Neutrophil to Lymphocyte and Platelet to Lymphocyte Ratios in Peritoneal Dialysis-Related Peritonitis

Periton Diyalizi İlişkili Peritonitlerde Nötrofil-Lenfosit ve Platelet-Lenfosit Oranları

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ABSTRACT

OBJECTIVE: Peritonitis is an important problem for peritoneal dialysis (PD) patients. It has been demonstrated that the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) increase nonspecifically in end-stage renal disease (ESRD) without infection. The neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have been recently investigated as a new alternative inflammatory parameter to distinguish infections and other inflammatory events in a number of studies. We aimed to investigate the diagnostic value of NLR and PLR in bacterial PD peritonitis.

MATERIAL and METHODS: In this study, we evaluated 40 peritonitis episodes that we treated. NLR and PLR were calculated from the same blood sample at the beginning and after the treatment of peritonitis. The same parameters were evaluated for 20 control subjects.

RESULTS: Classical inflammatory markers such as CRP and ESR; NLR and PLR decreased with the successful treatment of peritonitis, and levels of these parameters were significantly different between the periods ($p< 0.05$).

CONCLUSION: Both NLR and PLR are valuable markers to follow the course of peritonitis and response to the treatment of peritonitis in correlation with conventional inflammation markers of infection. NLR and PLR are also more simple to calculate and cheaper parameters than classical markers.

KEY WORDS: Peritoneal dialysis, Peritonitis, Neutrophil to lymphocyte ratio, Platelet to lymphocyte ratio

ÖZ

AMAÇ: Periton diyalizi (PD) hastaları için peritonit önemli bir sorundur. Son dönem böbrek hastalığı (SDBH) olgularında enfeksiyon olmaksızın, eritrosit sedimantasyon hızı (ESH) ve C- reaktif protein (CRP) düzeylerinin arttığı gösterilmiştir. Nötrofil-lenfosit (NLO) ve platelet-lenfosit oranları (PLO) güncel çalışmalarda enfeksiyöz ve öteki inflamatuvar olayların ayırımında yeni inflamatuvar belirteçler olarak çalışılmıştır. Bakteriyel PD peritonitlerinde NLO ve PLO'larının tanısal değeri araştırıldı.

GEREÇ ve YÖNTEMLER: Tedavi ettiğimiz 40 peritonit epizodunu değerlendirdik. NLO ve PLO başlangıçta ve peritonit tedavisi sonrası değerlendirildi. Aynı parametreler 20 kontrol olgusu için de hesaplandı.

BULGULAR: CRP ve ESH gibi klasik inflamasyon belirteçleri, NLO ve PLO peritonitin başarılı tedavisi sonrası anlamlı biçimde azaldı ($p< 0,05$).

SONUÇ: NLO ve PLO peritonit seyrinin takibinde değerli parametreler olup, peritonit tedavisi ile klasik inflamasyon belirteçleriyle korelasyon gösteren seyir izlemektedirler. Dahası NLO ve PLO, klasik belirteçlere kıyasla hem daha ucuz ve hem de hesaplanması kolay parametrelerdir.

ANAHTAR SÖZCÜKLER: Periton diyalizi, Peritonit, Nötrofil-lenfosit oranı, Platelet-lenfosit oranı

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INTRODUCTION

Peritoneal dialysis (PD) is an important renal replacement therapy modality, and for many patients it is simpler and better tolerated than in-center hemodialysis (HD) (1). However, peritonitis is one of the major complications of PD because it generally necessitates long-term antibiotherapy and sometimes removal of the PD catheter and disturbs the life quality of the patients.

End-stage renal disease (ESRD) patients have increased serum levels of inflammation mediators including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), tumor necrosis factor-alpha and interleukin-6 (2-4). Recently, the neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were introduced as potential markers to determine inflammation in various disorders (5,6). In addition, it was shown that NLR and PLR were closely associated with increased inflammation status in both HD and PD patients (7). During peritonitis, not only dialysate cell count but also increased levels of inflammation markers such as CRP and ESR may be valuable for diagnosis and follow-up (8). To date, any study about PLR/NLR and its association with inflammation is lacking in PD patients with peritonitis. We therefore aimed to determine PLR and NLR during peritonitis and after successful treatment for PD patients and to evaluate the diagnostic and follow-up value of these ratios in this population.

