The Effects of Magnesium Levels on Prognosis in Organophosphate Poisoning

İsmail AKTAŞ[1], Ramazan KÖYLÜ[1], Öznur KÖYLÜ[2], Başar CANDER[3]

[1] Department of Emergency Medicine, University of Health Sciences. Konya Education and Research Hospital, Konya, Turkey

[2] Department of Biochemistry, University of Health Sciences. Konya Education and Research Hospital, Konya , Turkey

[3] Department of Emergency Medicine, University of Necmettin Erbakan, Faculty of Medicine. Konya , Turkey

Abstract

Objectives: To investigate the predictive value of magnesium, neutrophil/lymphocyte ratios (NLR) in determining the severity of morbidity and mortality in patients with organophosphate poisoning (OP) admitted to the emergency department.

Materials ad Methods: This study was conducted retrospectively by scanning the medical recordings of patients aged over 18 years who were admitted to our emergency department with OP between 2010 and 2015. The demographic characteristics, medical history, laboratory findings, and Glasgow Coma Scale (GCS) scores of the patients were recorded.

Results:The data of 153 patients, 91 males and 62 females, were evaluated. There was no significant correlation between the changes in magnesium, hemoglobin, hematocrit, leukocytosis, platelets, potassium, calcium, glucose, alanine aminotransferase (ALT), troponin, and mortality in patients with OP (p>0.05). There was a significant relationship between the increase in lactate dehydrogenase (LDH) (p=0.004), low lymphocyte count (p=0.003), decreased cholinesterase (p=0.001), higher (NLR) (p=0.002), GCS (p<0.001), mechanical ventilator (MV) requirement (p<0.001), age (P=0.009), vasopressor treatment (p<0.001), and mortality.

Conclusion: No significant relationship determined between magnesium levels and prognosis. Low lymphocyte count, decreased cholinesterase, increased LDH and NLR in patients with OP were significantly correlated with mortality. Increased NLR ratio, one of the parameters in routine hemograms, may give information to physicians about the long-term follow-up of such patients with OP.

Keywords: emergency, organophosphate, magnesium, neutrophil lymphocyte ratio

Özet

Amaç: Bu çalışmada acil servise başvuran organofosfat zehirlenmesi (OP) ile başvuran hastalarda morbidite ve mortalitenin ciddiyetinin belirlenmesinde magnezyum, nötrofil / lenfosit oranlarının (NLR) prediktif değerini araştırmak amaçlanmıştır.

Gereç ve Yöntem: Bu çalışma 2010-2015 yılları arasında OP ile acil servise başvuran 18 yaş üstü hastaların tıbbi kayıtları retrospektif taranarak yapıldı. Hastaların Demografik özellikler, tıbbi öykü, laboratuvar bulguları ve Glasgow Koma Skalası (GKS) skorları kaydedildi.

Bulgular: 91 erkek ve 62 kadın 153 hastanın verileri değerlendirildi. OP'li hastalarda magnezyum, hemoglobin, hematokrit, lökositoz, trombosit, potasyum, kalsiyum, glukoz, alanin aminotransferaz (ALT), troponin ve mortalite değişiklikleri arasında anlamlı bir ilişki bulunmadı (p> 0.05). Laktat dehidrojenaz artışı (LDH) (p = 0.004), düşük lenfosit sayısı (p = 0.003), azalmış kolinesteraz (p = 0.001), yüksek NLR düzeyi (p = 0.002), GKS (p<0.001) mekanik ventilatör (MV) gereksinimi (p <0.001), yaş (P = 0.009), vazopressör tedavisi (p <0.001) ve mortalite arasında anlamlı bir ilişki vardı.

Sonuç: Magnezyum düzeyleri ile prognoz arasında anlamlı bir ilişki bulunamamıştır. OP'li hastalarda düşük lenfosit sayısı, azalmış kolinesteraz, LDH ve NLR artışı mortalite ile anlamlı olarak kore idi. Rutin hemogramlardaki parametrelerden biri olan artmış NLR oranı, OP hastalarının uzun süreli takibi hakkında hekimlere bilgi verebilir.

