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Editorial

Çok değerli meslektaşlarım,

Bir yılı aşkın süredir devam eden ve yeryüzündeki tüm insan popülasyonunu etkileyen Covid-19 salgını, maalesef çok sayıda insanın ölümüne, hastalanmasına, işsiz kalmasına sebep olduğu gibi dünyaya yıllar boyunca insanlar tarafından yapılan tahribatların sorgulanmasına da vesile oldu. Sosyal medyada hiçbir dönemde olmadığı kadar günlerce, aylarca yoğun bakımlar, kritik hastalar, mekanik ventilatörleri konuştu ve izledi.

Büyük bir otörün söylediği "Bir ülkenin kalkınmışlığı acil hastasına, kritik hastasına verdiği kaliteli sağlık hizmeti ile ölçülür." Sözünün ne kadar anlamlı ve gerçekçi olduğu bir kez daha görüldü.

Mortalite oranları, aşılama, yoğun bakım doluluk oranları ile birlikte yerküre adeta devasa bir yoğun bakım ünitesi gibi olmuştur.

Başta acil tıp ve kritik bakım uzmanları olmak üzere tüm sağlık çalışanları 7 gün 24 saat durmaksızın canhıraş bir şekilde insanlığı kurtarma adına seferde ve görevdedir.

"Hayat devam ediyor" sözü ne kadar güzel ifade ediyor; "sabır, azim ve ümitli değil mi?" Evet, kahramanlar bir taraftan sahada onurlu, gururlu sağlık hizmeti verirken, bir taraftan da bilime ışık tutmaya devam ediyor. Dergimizin bu sayısında yoğun bakım ünitelerinde merkezi sinir sistemi enfeksiyonları peruktan dilatasyon yöntemiyle yapılan trakeotomiler, hemodiyaliz hastaları, hastane dışı kardiyak arrestlerde mortalite belirleyiciler, Covid-19 ilişkili fungal enfeksiyonlar gibi araştırma makalelerinin yanı sıra non operatif takip edilen ateşli silah yaralanması, valproik asit zehirlenmesinde L-karnitin tedavisi gibi ilginç olgular yer almaktadır.

Bu sayının hazırlanmasında emeği geçen yayın kuruluna, değerli yazarlarımıza bilime katkıları nedeniyle teşekkür ederiz. Salgınla mücadelede mekanik destekler yanı sıra bu manalı iklimde insanların birbirine mekanik olmayan güçlü desteklerinin de sürmesini temenni ediyor, vefat edenlerin yakınlarına baş sağlığı, hastalara acil şifa diliyoruz.

Sağlıkla kalın.
Prof. Dr. Mehmet Gül

My dear colleagues,

The Covid-19 epidemic, which has been going on for more than a year and affecting the entire human population on the earth, unfortunately caused many people to die, become sick and unemployed, as well as questioning the destruction by people over the years. People talked and watched intensive care units, critically ill patients, mechanical ventilators for days and months on social media more than ever before.

Saying a great author, "The development of a country is measured by the quality health service it provides to its emergency patients and critical patients." It was once again seen how meaningful and realistic his word was.

With the mortality rates, vaccination, and intensive care occupancy rates, the world has become like a huge intensive care unit.

All healthcare professionals, especially emergency medicine and critical care specialists, are on duty to save humanity 24 hours a day, 7 days a week.

How beautifully expresses the phrase "life goes on"; "Isn't patience, determination and hope?" Yes, the heroes continue to shed light on science while providing honorable and proud health services on the field. In this issue of our journal, besides research articles such as central nervous system infections in intensive care units, tracheotomies performed with percutaneous dilatation method, hemodialysis patients, mortality determinants in out-of-hospital cardiac arrest, Covid-19 related fungal infections, non-operatively followed gunshot injury, L- in valproic acid poisoning. There are interesting cases such as carnitine therapy.

We would like to thank the editorial board and valuable authors for their contribution to science, who contributed to the preparation of this issue. In addition to mechanical support in the fight against the epidemic, we hope that people will continue to support each other in this meaningful climate, and we wish the relatives of the deceased to have a head health and urgent recovery to the patients.

Stay healthy.
Professor Doctor Mehmet Gül

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Central Nervous System Infections in the Intensive Care Units and Risk Factors for Mortality; Retrospective Study

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Abstract

Aim: This study was designed to analyze demographic, clinical and laboratory characteristics beside risk factors that affect the mortality rate of patients hospitalized in ICUs with diagnosis of CNS infection.

Methods: Patients that have been hospitalized at ICU on pre-CNS infection were retrospectively studied. Beside the clinical laboratory characteristics of the patients, mortality rate and risk factors that affect the mortality were recorded to be analyzed later.

Results: Following the evaluation of 118 ICU patients who were suspected to have CNS infection, 62 of them, with full diagnosis of CNS infection, were included in the study. Bacterial meningitis was the diagnosis for 40 (66%) of these patients while 18 of the total (30%) was diagnosed with viral encephalitis and 3 of them (4%) was diagnosed with tuberculous meningitis. When these factors were investigated in a multivariable study, age and time from the onset of symptoms to hospital admission were independent risk factors (CI: 1,098(1,031-1,169), 1,614(1,037-1,278).