MATERIALS and METHODS

We retrospectively evaluated 40 peritonitis cases that we treated in past three years in Firat University Nephrology Clinic, Elazig, Turkey and compared their results with 20 healthy subjects. Our population consisted of PD patients aged 18-75 years with an acute bacterial peritonitis attack. Peritonitis was defined as the development of cloudy dialysate with or without abdominal pain, fever, nausea, dialysate white blood cell (WBC) count higher than 100/mm^3 and the presence of microorganisms (9). Patients with acute comorbidites such as active infection of other sites of the body, sepsis, acute cardiac disorders, and diabetic ketoacidosis were excluded. Urea, creatinine, hemoglobin, albumin, uric acid, phosphorus, total cholesterol, CRP, ESR levels were collected from the database of our hospital. NLR and PLR were calculated from the same blood sample at the beginning and approximately 15 days after the completion of successful treatment of peritonitis. Although 15 days may be thought to be early to check the inflammation parameters, it was the most suitable time in order to obtain laboratory parameters for all patients in this regard and this is a limitation of this study. We therefore evaluated our NLR and PLR ratios in two periods as acute and healed period of peritonitis. For the calculations of these ratios, neutrophil and platelet counts were divided to lymphocyte counts, respectively.

Statistical analysis was performed by using SPSS 12 (SPSS Inc., Chicago, IL, USA). The data are expressed as mean ± standard deviation. A p value < 0.05 was considered as significant. Parameters during the periods (acute and healed period of peritonitis) were compared with the paired T-test and parameters of patients' healed period and control group were analyzed with the independent T-test. Correlations were analyzed with Pearson's correlation test.

RESULTS

Demographic characteristics of our subjects are shown in Table I.

Table I: Demographic characteristics of the patient and control groups.

	Patients (n= 40)	**Control group (n=20)**
Age (years)	50.93 ± 14.78	39.65 ± 10.61
Gender (male/female)	25/15 (62.5% / 37.5%)	17/3 (85% / 15%)

In this study, the levels of conventional inflammation markers such as CRP and ESR were increased and the elevated NLR and PLR levels decreased with the successful treatment of peritonitis while the levels of these parameters between periods were significantly different (p< 0.05 for all parameters). Additionally albumin, uric acid and phosphorus levels increased after the successful treatment of peritonitis with a statistically significant difference between the periods (p< 0.05 for each parameter). Levels of total cholesterol were not significantly different between the periods (p> 0.05) as shown in Table II.

Table II: Laboratory values during peritonitis and after treatment for patient group (n=40).

	Peritonitis	**After treatment**
Albumin (g/dl)	3.03 ± 0.59	3.62 ± 0.60 ***
Uric acid (mg/dl)	5.32 ± 1.28	6.62 ± 1.53 ***
Phosphorus (mg/dl)	4.14 ± 1.14	5.33 ± 1.31 ***
Total cholesterol (mg/dl)	211.33 ± 252.50	205.78 ± 44.21
CRP(mg/dl)	15.38 ± 7.91	1.80 ± 1.38 ***
ESR (mm/h)	110.83 ± 23.68	43.43 ± 19.45 ***
NLR	14.15 ± 12.67	4.24 ± 4.36 ***
PLR	396.18 ± 330.23	189.44 ± 77.03 ***

***p<0.001; values during peritonitis vs. after treatment.

We observed that PD patients had higher NLR, PLR and ESR levels than control subjects ($p<0.05$). CRP and ESR decrease was compatible and in correlation with NLR and PLR decrease after the treatment of peritonitis, although without statistical significance. Interestingly, CRP levels after the treatment of peritonitis were not different from control group. On the other hand, NLR and PLR after treatment were significantly higher than the control group as shown in Table III (4.24 ± 4.36 vs. 1.63 ± 0.34 and 189.4 ± 77 vs. 117.5 ± 36.6, respectively).

Table III: Comparison of laboratory values between the patient and control groups.

	After treatment	Control group (n=20)
Urea (mg/dl)	138.77 ± 38.39	28.5 ± 6.39 ***
Creatinine (mg/dl)	9.21 ± 2.61	0.89 ± 0.19 ***
Hemoglobin (g/dl)	10.39 ± 1.61	14.89 ± 1.25 ***
Albumin (g/dl)	3.62 ± 0.60	4.62 ± 0.35
Uric acid (mg/dl)	6.62 ± 1.53	5.42 ± 1.33 **
Phosphorus (mg/dl)	5.33 ± 1.31	3.47 ± 0.61 ***
Total cholesterol (mg/dl)	205.78 ± 44.21	181.45 ± 44.08 *
CRP (mg/dl)	1.80 ± 1.38	2.29 ± 1.11
ESR (mm/h)	43.43 ± 19.45	7.7 ± 6.6 ***
NLR	4.24 ± 4.36	1.63 ± 0.34 *
PLR	189.44 ± 77.03	117.54 ± 36.6 ***

* $p<0.05$; ** $p<0.01$; ***$p<0.001$; patient group vs. control group.