Anahtar kelimeler: acil, organofosfat, magnezyum, nötrofil lenfosit oranı

Introduction

Organophosphate compounds are widely used in agriculture[1] and poisoning with these compounds is more common in developing countries such as our country, Turkey, although it is also known to be a major problem in industrialized countries[2,3]. Poisoning can occur accidentally in agricultural areas, in industry, in animal husbandry or due to contaminated food, and may also occur in suicide[4]. It is reported that three million people in the world are poisoned with pesticides every year and nearly 200,000 of these die[5]. Orga-

Aktas et al.
The effects of magnesium levels on prognosis
in organophosphate poisoning

8

Eurasian J Tox. 2019; 1 (1): 7-10

nophosphate poisoning (OP) is frequently seen in Turkey in accidental poisoning or suicides. Poisoning with these chemicals affects all vital functions and requires early diagnosis and treatment[6, 7].

In recent years, in addition to clinical tests in which the neutrophil/lymphocyte ratio (NLR) is used as an inflammatory marker, the relationship of the NLR with many diseases has been investigated. The basis of these studies is the physiologic response of leukocytes to stimuli, the increase in the neutrophil count, and the relative decrease in lymphocyte counts associated with neutrophilia[8]. The NLR is frequently used as a prognostic factor in cardiovascular system diseases. An increase in the NLR in patients undergoing cardiovascular interventions was found to be an indicator of poor prognosis. Similarly, there are studies that showed an increase in the NLR could be associated with increased mortality in acute coronary syndrome[9, 10]. In some studies, the NLR was found to be useful for predicting prognosis in some types of cancer[9, 11]. As we guess that as a result of OP, inflammation begins in the body, the severity of the poisoning will be in correlation with the severity of the inflammatory process, and that there will be significant changes in NLR. In this study, we aimed to investigate the predictive value of the NLR in determining the severity of morbidity and mortality in patients with OP admitted to the emergency department.

It is stated that organophosphates cause acetylcholine (Ach) accumulation in synapses by irreversibly inhibiting the acetylcholinesterase enzyme (AchE)[12,13], and that the clinical presentation is caused by the excessive stimulation of nicotinic and muscarinic cholinergic receptors with Ach in central nervous system, in the autonomic nervous system, and at neuromuscular junctions[12, 13]. It is reported that the stimulation of muscarinic receptors causes myosis (<3 mm), bradycardia, and increased bronchial secretion, and the stimulation of nicotinic receptors causes fasciculation in muscles, cramps, weakness in respiratory muscles, seizures and loss of consciousness[12].

The diagnosis of OP is based on clinical findings and the level of cholinesterase in the serum. The treatment includes administering drugs including atropine and oxime and supportive care. However, atropine and oximes used in the treatment of OP may be insufficient to reduce morbidity and mortality in some cases. The mortality rate in OP can reach up to 30%[6]. We aimed to investigate the predictive value of NLR) in determining the severity of morbidity and mortality in patients with OP admitted to the emergency department.

Materials and Methods

This retrospective study was approved by the local ethics committee (Number: 2016/496). The study was performed by scanning the medical records of 153 patients who were diagnosed as having OP in the Emergency Medicine Clinic between January 2010 and January 2016. Patients aged under 18 years, pregnant females, and those with previously known cardiac disease were excluded from the study. Demographic characteristics, medical history, vital signs, laboratory findings, hospitalization and intensive care unit stay durations, mechanical ventilator and vasopressor requirements, mortality rates, and Glasgow Coma Scale (GCS) scores of the patients were recorded. The Statistical Package for the Social Sciences (SPSS) for Windows Ver. 15.0 (SPSS Inc, Chicago, IL) was used for statistical analyses of the data. Descriptive statistics were presented as mean±standard deviation, median (min-max), frequency distribution, and percentage. The normality of distribution of the variables was evaluated with visual (histogram and probability plots) and analytical (Kolmogorov-Smirnov/Shapiro-Wilk tests) methods. For variables that did not have normal distribution, the Mann-Whitney U test was used to search for the relation between two independent variables, and the Kruskal Wallis test was used to investigation relations between three independent variables. When a significant difference was detected between three independent groups, Bonferroni correction was used to determine the source of the difference. The relationship between the variables was evaluated using the Spearman's correlation test. P<0.05 was considered as statistically significance.

