

Association Between the Inflammatory Parameters and Prognosis of Bell's Palsy

Enflamatuar Parametreler ve Bell Paralizi Prognozu Arasındaki İlişki

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ABSTRACT

Objective: Bell's palsy is paresis or paralysis of facial nerve associated with peripheral nerve dysfunction. The aim of this study is to investigate the role of the inflammatory parameters in predicting the prognosis of the patients with Bell's palsy.

Method: A total of 58 Bell's palsy Grade \geq III patients, according to the House-Brackmann classification, on the first presentation were taken as the study group, and 60 age and gender-matched healthy people without any disease formed the control group. The corticosteroid treatment was accepted as successful if House-Brackmann grades I and II were achieved in the post-treatment follow-up, and grades III to VI patients were evaluated as partial-not meaningful recovery. In addition, pretreatment hemogram and biochemistry tests were recorded, and the C-reactive protein (CRP)/albumin ratio, Neutrophil to lymphocyte ratio (NLR), red blood cell distribution width (RDW), and mean platelet volume (MPV) of the patients were compared.

Results: In the study group, the CRP/albumin ratio and the mean RDW were statistically significantly higher than the control group (0.958 \pm 0.91 vs. 0.478 \pm 0.322, p=0.029; 13.89 \pm 1.27 vs. 12.98 \pm 0.72, p<0.001). RDW was statistically significantly higher in those with partial-not meaningful recovery than the successfully treated patients (14.43 \pm 1.59 vs. 13.67 \pm 1.06, p=0.030). Other laboratory parameters were not significantly different (P>0.05).

Conclusion: Higher CRP/albumin, RDW, NLR, MPV were related to a poor prognosis for Bell's palsy. RDW, which to date has been a widely used marker for inflammation, could be a potentially promising marker for use in predicting prognosis in Bell's palsy.

Keywords: Albumin, Bell's palsy, C-reactive protein, red blood cell distribution width

ÖZ

Amaç: Bell paralizi periferik sinir disfonksiyonu ile ilişkili fasiyal sinirin akut parazi veya paralizisidir. Bu çalışmanın amacı, Bell paralizi olan hastaların prognozunu tahmin etmede enflamatuar parametrelerin önemini araştırmaktır.

Yöntem: House-Brackman sınıflandırmasına göre Bell paralizi \geq III olan toplam 58 hasta çalışma grubu olarak alınmış, kontrol grubunu ise yaş ve cinsiyet açısından eşleştirilmiş 60 sağlıklı gönüllü oluşturmuştur. Tedavi sonrası takipte kortikosteroid tedavisinin başarısı House-Brackmann grade I ve II olarak kabul edildi ve grade III ile VI olan hastalar kısmi-anlamli olmayan iyileşme olarak değerlendirildi. Tedavi öncesi hemogram ve biyokimya testleri kaydedildi. Çalışma ve kontrol gruplarının C-reaktif protein (CRP)/albümin oranı, nötrofil/lenfosit oranı (NLO), kırmızı kan hücresi dağılım genişliği (RDW) ve ortalama trombosit hacmi (MPV) değerleri karşılaştırıldı.

Bulgular: C-reaktif protein/albümin çalışma grubunda kontrol grubuna göre istatistiksel olarak anlamlı derecede yüksekti (0,958 \pm 0,91'e karşı 0,478 \pm 0,322, P=0,029). Ortalama RDW, çalışma grubunda kontrol grubuna göre anlamlı olarak daha yüksekti (13.89 \pm 1.27'ye karşı 12.98 \pm 0.72, P<0.001). RDW değeri, kısmi- anlamlı olmayan iyileşme gösterenlerde, başarıyla tedavi edilen hastalara kıyasla istatistiksel olarak anlamlı derecede daha yüksekti (14.43 \pm 1.59'a karşı 13.67 \pm 1.06, p=0.030). Diğer laboratuvar parametrelerinde gruplar arasında anlamlı farklılık tespit edilmedi (P>0.05).

Sonuç: CRP/albümin, RDW, NLO ve MPV yüksekliği Bell paralizisinde kötü prognozla ilişkilidir. Bugüne kadar yaygın olarak kullanılan enflamatuar bir belirteç olan RDW, Bell paralizisinde prognozu tahmin etmede umut verici bir belirteç olabilir.