DISCUSSION

Peritonitis is one of the major problems for PD patients. It increases the morbidity and mortality rates in this patient group (10). Although clinical manifestations can vary from patient to patient, abdominal pain, fever, nausea and vomiting are the most common symptoms. For the diagnosis of peritonitis, 2 of these 3 criteria are essential: i- Symptoms and signs of peritoneal inflammation, ii- Increased WBC in peritoneal fluid (leucocyte > 100/mm^3 and polymorphonuclear leucocytes making up >50 % of cells) and cloudy dialysate, iii- Demonstrating the infectious agent with gram staining or culture (1). Among PD patients, gram (+) bacteria are the most common infective agents and Staphylococcus epidermidis is the most common. Peritonitis with gram (-) bacteria and fungi is relatively rare. In general, intravenous or intraperitoneal antibiotherapy is effective for the treatment of peritonitis (11).

In ESRD patients including HD and PD, inflammation markers such as CRP, NLR, PLR were observed to be elevated (7). During the follow-up of the peritonitis not only dialysate cell count, but also inflammation markers are the cornerstones for evaluating the response to the treatment. In several chronic diseases including ESRD, low-grade inflammation without an infectious process has been known for a long time. Low-grade inflammation is probably a contributing factor in the malnutrition-inflammation-atherosclerosis syndrome in ESRD patients. In this population, NLR is shown to be a novel inflammation marker especially for cardiovascular events and a predictor of mortality (12,13).

It is known that in PD patients, about 90% have high ESR and 25%-60% have high CRP levels (14). In ESRD patients, most factors such as anemia, which are supposed to affect ESR, have no influence on CRP values. Nevertheless, the increase in CRP levels can be under the influence of inflammation and tissue damage, as well as infection (15). In this study, we observed that conventional markers of inflammation associated with infection such as CRP and ESR were elevated especially in active period of the infectious process and returned to nearly baseline levels after the treatment of peritonitis. In accordance with CRP and ESR, NLR and PLR were both increased in active peritonitis period and decreased after the treatment. Because of the fact that chronic kidney disease is a disorder with low-grade inflammation, NLR and PLR are higher than healthy subjects. In the present study we observed spikes for these two parameters during active peritonitis period and a subsiding after successful treatment.

In several past studies, NLR and PLR were evaluated in ESRD, HD and PD patients and in all these conditions, these parameters were observed to be higher than in healthy subjects. Additionally PD patients had higher NLR and PLR levels than HD patients (7,14,16). Also in this study, we observed that PD patients have higher NLR, PLR, and ESR levels than control subjects.

In many previous studies, NLR was observed to be an important diagnostic and prognostic determinant for several diseases including psoriasis (17), infective endocarditis (18), pneumonia (19), bacteremia (20,21) and acute appendicitis (22).

Peritonitis is not a rare morbid condition for PD patients. During peritonitis, it is important to evaluate inflammation markers periodically to follow the efficiency of treatment. Classical markers such as ESR, CRP and others necessitate a relatively big expense. On the other hand both NLR and PLR are simpler to calculate and more affordable.

Beside the reduction of NLR and PLR in correlation with ESR and CRP reduction after the treatment of infectious peritonitis; elevated levels of albumin, uric acid and phosphorus can be attributed to the reduction of inflammation and healing of the nutrition and nutritional parameters.

CONCLUSION

According to the results of our present study, NLR and PLR are both valuable markers to follow the course of peritonitis and response to the treatment of peritonitis in correlation with conventional inflammation markers. Both NLR and PLR are more simple to calculate and cheaper parameters than classical markers such as ESR, CRP and others. This was a retrospective study with small sample size and new, large and randomized controlled trials may be useful in this field.

