Research Article / Özgün Araştırma

Neutrophil-lymphocyte and Platelet-lymphocyte Ratios in Febrile Seizures

Febril Konvülziyonlarda Nötrofil-lenfosit ve Platelet-lenfosit Oranları

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Abstract

Introduction: The neutrophil-lymphocyte ratio (NLR) and the platelet-lymphocyte ratio (PLR) are accepted as the indicators of systemic inflammatory response. The aim of this study was to evaluate the value of the changes in NLR and PLR values as a biomarker in patients presenting with febrile seizure.

Methods: Patients with a diagnosis of febrile seizure were retrospectively evaluated. A total of 175 febrile seizure patients and 150 healthy children constituting the control group were included in the study. The febrile seizure type was simple in 113 and complicated in 62 subjects.

Results: The NLR value was higher in the febrile seizure group (3.36±3.28) than in the control group (1.82±2.21) with statistical significance (p=0.000). The PLR value was also higher in the febrile seizure group (135.10±80.44) than in the control group (123.43±67.06) but without statistical significance (p>0.05). There was no statistically significant relationship between the NLR or PLR values and age. The main characteristic influencing the NLR and PLR values in the febrile seizure group was found to be the type of febrile seizure.

Conclusion: Febrile seizure diagnosis and typing is done clinically, if the examination is performed for any reason, the NLR and PLR values can provide guidance in the differentiation of simple and complex febrile seizures.

Keywords: Febrile seizure, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio

Öz

Giriş: Nötrofil/lenfosit oranı (NLO) ve platelet/lenfosit oranı (PLO) sistemik enflamatuvar cevabın göstergesi olarak kabul edilmektedir. Burada febril konvülziyon ile başvuran hastalarda NLO ve PLO değerlerinde meydana gelen değişikliklerin ve bir biyobelirteç olarak kullanılabilirliğinin değerlendirilmesi amaçlandı.

Yöntemler: Febril konvülziyon tanısı alan hastalar geriye dönük olarak incelendi. Çalışmaya febril konvülziyonlu 175 hasta ile kontrol grubu olarak sağlıklı 150 çocuk alındı. Febril konvülziyon tipi, hastaların 113'ünde basit, 62'sinde komplike idi.

Bulgular: Febril konvülziyon grubunda NLO değeri (3,36±3,28), kontrol grubuna (1,82±2,21) göre yüksekti ve bu yükseklik istatistiksel olarak anlamlı saptandı (p=0,000). PLO değeri de febril konvülziyon grubunda (135,10±80,44) kontrol grubuna (123,43±67,06) göre yüksek saptandı, ancak bu farklılık istatistiksel olarak anlamlı saptanmadı (p>0,05). Yaş ile NLO-PLO değerleri arasında ilişki saptanmadı. Febril konvülziyonlu hastalarda NLO ve PLO değerini etkileyen temel özelliğin febril konvülziyonun tipi olduğu saptandı.

Sonuç: Febril konvülziyon tanısı ve tiplemesi klinik olarak yapılır, herhangi bir nedenle tetkik yapıldıysa NLO ve PLO değerleri basit ve komplike febril konvülziyon ayrımında yol gösterici olabilir.

Anahtar Kelimeler: Febril konvülziyon, nötrofil-lenfosit oranı, platelet-lenfosit oranı

Introduction

Febrile seizure (FS) is the most common seizure of childhood between 6 months-6 years age group. In the definition of American Academy of Pediatrics (AAP), there should be no intracranial infection, metabolic disorder, or history of afebrile seizure to diagnose FS. The condition is called simple febrile seizures (SFS) if the seizures are generalized and last less than 15 minutes and do not recur within 24 hours while other cases are called complex febrile seizures (CFS).[1] The typing of the FS is important for patient management and determining the condition's prognosis.[2] Both types are generally not

expected to have long-term sequela on motor or cognitive development, although CFS has been associated with a slightly higher rate of epilepsy.

The most of FS occurs at home or on the way to the hospital so anamnesis is very important for diagnosis. Serious anxiety, panic and fear caused by FS in parents cause a decrease in anamnesis reliability. In addition, physical examination findings have often changed or resolved upon admission. Therefore, there is difficulties in the differential diagnosis with events such as febrile reaction, cutis marmorata, hyporesponsive state, breath holding spell as well as the clinical typing of FS types. A side from clinical identification, some recent research evaluated the laboratory parameters in description of seizure types and in determining the prognosis and medical treatment to be used. The neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are inexpensive and simple inflammation indicators with gradually increasing popularity and can easily be calculated using the neutrophil, lymphocyte, and platelet values from the complete blood count test. Neutrophils can only survive for a short time, about one day, in the blood and their numbers increase in systemic infection or inflammatory response. There are many studies in the literature on the association of the NLR value with various clinical conditions.[3-7] Platelet activation increases in case of inflammation. Increased mean platelet volume is an indicator of platelet activation in FS.[8] The possibility of using the PLR value as an inflammation indicator is also recognized.[9-11] In this study, we aimed to evaluate the NLR and the PLR for differentiating of FS types.