Anahtar kelimeler: Bell paralizi, C-reaktif protein, albümin, kırmızı kan hücresi dağılım genişliği

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INTRODUCTION

Bell's palsy is a facial deficiency and paralysis related to peripheral nerve dysfunction. Although genetic, immunological, vascular, and infectious etiologies have been suggested in Bell's palsy, novel researches have associated Bell's palsy with herpes simplex virus-1 (HSV-1) (1, 2). The mostly emphasized theory is that edema and ischemia cause impingement of the facial nerve within the canal of the facial bone. This edema could be seen on magnetic resonance imaging (MRI) scans, focusing on the facial nerves. Impingement of the facial nerves in the labyrinth segment due to the inflammatory reaction is the leading etiopathogenetic factor (3). Previous studies have proven that Bell's palsy develops because of the inflammation of the facial nerves (4).

In recent years, the neutrophil-lymphocyte ratio (NLR) has been recognized as an inflammation marker in Bell's palsy (5). Red blood cell distribution width (RDW) is a value commonly estimated in the blood tests and refers to the variation in the volume and size of circulating erythrocytes (6). The importance of RDW in inflammation and disease prognosis has previously been investigated in detail (6, 7). As a positive acute-phase reactant, C-reactive protein (CRP) is used for diagnosing and evaluating treatment effectiveness in patients with infection/inflammation (8). Albumin is also known as a negative acute-phase protein. In addition to the fact that patients with acute inflammation show decreased albumin levels, this decrease has also been observed in patients with chronic malnutrition and inflammation (9). Therefore, it has been thought that measurements of CRP and albumin could be used in combination for predicting the prognosis in acute or chronic inflammation periods (10, 11).

This study evaluates the effectiveness of RDW and the CRP/albumin ratio, which are reproducible, inexpensive, and easily available markers as they can be obtained from routine blood tests in predicting the Bell's palsy prognosis.

MATERIAL AND METHODS

Our retrospective study was conducted in the Otorhinolaryngology Clinic covering the period between January 2017 and February 2020. All study procedures were applied in compliance with the principles of the Declaration of Helsinki. The Institutional Review Board (decision no:2020/34) granted the study approval. The clinic archives were scanned for identification of cases with Bell's palsy. Exclusion criteria included the presence of any inflammatory or nutritional disorders that could change blood parameters, acute infection or inflammation, pneumonia, acute/chronic kidney failure, diabetes mellitus, chronic liver disease, chronic obstructive pulmonary disease, obstructive sleep apnea, connective tissue disease, inflammatory bowel disease, central facial paralysis, traumatic facial paralysis, Ramsay-Hunt syndrome, previous otological surgery or active otological disease, and also smokers and alcohol users, or patients who had presented five days after the first episode of Bell's palsy were not enrolled in the study.

According to the House-Brackmann (12) classification on the first presentation, 58 patients with Bell's palsy Grade III were taken as the study group, and 60 age and gender-matched healthy people without any disease formed the control group. According to physical examination and patient records, healthy subjects without any chronic illness or drug history were selected from the check-up clinic of the hospital. The corticosteroid treatment was accepted as successful if House-Brackmann grades I and II were achieved in the post-treatment follow-up, and patients with grades III to VI were evaluated as partial-not meaningful recovery. Pretreatment hemogram and biochemistry tests were recorded. In addition, the patients were assessed with gadolinium-enhanced MRI on the day of admission. Based on the facial nerve contrast involvement in the T1-weighted MRI reports, patients were separated into two subgroups: Bell's palsy with (BPWE) and without (BPWOE) edema. All selected patients were treated with corticosteroids (1 mg/kg/day prednisone as the

initial dose), with a gradual dose decrease continued for at least two weeks.

Laboratory analyses

Data related to blood test parameters such as neutrophil count, CRP, platelet count, lymphocyte count, MPV, RDW, and albumin were scanned from files. In addition, the CRP to albumin ratio was estimated, and the result was compared with the NLR, RDW, and MPV values in both groups.

Statistical analysis

Study data were analyzed statistically using R 3.2.1 for Windows, and Excel 2016 software. Descriptive statistics of the quantitative variables were stated as standard deviation, median, mean, min-max. Qualitative variables were expressed as percentages and frequencies. The Shapiro-Wilk test was used for computing conformity of quantitative variables to normal distribution. The comparisons of two groups of quantitative variables not showing normal distribution were conducted via Mann-Whitney U test, and for variables with normal distribution, the independent samples t-test was used. The Yates chi-square test was used for intergroup comparisons of qualitative variables. In all statistical analyses, a statistically significant value of $P < 0.05$ was taken into consideration.

RESULTS

A total of 118 subjects, including 60 healthy individuals in the control and 58 cases with Bell's palsy in the patient groups were examined in the study. The demographic information and laboratory findings of the groups are shown in Table 1. In both groups, mean gender and age distributions were similar ($P > 0.05$).

