnancy. Prothrombotic changes and thrombosis prevent this process and may cause miscarriage [2]. Since hypercoagulability might result in recurrent miscarriage, anticoagulant agents could potentially increase the live-birth rate in subsequent pregnancies in women with either inherited thrombophilia or unexplained recurrent miscarriage. However, efficacy and safety of thromboprophylaxis with anticoagulant therapy is too limited to recommend and controversial the use of anticoagulants in recurrent pregnancy loss [1].

Platelets play an important role in the pathogenesis of vascular diseases [3]. Mean platelet volume (MPV) and platelet distribution width (PDW) are physiological variables with haemostatic importance. The MPV test is an indicator of platelet size. Increased MPV indicates that platelet diameters are greater. An increase in MPV shows that new platelet synthesis in bone marrow has increased. Thus bigger, younger and more functional platelets are produced and MPV increases. MPV tests are generally requested for differential diagnosis of thrombocytopenia. Young and big platelets are more reactive, produce more prothrombotic factor and group more easily. They contain denser granules than small platelets and secrete more serotonin, thromboxane A2, PF4 and β-thromboglobulin [4, 5].

Increased MPV values are seen in cases of cardiovascular disease [4, 6], diabetes [4], pregnancies with growth retardation [7], polycystic ovarian disease [8], anti-phospholipids antibody syndrome (APAS) [9], preeclampsia [10] and in cases of missed aborts [11].

Complete blood count (CBC) is an easily accessible, cheap and easily evaluated method. To our knowledge there is no study at present on the MPV and PDW values in RPL patients.

The aim of this cohort study is to investigate whether any hematologic changes detectable by simple CBC precede recurrent miscarriage development.

Material and Method

This study comprises patients who attended Harran University Medical Faculty Hospital and Canakkale Onsekiz Mart University Medical Faculty Hospital Infertility and Gynecology clinics between January 2011 and June 2011. The CBC and clinical findings of these patients were evaluated retrospectively. Permission was granted by Canakkale Onsekiz Mart University Medical Faculty Ethics Committee.

Patient Selection:

The study included 50 women with at least two subsequent miscarriages and a control group of 49 women who gave birth without experiencing any miscarriages. Patients applying to the hospital with high fever or infection history within the first five days were excluded from the study. Liver, kidney disease, myeloproliferative disease, additional systemic infection or malignancy cases were excluded. Patients who had taken non-steroid anti-inflammatories, aspirin, oral anti-coagulants or oral contraceptives that may affect platelet count and functions or the coagulation system and patients who smoked were excluded from the study. For automatic blood count EDTA tubes (15% K3 EDTA 0.054ml/4.5 ml blood) were used. Samples taken from the antecubital vein were processed within 30 minutes. Full blood measurements were done on an automatic blood count machine (LH 750, Beckman Coulter, England). Normal MPV values were accepted as 7.4-12 fl (femtolitre, μm3) in the laboratories.

Statistical analysis:

All data were analyzed with SPSS 20 software (SPSS, Inc., Chicago, IL). The variables were investigated using visual (histogram, probability plots) and analytic methods (Kolmogorov-Smirnov test) to determine whether they were normally distributed. Descriptive analyses were presented using means and standard errors of mean (SEM) for normally distributed variables. The Student's t-test was used to compare these parameters between the RPL and control groups. A p-value of less than 0.05 was considered to indicate a statistically significant difference.

Results

The study comprised a total of 99 women; 50 with repeated miscarriages and 49 in the control group. The average age of women in the study was 26.18±3.63 (23-30) for the RPL group and 26.57±3.74 (23.5-29.5) in the control group. The average number of previous miscarriages in the RPL group was 3 (2-5). There was no difference between the two groups in terms of age, TSH, hemoglobin, white blood cells, hematocrit and platelet counts. The MPV values of the RPL and control groups were 8.06±1.56 and 7.72±1.10, respectively, and there was no statistically significant difference between them (p:0.346). The PDW values for the groups were 17.85±1.75 (16.5-19.3) and 17.96±2.27 (16.5-19.5), respectively, and there was no significant difference between them (p:0.823). However from the point of view of RDW values were 13.8±0.4 and 15.1±0.3, respectively, and this situation was statistically significant (p:0.023) (Table 1).