Results

Ninety-nine of the 153 patients included in the study were males (59.5%) and 62 were females (40.5%). The mean age of the males and females was 43.10±18.41 and 40.32±17.27 years, respectively, and the age range was 18-82 years. When we examined the routes of OP, in male patients it was observed that 40 had OP by ingestion , 40 by inhalation, and 11 through skin exposure, and in female patients 34 had had OP by ingestion, 21 had OP by inhalation, and 7 through skin exposure. Thirty-two males and 23 females had OP in suicide attempts. Fifty-nine males and 39 females were had OP accidentally. When the clinical findings of the patients were examined at admission to the emergency room, 92 (60.1%) patients had nausea, 66 (43.1%) vomiting, 14 (9.2%) abdominal pain, 32 (20.9%) shortness of breath, 17 (11.1%) dizziness, 10 (6.5%) diarrhea, 11 (7.2%) headache, 13 (8.5%) burning and redness in the body, 18 (11.8%) confusion, 8 (5.2%) coma, 1 (0.7%) hemoptysis, and 1 (0,7) chest pain.

Complete blood count findings of the patients were as follows: the mean leukocyte value was 8.8±2.86x10^3/uL (min-max: 3.9-19.2x10^3/uL), the mean hemoglobin value was 13.2±1.9 g/dL (min-max: 8.1-17.5 g/dL), the mean hematocrit value was 39.2±5.03% (min-max: 26.7-50.9%), the mean neutrophil value was 6.2±2.9x10^3/uL (min-max:

Eurasian J Tox. 2019; 1 (1): 7-10

Aktas et al.
The effects of magnesium levels on prognosis
in organophosphate poisoning

9

1.54-17.3 x10³/uL), the mean lymphocyte value was 1.8±0.8 x103/uL (min-max: 0.34-4.62x10³/uL), and the mean platelet (PLT) value was 234.9±80.02x10³/uL (min-max: 26.7-50.9x10³/uL). There was a significant correlation between low lymphocyte counts and mortality (p=0.003). There was a significant correlation between high NLR and mortality (p=0.002) (Table 1).

Table 1. The relationship between the NLR, lymphocyte count, and mortality

Parameter	Discharge	Ex	P value
Lymphocyte, mean±SD	1.92±0.79	0.83±0.38	0.003
NLR, median (IQR)	2.81 (2.74)	9.24 (11.96)	0.002

Discussion

No significant relationship determined between magnesium levels and prognosis.In this article want to take attention to predictivity between NLO and organophosphate poisoning.

To the best of our knowledge, there are no studies on the effects of NLR on prognosis in OP. In our study, the effect of NLR on mortality and prognosis was investigated. A significant correlation was found between NLR and mortality and prognosis.

Recently, lymphocytopenia and NLR have been noted as an independent predictor in a wide conditions ranging from oncologic diseases to cardiovascular system diseases. Tamhane et al.[10] showed that a high NLR was correlated with intra-hospital and 6 months mortality and reinfarction, and also increased incidence of stroke. The NLR is frequently used as a prognostic factor in cardiovascular system diseases. Increased NLR in patients undergoing cardiovascular interventions was shown as an indicator of poor prognosis. Similarly, an increased NLR was found correlated with increased mortality in acute coronary syndrome in some studies[9, 10]. Goodman et al. showed that the NLR was more sensitive than white blood cell (WBC) counts in appendicitis[14]. Neutrophilia was found correlated with acute decompensated heart failure in patients with acute myocardial infarction, and together with relative lymphopenia, they were good markers of mortality in heart failure[15]. The NLR is considered to be indicative of subclinical inflammation[16]. In some studies, the NLR was found to be useful for predicting prognosis in some types of cancer[11].