Conclusion: The mortality rate of the patients that were subjects of the study was 52,5%. Age and time from the onset of symptoms to hospital admission were independent risk factors that affect the mortality.

Key words: Intensive Care, Meningitis, Encephalitis,

Introduction

Central nervous system infections like meningitis, encephalitis and brain abscess are rare in ICUs; they are not easy to diagnose and they have high mortality rates. These pathologies require fast diagnosis and, more importantly, on-time administration of proper antimicrobial treatments in order to decrease morbidity and mortality rates.

Many patients with CNS infection encounter increased intracranial pressure, status epilepticus, deep coma and respiratory paralysis, and they must be treated in ICU due to high mortality rate. It was reported that the mortality rate of bacterial meningitis is between 20 and 45% while it is 70% in the untreated herpes simplex encephalitis and 30% in treated ones.[1-7]

In a study conducted in Africa, it was stated that the mortality rate of ICU requiring CNS infection patients was 39%, and many of the patients were infected with HIV and cryptococcus.[8]

Another report from Portugal revealed that secondary infection (pneumonia, endocarditis and sinusitis) rates of patients with bacterial meningitis who need intensive care were high. The mortality rate of these patients were 40%, and the most important factor that affected this rate was old age and APACHE II scores.[6]

In a retrospective study conducted in the USA, the mortality rate was 18 while the most important factors affecting the mortality were cerebral edema, status epilepticus and thrombocytopenia.[9]

Causes, characteristics and mortality rates of CNS infections are various in different geographical areas. Therefore, the spectrum and results of CNS infections in ICUs need to be documented.

This study was designed to analyze demographic, clinical and laboratory characteristics beside risk factors that affect the mortality rate of patients hospitalized in ICUs on diagnosis of central nervous system infection; it is rare, difficult to diagnose, highly mortal and fast in progress with possible sequels.

Patients and Methods

This study was conducted on patients who were hospitalized in Erciyes University Faculty of Medicine Department of Internal Medicine, Anesthesiology and Reanimation ICU between 6 January 2010 and 1 April 2020 on diagnosis of CNS infection. The ethical approval of this study was given by the Ethics Committee of Erciyes University (283/2020).

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The diagnoses of CNS infections were based on clinical and radiological examinations, cerebrospinal fluid analyses and CNS imaging findings.

The CSF WBC count of negative culture was accepted as >100/mm3 based on the clinical symptoms and findings of bacterial meningitis and acute bacterial meningitis. The conclusive diagnosis of bacterial meningitis depends of either gram or culture positivity, or both, for bacteria known to cause meningitis.

The criteria for viral meningitis/encephalitis were high fever and altered sensorium or behavioral abnormality along with CSF pleocytosis. The specific cause of encephalitis was verified by CSF PCR (herpes simplex virus) test.

Diagnosis of TBM (tuberculous meningitis) was based on MR and CSF findings. Basic criteria for TBM were high fever, neck stiffness and altered mental status. Supporting findings for TBM were; 1. CSF cells .2×109 /L with lymphocytic predominance, protein 1 g/L, sterile bacterial and fungal culture and absence of cryptococcal antigen; 2. CT or MRI showing exudates, hydrocephalus, tuberculoma or infarction; 3. extra-CNS tuberculosis. Presence of any two of the basic or supporting criteria was accepted as a TBM diagnosis. Presence of acid fast bacilli (AFB) in BOS staining or culture, PCR and/or IgM ELISA was the conclusive indicator of TBM.

Demographical characteristics of patients, duration of disease, fever, headache, vomiting, seizure, focal neurological deficit, difficult breathing, intracranial pressure level, neuroradiological findings and laboratory results of the patients were obtained from electronic medical records. Age, gender, comormidity features and Charlson Comorbidity indices of the patients were recorded. Consciousness was analyzed through Glasgow Coma Scale (GCS). The SOFA score at hospitalization, GCS, symptoms, neck stiffness, Kerning's sign, total blood count, liver and kidney functions, electrolyte levels, prothrombin times, INR, procalcitonin, C-reactive Protein (CRP) levels and APACHE II scores on the first day were also recorded. Invasive mechanical ventilation requirement, length of mechanical ventilator days, length of in-bed period, and length of ICU period, mortality rate and risk factors affecting the mortality were evaluated as well.

Statistical

Continuous variables were summarized as medians and interquartile ranges. Statistical analyses of obtained data were performed using SPSS software, version 22.0 (SPSS, Chicago, IL). Data were analyzed using chi-square test, Fisher exact test, and independent *t* test. P□value < 0.05 was considered statistically significant.

The predictors of death were analyzed using univariate regression analysis; the variables included were age, time from the onset of symptoms to hospital admission GCS score, APACHE II score, SOFA, IMV, length of mechanical ventilation, ICU length of stay, hospital length of stay. Variables with a p value of 0.1 in univariate analysis were included in the multivariate regression analysis using Hosser–Lemeshow goodness-of-fit. A variable was considered significant if the two-tailed p value was 0.05.