Table 1. Comparison of RPL and control groups

Variable	RPL (n=50)	Control (n=49)	P
Age (years)	26,18±3,63	26,57±3,74	0.774
TSH (mIU/L)	1,58±0,73	1,50±0,65	0.456
Hemoglobin (g/dL)	12,18±1,33	11,71±0,86	0.181
WBC (K/ml)	7917,42±1467,33	8062,32±1711,42	0.734
PDW (%)	17,85±1,75	17,96±2,27	0.823
MPV (fL)	8,06±1,56	7,72±1,10	0.346
Hematocrit (%)	36.9 ± 0.5	36.2 ± 0.4	0.272
Platelet (K/ml)	268,000 ± 7,200	273,000 ± 8,200	0.685
RDW (%)	13.8 ± 0.4	15.1 ± 0.3	0.023

RPL: recurrent pregnancy loss, TSH: thyroid stimulating hormone, WBC: white blood cell; PDW: platelet distribution width; MPV: mean platelet volume; RDW: red distribution width
*Data reported as mean ± SEM

Discussion

In this first study on RPL and platelet activity in the literatu-

re; while there was no significant difference between RPL and control groups in terms of MPV and PDW values, there was a significant difference in RDW values between the two groups.

CBC, a simple, easily accessible and relatively economic test, includes routine parameters MPV, PDW and RDW which have been researched in various pathologic situations and interesting results have been published. While increased MPV values have been found especially in many vascular, autoimmune or thrombophilic diseases, MPV is known as a prognostic marker for some diseases [4, 6, 12].

While recent studies have found increased MPV in cases of deep vein thrombosis [3], severe anemia [5], APAS [9], PCOS [8], low birth weight pregnancies and pre-eclamptic pregnancies [7, 10], it decreases in cases of Kawasaki disease [13]. In a study of third-trimester pregnancies, MPV values were higher in pregnancies with impaired uterine artery identified by Doppler measurements compared to normal pregnancies [7]. A study of PCOS patients found MPV was linked to insulin resistance, DHEA-S and increased ovarian volume and determined that this situation may be related to increased hypercoagulobility and increased risk of cardiovascular diseases [8, 14]. However our study found no difference between MPV values between women with RPL and the control group.

As PDW does not increase with platelet distension, it is suggested to be a more specific marker of platelet activation than MPV. It is thought that MPV and PDW together are more meaningful for coagulation activation [15].

To our knowledge in the English-language literature to date while there is no study of the evaluation of PDW related to RPL, there are very limited dated studies available on PDW values in pregnancy. A study evaluating PDW in second trimester pregnancies determined PDW increased significantly and progressively [16]. PDW values decrease in children with pulmonary artery hypertension and Kawasaki disease [17].

A broad participation study on coronary artery disease found increased PDW values were significant in elderly, overweight, diabetic, dilated cardiomyopathy or valvular heart disease patients and also in patients using statin and diuretics [4]. Our study found no significant difference between the RPL and control groups.

RDW is determined by calculating the variation in erythrocyte sizes. RDW is a parameter with prognostic importance for idiopathic pulmonary fibrosis and liver disease [18]. It is known as an independent marker for the mortality risk of resuscitation patients [19]. A study in hypertension patients found increased RDW values correlated strongly with heightened systolic and diastolic blood pressure. Researchers have found RDW values have positive correlation for serum bilirubin levels, prothrombin time and creatinine levels and negative correlation with serum albumin concentrations in liver disease [20]. A study comparing AA amyloidosis patients with a healthy control group found RDW values were significantly increased [21]. To our knowledge there is no study in the literature on RDW values in RPL cases. Our study found RDW values were significantly lower than the control group. Current data from RPL patients indicate future studies may be valuable.

In summary; this is the first study to compare RPL patients with a healthy control group to determine whether there is a relationship between MPV, PDW and RDW values. There was no significant difference found between the RPL and control groups in terms of MPV and PDW values. The RDW values of the RPL group were significantly higher than the control group.

Competing interests

The authors declare that they have no competing interests.

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