The low number of lymphocytes in colorectal tumors is associated with poor prognosis because the presence of T-lymphocytes in a tumor is indicative of a significant immune response against the lesion. It was shown that the NLR was a good prognostic factor in determining mortality in colorectal and ovarian cancers[11]. In a study by Buck et al., complete blood counts from peripheral blood samples were measured at 24 hours in patients who were diagnosed as having ischemic stroke. It was shown that high peripheral leukocyte and neutrophil numbers were associated with the existing ischemic infarct volume. In that study, no relation was found between the number of lymphocytes and infarct volume[17]. In addition to infectious diseases, the NLR has been investigated in metabolic syndrome, chronic obstructive pulmonary disease, end-stage renal failure, subdural hemorrhage, Behcet's disease, malignancy, and keratoconjunctivitis[18-20].
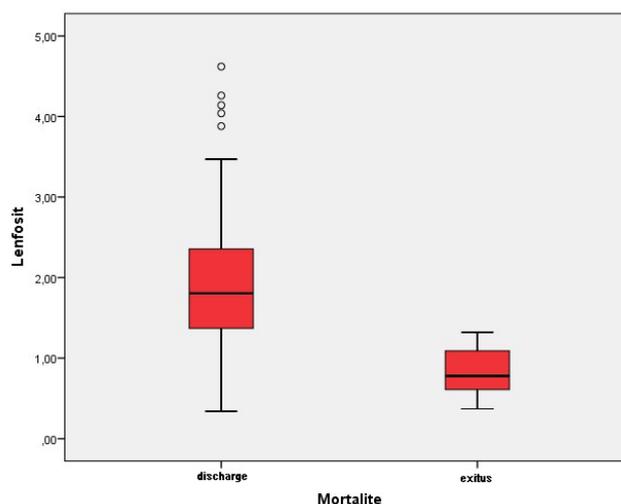

Figure 1. Boxplot showing the relationship between lymphocyte count and mortality
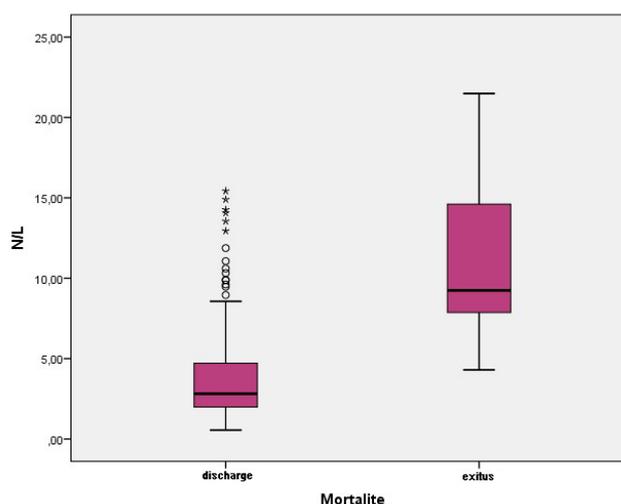

Figure 2. Boxplot showing the relationship between NLR and mortality

In our study, we found increased NLR and low lymphocyte counts in patients with OP. In the literature, we found no information about the use NLR in OP; therefore, comparisons were made with the use of NLR in other diseases to show the inflammatory process and prognosis. We conc-

Aktas et al.
The effects of magnesium levels on prognosis
in organophosphate poisoning

10

Eurasian J Tox. 2019; 1 (1): 7-10

luded that prognosis is worse in patients with an increased NLR and low lymphocyte count, and these patients should be followed up for longer. These findings should be validated by future studies because there are no similar studies in the literature.

References

1. Sogorb MA, Vilanova E, Carrera V. Future applications of phosphotriesterases in the prophylaxis and treatment of organosporus insecticide and nerve agent poisonings. Toxicology letters. 2004;151(1):219-33.