A statistically significantly higher CRP/albumin ratio and mean RDW were observed in the study group (0.958 ± 0.91 vs. 0.478 ± 0.322 , $P = 0.029$; 13.89 ± 1.27 vs. 12.98 ± 0.72 , $P < 0.001$). A higher MPV was also observed in the study group, however it was not determined as a significant biomarker ($P = 0.260$). A higher NLR in the study group was also observed, which was statically significant ($P = 0.001$). The results of patients with successful treatment and those with partial-not meaningful recovery are summarized in Table 2.

A statistically significant RDW value was seen in those with partial-not meaningful recovery compared to the successfully treated patients (14.43 ± 1.59 vs. 13.67 ± 1.06 , $P = 0.030$). However, no significant differences were determined among the other laboratory parameters ($P > 0.05$).

Table 1. Demographic characteristics of the patients in both groups

	Patients	Control	p
Age	45.25±12.62	44.12±16.18	0.674
Gender			
Male	26 (43.3%)	24 (41.4%)	0.830
Female	34 (56.7%)	34 (58.6%)	
RDW	12.98±0.72 13.05 (10.5-14.5)	13.89±1.27 13.90 (10.5-17.6)	<0.001
MPV	8.76±0.97 8.70 (6.4-10.8)	8.99±1.04 8.90 (7.2-12.2)	0.260
CRP / albumin	0.478±0.322 0.42 (0-1.36)	0.958±0.91 0.71 (0-3.00)	0.029
Neutrophil / lymphocyte	1.833±0.820 1.69 (0.92-7.00)	2.492±1.49 1.99 (0.26-9.14)	0.001

Independent sample t- test (Age)

Pearson's chi-square test (Gender)

Mann -Whitney U test (RDW, MPV, CRP/albumin, Neutrophil/lymphocyte)

CRP; C-reactive protein, NLR; neutrophil to lymphocyte ratio, MPV; mean platelet volume, RDW; red blood cell distribution width

Table 2. Clinical characteristics of patients in the successful treatment and partial-not meaningful recovery groups

	Successful treatment	Partial-not meaningful recovery	p
RDW	13.67±1.06 13.70 (11.90-15.90)	14.43±1.59 14.20 (10.5-17.6)	0.030
MPV	8.85±1.02 8.70 (7.20-10.90)	9.34±1.03 9.30 (7.80-12.20)	0.137
CRP / albumin	0.902±0.944 0.50 (0-3.00)	1.090±0.828 0.809 (0.14-3.00)	0.151
Neutrophil / lymphocyte	2.270±1.219 1.94 (0.26-6.69)	3.025±1.944 2.55 (1.35-9.14)	0.081

#Mann-Whitney U test

CRP; C-reactive protein, NLR; neutrophil to lymphocyte ratio, MPV; mean platelet volume, RDW; red blood cell distribution width

Table 3. Recovery status of patients in correlation with the facial nerve enhancement on contrasted MRI.

	Successful treatment	Partial-not meaningful recovery
BPWE	8 (19.5%)	12 (70.6%)
BPWOE	33 (80.5%)	5 (29.4%)

Yates chi-square test

BPWE; Bell's palsy with edema BPWOE; Bell's palsy without edema.

Significant differences were reported on MRI among patients with complete and partial-not meaningful recovery ($P < 0.001$). The rate of BPWE in those with complete recovery was 19.5%, while this rate was 70.46% for those with partial-not meaningful recovery (Table 3, Figure 1). In addition, a higher but non-significant NLR was reported in patients with BPWE ($P = 0.330$, Figure 2).

DISCUSSION

Although pathophysiology of Bell's palsy has not been elucidated yet, viral facial nerve inflammation, microvascular failure, and autoimmune diseases have been cited as possible causes (13,14). Inflammatory and immunological causes are the most studied mechanisms which have been accepted as a major factor in the pathogenesis of Bell's palsy (15). The most likely cause of Bell's palsy has been reported to be facial nerve edema caused by varicella-zoster virus and herpes virus (16).