Materials and Methods

Patients who had referred to the Ankara Yıldırım Beyazıt University Yenimahalle Training and Research Hospital's Pediatric Emergency Department with FS between 1 January 2015 and 1 November 2016 were evaluated. Medical data of the patients who had complete blood count examination was reviewed retrospectively. Age matched healthy children were evaluated as a control group. AAP criteria was used to confirm the diagnosis of FS. Patients with a history of afebrile seizure, a structural or developmental anomaly, metabolic disorder, central nervous system infection findings or toxic encephalopathy were excluded. The demographic features, seizure type, and complete blood count results were evaluated. Routine laboratory testing is not required for patients presenting with FS. Therefore, the complete blood count of the patients who were requested in relation to the current infection at the time of admission was evaluated. The NLR and PLR values were calculated by dividing the neutrophil and platelet count to the lymphocyte count, as obtained from the complete blood count test results.

The ethics committee approval for the study was obtained from the Ankara Yıldırım Beyazıt University Yenimahalle Training and Research Hospital's Clinical Studies Ethics Committee (2016/59). Written informed consent could not be obtained from the patients because it was a retrospective study.

Statistical Analysis

We used IBM SPSS Statistics for Windows 21.0 (Armonk, NY: IBM Corp) to analyze the data. Descriptive statistics were used for the demographic characteristics of the patients. The categorical variables were expressed as numbers and percentages; the numerical data were expressed as mean ± standard deviation. The student's t-test was used for normally distributed variables, and Mann-Whitney U test was used for quantitative or ordinary scaled variables. The chi-square or Fisher's Exact tests was used to analyze the proportions accurately. P-value <0.05 was accepted statistically significant.

Results

One hundred and seventy-five patients were included in the study. The mean age of patients was 23.1±1.36 months, and 100 (57.1%) subjects were male. The control group included 150 healthy children. The FS type was simple in 113 patients and complex in 62 patients. The mean age was higher in the CFS group while there was no difference regarding gender. A family history of FS was present in 43 patients (24.6%) and of epilepsy in 26 patients (14.9%).

Comparison of the FS and control group showed a statistically significant difference regarding the leukocyte, neutrophil, lymphocyte, and platelet counts (p<0.05). The mean NLR value was 3.36±3.28 in the FS group and 1.82±2.21 in the control group with a statistically significant difference (p<0.001). The mean PLR value was 135.10±80.44 in the FS group and 123.43±67.06 in the control group with no statistically significant difference (p>0.05) (Table 1).

Separating the FS patients into SFS and CFS groups revealed a statistically significant difference between the groups for both the NLR and PLR values (Table 2). The increase in the neutrophil count was not significant while there was a statistically significant decrease in the lymphocyte count in the CFS group.

Discussion

The etiopathogenesis of FS has not been fully explained but some immune mechanisms are thought to be involved. The NLR and the PLR are accepted as an indicator of the systemic inflammatory response. The neutrophils and lymphocytes are the main cells of the immune system and can initiate and

Table 1. Demographic and laboratory results of febrile seizure and control groups

	Febrile seizure (n=175)	Control (n=150)	p
Age (month)	23.1±1.36	23.7±1.61	0.762
Gender (male)	100 (57.1%)	79 (52.6%)	0.435
White blood cell count (10³/mm³)	11.08±4.83	7.99±1.93	**0.000**
Neutrophil count (10³/mm³)	7.27±4.61	3.93±2.13	**0.000**
Lymphocyte count (10³/mm³)	2.93±1.64	3.18±1.36	**0.017**
Platelet (10³/mm³)	312.52±103.27	328.94±85.99	**0.033**
Neutrophil to lymphocyte ratio	3.36±3.28	1.82±2.21	**0.000**
Platelet lymphocyte ratio	135.10±80.44	123.43±67.06	0.134

increase the release of cytokines that leads to the start of inflammation. Recently, NLR has been used as a predictor for differentiating FS types.[12,13] We evaluated whether NLR and PLR had any diagnostic importance in patients with FS and whether they could be used as a biomarker in differentiating SFS and CFS. We determined that the PLR value could be used as a marker to differentiate SFS and CFS while the NLR value could be used to differentiate both SFS and CFS and the FS and control groups. FS patients may have neutrophil and lymphocyte concentration changes as an indicator of their cellular stress due to the underlying infection.