REFERENCES

1. Bargman JM: Advances in peritoneal dialysis: A review. Semin Dial 2012;25(5):545-549
2. Steinvinkel P, etteler M, Johnson RJ, Lindholm B, Pecoits-Filho R, Riella M, Heimbürger O, Cederholm T, Girndt M: IL-10, IL-6, and TNF-alpha: Central factors in the altered cytokine network of uremia-the good, the bad, and the ugly. Kidney Int 2005;67:1216-1233
3. Bathon J, Graves Jens P, Hamrick R, Mayes M: The erytrocite sedimentation rate in end-stage renal failure. Am J Kidney Dis 1987;10:34-40
4. Haubitz M, Schulze M, Koch KM: Increase of C-reactive protein serum values following haemodialysis. Nephrol Dial Transplant 1990;5(7):500-503
5. Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS: Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol 2008;102:653-657
6. Walsh SR, Cook EJ, Goulder F, Justin TA, Keeling NJ: Neutrophil-lymphocyte ratio as a prognostic factor in colorectal cancer. J Surg Oncol 2005;91:181-184
7. Turkmen K, Guney I, Yerlikaya FH, Tonbul HZ: The relationship between neutrophil-to- lymphocyte ratio and inflammation in end-stage renal disease patients. Ren Fail 2012;34(2): 155-159
8. Ozturk R, Yilmaz GR, Bulut C, Parpucu H, Kinikli S, Duranay M, Demiroz AP: Assessment of procalcitonin and other inflammatory markers in peritoneal dialysis-related peritonitis. Turk J Med Sci 2010;40(2):199-206
9. Levison ME, Bush LM: Peritonitis and intraperitoneal abscesses. In: Mandell GL, Bennett JE (eds), Principles and Practice of Infectious Diseases. (6th ed). New York: Churchill Livingstone, 2005; 927-951
10. Sipahioglu MH, Aybal A, Unal A, Tokgoz B, Oymak O, Utas C: Patient and technique survival and factors affecting mortality on peritoneal dialysis in Turkey: 12 years' experience in a single center. Perit Dial Int 2008;28(3):238-245
11. Çelik A, Çamsarı T: CAPD peritonitis and its treatment. Turk Neph Dial Transpl 1994;3:1-4
12. An X, Mao HP, Wei X, Chen JH, Yang X, Li ZB, Yu XQ, Li ZJ: Elevated neutrophil to lymphocyte ratio predicts overall and cardiovascular mortality in maintenance peritoneal dialysis patients. Int Urol Nephrol 2012;44:1521-1528
13. Okyay GU, Inal S, Oneç K, Er RE, Paşaoğlu O, Paşaoğlu H, Derici U, Erten Y: Neutrophil to lymphocyte ratio in evaluation of inflammation in patients with chronic kidney disease. Ren Fail 2013;35(1):29-36
14. Fine A: Relevance of C-reactive protein levels in peritoneal dialysis patients. Kidney Int 2002;61:615-620
15. Hind CRK, Thomson SP, Winearls CG, Pepys MB: Serum C-reactive protein concentration in the management of infection in patients treated by CAPD. J Clin Pathol 1985;38:459-463
16. Turkmen K, Erdur FM, Ozcicek F, Ozcicek A, Akbas EM, Ozbicer A, Demirtas L, Turk S, Tonbul HZ: Platelet-to-lymphocyte ratio better predicts inflammation than neutrophil-to-lymphocyte ratio in end-stage renal disease patients. Hemodial Int 2013;17:391-396
17. Sen BB, Rifaioglu EN, Ekiz O, Inan MU, Sen T, Sen N: Neutrophil to lymphocyte ratio as a measure of systemic inflammation in psoriasis. Cutan Ocul Toxicol 2014;33(3):223-227
18. Turak O, Özcan F, Işleyen A, Başar FN, Gül M, Yilmaz S, Sökmen E, Yüzgeçer H, Lafçi G, Topaloğlu S, Aydoğdu S: Usefulness of Neutrophil to lymphocyte ratio to predict ın- hospital outcomes in infective endocarditis. Can J Cardiol 2013;29(12):1672-1678
19. de Jager CP, Wever PC, Gemen EF, Kusters R, van Gageldonk-Lafeber AB, van der Poll T, Laheij RJ: The neutrophil- lymphocyte count ratio in patients with community- acquired pneumonia. PLoS One 2012;7(10):e46561
20. Terradas R, Grau S, Blanch J, Riu M, Saballs P, Castells X, Horcajada JP, Knobel H: Eosinophil count and neutrophil- lymphocyte count ratio as prognostic markers in patients with bacteremia: A retrospective cohort study. PLoS One 2012;7(8):e42860
21. de Jager CP, van Wijk PT, Mathoera RB, de Jongh- Leuvenink J, van der Poll T, Wever PC: Lymphocytopenia and neutrophil- lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. Crit Care 2010;14(5):R192
22. Markar SR, Karthikesalingam A, Falzon A, Kan Y: The diagnostic value of neutrophil: Lymphocyte ratio in adults with suspected acute appendicitis. Acta Chir Belg 2010;110(5):543-547