Many clinical studies have showed that RDW could be a predictor of mortality and length of hospital stay (17). In addition, RDW values have

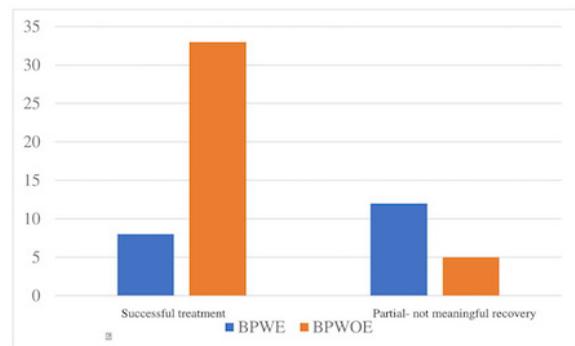


Figure 1. Graph of MR groups according to the recovery status

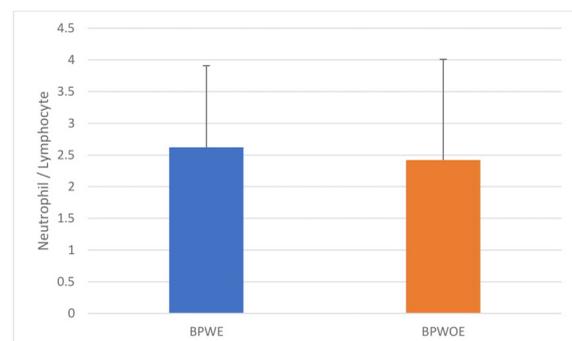


Figure 2. Graph of relationship between MR groups and neutrophil/ lymphocyte

been associated with markers of inflammation such as C-reactive protein and erythrocyte sedimentation rate (18). Thus, RDW can predict the association between current pathology and an inflammatory event, and recent studies have identified RDW as a new inflammatory marker (6, 7). Although high RDW values in Bell's palsy patients appears to be due to inflammation, this situation is still uncertain. Our study reported a significantly higher median RDW for Bell's palsy patients. It was also demonstrated that partial-not meaningful Bell's palsy recovery caused a significant increase in RDW values.

The CRP/albumin ratio is currently a widely used marker of inflammatory processes in various diseases. CRP levels increase depending on the severity of inflammation and infection (19), and albumin as a negative acute-phase protein related to oxidative stress, provides an idea about diagnosing infection and inflammatory complications (20). In a previous study, a significantly higher CRP/albumin ratio was determined in patients with Bell's palsy than in the control group, and CRP/albumin ratio was also significantly higher in unrecovered patients (21). In our study, the CRP/albumin ratio was statistically significantly higher in the patient group than in the control group. Regardless of a higher CRP/albumin ratio detected in patients with a partial not-meaningful recovery than successfully treated cases, the intergroup difference was not significant.

Use of NLR and CRP-albumin ratios has been reported to predict inflammation (11,22). Neutrophils are essential factors in the production of cytokines and they are often increased in inflammatory disorders, whereas the lymphocyte count may decrease during inflammation. The NLR which is a potential predictor of Bell's palsy was reportedly higher in unhealed patients in previous studies (23,24). Bucak et al.⁵ showed that NLR levels were significantly higher in patients with Bell's palsy, and patients with unsatisfactory recovery had higher NLR levels. Similar to that study, Cayir et al.²¹ stated an association between high NLR levels and poor prognosis. Conversely, Horibe et al.²⁵ claimed

that NLR was not a significant marker. In the current study, a significantly higher mean NLR was observed in the study group. Although the NLR was higher in the patients with partial-not meaningful recovery, it was not determined to be a statistically significant biomarker.

Gadolinium-enhanced MRI scans of the normal facial nerve could not be achieved, however these scans are recommended as a diagnostic tool for evaluating Bell's palsy (26). Because of the increased extracellular fluid from edema and inflammation, contrast-enhancement of the facial nerve may have a diagnostic value in Bell's palsy. However, in a previous study, prognostic significance of gadolinium-enhanced MRI of the facial nerve in patients with Bell's palsy was not observed (27). In the current study, regarding Bell's palsy patients with (BPWE) and without (BPWOE) edema, a statistically significant difference was observed between those who recovered completely and those with partial-not meaningful recovery ($p = 0.001$). The rate of BPWOE was 80.5% in successful treatment and 29.4% in partial not-meaningful recovery subgroups. In comparing NLR in the BPWOE and BPWE subgroups, although NLR was higher in patients with BPWE, this difference was not statistically significant. These results may show that the diagnostic power of the gadolinium enhanced-MRI is dependent on the severity of the nerve damage.

This study has some limitations that should be further explored in future studies. There is also a necessity for a longitudinal follow-up to ascertain whether variations in the inflammatory biomarkers have predictive value in the prognosis of Bell's palsy. Nevertheless, this study could guide future studies on blood test parameters related to inflammation of Bell's palsy patients.

CONCLUSION

The results of the present study indicated that a higher CRP-albumin ratio, RDW, NLR, and MPV were related to a poor prognosis for Bell's palsy patients. Thus, RDW, which to date has been a widely used marker for inflammation, could be a

potentially promising marker for use in predicting prognosis in Bell's palsy. Nevertheless, there is a need for further studies on this subject.

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