Studies from our country have revealed that FS is more common in males and that the mean age of CFS patients is low but without statistical significance.[12,13] We also found no difference regarding gender in our study and the mean age of the CFS patients was higher than the SFS group.

Aydin et al.[14] have reported that NLR values are the lowest in the ≤1 years age group and increase with age. The highest value was found to be 1.86 in the ≤1 years age group and 1.97 in the 1-2 years age group. They also found a significant difference in the NLR values between the genders between the ages of 1 and 10 years.[14] The NLR value of the FS group in our study where most of the subjects were aged 2 years or below was above the normal reference value.

The NLR value has been shown to increase in disorders such as asthma, cardiovascular diseases, Kawasaki disease, familial Mediterranean fever and *Brucellosis* in children [3-7], and acute pancreatitis, septicemia, status epilepticus and restless legs syndrome in adults.[15-18] It is known that the PLR value can be used as an inflammatory marker in disorders such as pneumonia, Guillain-Barré syndrome, and rheumatoid arthritis.[9-11] The PLR value has been shown to increase with increasing cancer stage in adult gastric cancer patients.[19] A review of previous studies reveals that the common mechanism is a response to increased inflammation. We are not aware of a previous study evaluating the status of the PLR value in FS. We have demonstrated that the PLR value can help when determining the type of FS in this study.

Table 2. Demographic and laboratory results of SFS and CFS groups

	SFS (n=113)	CFS (n=62)	p
Age (month)	20.98±1.21	26.96±1.53	**0.011**
Gender (male)	64 (56.6%)	36 (58.0%)	0.855
White blood cell count (10³/mm³)	11.19±4.77	10.88±4.96	0.625
Neutrophil count (10³/mm³)	7.22±4.83	7.35±4.20	0.571
Lymphocyte count (10³/mm³)	3.15±1.74	2.51±1.35	**0.019**
Platelet (10³/mm³)	305.38±102.20	325.53±104.77	0.162
Neutrophil to lymphocyte ratio	3.16±3.23	3.74±3.37	**0.043**
Platelet lymphocyte ratio	121.84±65.89	159.27±97.81	**0.002**

SFS: Simple febrile seizures, CFS: Complex febrile seizures

Goksugur et al.[12] and Yigit et al.[13] have reported different NLR values in the SFS and CFS groups. We similarly found a significant difference in NLR values. Liu et al.[20] reported that elevated NLR and MPV/PLT ratio (MPR) effect the FS risk. They confirmed that NLR is an independent predictor in differentiating of FS types and emphasized that NLR and MPR may have a synergistic effect.[20] This state may be related to increased neutrophil-mediated inflammation and reduced anti-inflammation response.[21,22]

Infection-related tests were requested to some patients for the treatment and follow-up of the concomitant infection is independent of the diagnosis of FS and is related to the follow-up and treatment process of the infection. Therefore, there is no routine laboratory test for patients with FS in our center, as is the case all over the world.

Study Limitations

The limitations of our study were low patient numbers and retrospective nature. Further longitudinal studies on a larger sample are needed to validate the present results and postulate a possible diagnostic potential.

Conclusion

FS diagnosis and typing is done clinically, if the examination is performed for any reason, the neutrophil-lymphocyte and PLRs can provide guidance in the differentiation of simple and complex FS.

Ethics

Ethics Committee Approval: The ethics committee approval for the study was obtained from the Ankara Yıldırım Beyazıt University Yenimahalle Training and Research Hospital's Clinical Studies Ethics Committee (2016/59).

Informed Consent: Written informed consent could not be obtained from the patients because it was a retrospective study.

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Authorship Contributions

Surgical and Medical Practices: S.İ.Ö., H.A., A.N.Ç.K., Concept: S.İ.Ö., H.A., A.N.Ç.K., Design: S.İ.Ö., H.A., A.N.Ç.K., Data Collection or Processing: S.İ.Ö., H.A., A.N.Ç.K., Analysis or Interpretation: S.İ.Ö., H.A., A.N.Ç.K., Literature Search: S.İ.Ö., H.A., A.N.Ç.K., Writing: S.İ.Ö., H.A., A.N.Ç.K.

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