2. Langley R, Sumner D. Pesticide mortality in the United States 1979-1998. Veterinary and human toxicology. 2002;44(2):101-5.

3. Öztürk MA, Kelestimur F, Kurtoglu S, Güven K, Arslan D. Anticholinesterase poisoning in Turkey-clinical, laboratory and adiologic evaluation of 269 cases. Human & experimental toxicology. 1990;9(5):273-9.

4. K"aralliedde L. Organophosphorus poisoning and anaesthesia. Anaesthesia. 1999;54(11):1073-88.

5. Jeyaratnam J. Acute pesticide poisoning: a major global health problem. World Health Stat Q. 1990;43(3):139-44.

6. Güven M, Sungur M. Organophosphorus poisonings and future directions. Current Topics in Toxicology, Volume 2. 2005:57-65.

7. Kwong TC. Organophosphate pesticides: biochemistry and clinical toxicology. Therapeutic drug monitoring. 2002;24(1):144-9.

8. Lowsby R, Gomes C, Jarman I, Lisboa P, Nee PA, Vardhan M, Eckersley T, Saleh R, Mills H. (2015). Neutrophil to lymphocyte count ratio as an early indicator of blood stream infection in the emergency department. Emerg Med J. 32(7):531-4.

9. Duffy BK, Gurm HS, Rajagopal V. (2006). Usefulness of an elevated neutrophil to lymphocyte ratio in predicting long-term mortality after percutaneous coronary intervention. Am J Cardiol 97:993-6, 996.

10. Tamhane UU, Aneja S, Montgomery D. (2010). Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol 102:653-7.

11. Tsujimura A, Kawamura N, Ichimura T, et al. (2002). Telomerase activity in needle biopsied uterine myoma-like tumors: differential diagnosis between uterine sarcomas and leiomyomas. Int J Oncol; 20:361-365.

12. Clark RF. Insecticides: organic phosphorus compounds and carbamates. Goldfrank's toxicologic emergencies. 2002;8:1497-512.

13. Peter JV, Moran JL, Graham P. Oxime therapy and outcomes in human organophosphate poisoning: an evaluation using meta-analytic techniques. Critical care medicine. 2006;34(2):502-10.

14. Goodman DA, Goodman CB, Monk JS. Use of the neutrophil:lymphocyte ratio in the diagnosis of appendicitis. Am Surg 1995; 61:257-259.

15. Raungkaewmanee S, Tangjitgamol S, Manusirivithaya S, Srijaipracharoen S. (2012). T. Platelet to lymphocyte ratio as a prognostic factor for epithelial ovarian cancer. J Gynecol Oncol 23: 265-73

16. Jilma B, Blann A, Pernerstorfer T. (1999). Regulation of adhesion molecules during human endotoxemia. No acute effects of aspirin. Am J Respir Crit Care Med 159:857-63.

17. Buck BH, Liebeskind DS, Saver JL, Bang OY, Yun SW, Starkman S, et al. Early neutrophilia is associated with volume of ischemic tissue in acute stroke. Stroke. 2008;39(2):355-60.

18. Sönmez O, Ertaş G, Bacaksız A, Tasal A, Erdoğan E, Asoğlu E. (2013). Relation of neutrophil-to-lymphocyte ratio with the presence and complexity of coronary artery disease: an observational study. Anadolu Kardiyol Derg. 13:662-7.

19. Kılıçaslan B, Dursun H, Kaymak S, Aydın M, Ekmekçi C, Susam İ. (2015). The relationship between neutrophil to lymphocyte ratio and blood pressure variability in hypertensive and normotensive subjecs. Turk Kardiyol Dern Ars. 43(1):18-24

20. Elbey B, Yazgan ÜC, Yıldırım A, Karaalp Ü, Şahin A. (2015). Vernal keratokonjonktivitli olgularda ortalama trombosit hacmi ve nötrofil/lenfosit oranı. Journal of Clinical and Experimental Investigations. 6(1):40-3.