Results

This retrospective study was conducted on 118 patients who were hospitalized at ICU of Erciyes University School of Medicine Department of Internal Medicina and Anesthesiology in the last 10 years with pre-diagnosis of CNS infection. CNS was excluded from 57 of these patients. Average age of our patients was 55 (range 38-71) and 43 of them (71%) were male. Median Charlson morbidity index of our patients was 2 (range 0-4) and 38 of them (61%) had risk factors in terms of CNS infection. The time from the onset of symptoms to hospital admission median was 2 (range 1-7); the most common symptoms were mental impairment (93%) and body temperature (84%).

The most common finding in physical examination was low GCS (98%) and 62% of them had neck stiffness.

The SOFA score of our patients at hospital admission was 4 (range 2-5) while the APACHE II value was 17 (range 10-21).

Considering the laboratory results, the median of blood glucose was 120 (range; 94-154) and WBC level was 11490 (range 7660-17420). Procalcitonin level was low (0,2 range 0,08-1,75) while CRP was high (median 59, range 26-155). LDH levels of these patients were high as well (median 356, range 283-465). CSF and blood cultures were obtained from these patients. There was no growth in blood samples of 77% of the patients and no growth in CSF of 82% of the patients. CSF results of six patients (10%) revealed viral PCR (HSV1) and results of two patients (3%) revealed positive mycobacterial PCR.

There were positive findings in the MR images of 54 patients (89%) accordant with their diagnoses. Forty patients (66%) were diagnosed with bacterial meningitis while eighteen patients (30%) were diagnosed with viral encephalitis and three of them (4%) with tuberculous meningitis. Thirty patients received Acyclovir, twenty-six patients received Meronem, twenty-one patients received Seftriakson, and three patients received anti-TBC treatment. Nineteen patients received Vancomycin and two patients received Linezolid medications part in addition the abovementioned medications.

Thirty-four patients (56%) needed mechanical ventilation and the median of length of mechanical ventilation was 14 (range 5-18).

The median length of ICU stay was 10 (range 4-17) and the length of hospitalization was 15 (range 10-22). The mortality rate determined during the study was 52, 5%.

The comparison of laboratory and clinical findings of bacterial meningitis and viral meningitis/encephalitis patients were given in Table 2. The WBC median of CSF for bacterial meningitis patients was 303 (range 55-1465) while it was 60 (range 9-119) for viral meningitis/encephalitis incidents (p: 0,004). The glucose levels of bacterial meningitis patients were lower in CSF were lower than that of viral meningitis/encephalitis patients (p: 0,011). As the number of tuberculous meningitis patients was very few, their characteristics were not compared with that of bacterial meningitis patients and viral meningitis/encephalitis patients. The findings of TBM patients were given in Table 3. All of TBM patients needed invasive mechanical ventilation and they all died.

The univariable and multivariable analyses of factors effective on mortality were given in Table 4. Considering these factors, the univariable analysis revealed that age, GCS, SOFA and APACHE II scores, Charlson Morbidity Index, time from the onset of symptoms to hospital admission, and IMV need were effective on mortality (p<0,05).

When the multivariable analyses was done, age and time from the onset of symptoms to hospital admission were independent risk factors (respectively CI: 1,098(1,031-1,169), 1,614(1,037-1,278)).

Table 1. Demographical characteristics, clinical characteristics and treatment codes of patients with CNS infection

Characteristics	Patients n:61
Age, y median (IQR)	55(38-71)
Male sex no.(%)	43(71)
Charlson Comorbidity Index no.(%)	2(0-4)
Risk factors no.(%)	38(61)
Immune-compromised state	9(15)
Old age	9(15)
Sinusitis	5(8)
Otitis	6(9)
CNS surgery	7(10)
Head trauma	1(2)
Spinal anesthesia	1(2)
Time of onset of Symptom day, median (IQR)	2(1-7)
Presenting symptoms no.(%)	
Fever	51(84)
Headache	30(49)
Altered mental status	57(93)
Seizure	16(26)
Nausea and Vomiting	32(52)
Examination	
Stiff neck,	38(62)
Kerning's sign	20(32)
Focal neurologic deficits	19(31)
GCS<15	59(98)
SOFA	4(2-5)
APACHE II	17(10-21)
Blood glucose	120(94-154)
White Cell count per mm3 median (IQR)	11490(7660-17420)
C reactive protein mg/l median (IQR)	59(26-155)
Procalcitonin ng/ml median (IQR)	0,2(0,08-1,75)
LDH U/L median (IQR)	356(283-465)
Blood cultures no.(%)	
No bacteria	47(77)
Staphylococcus sp.	9(15)
Acinetobacter sp.	3(6)
S. Pneumonia	1(2)
CSF cultures no.(%)	
No bacteria	50(82)
S. Pneumonia	7(10)
N. Meningitis	1(2)
E. Coli	1(2)
Acinetobacter sp.	1(2)
Staphylococcus sp.	1(2)
CSF Viral PCR (HSV 1) no.(%)	6(10)
CSF mycobacteria PCR no.(%)	2(3)
Positive MR findings	54(89)
Bacterial meningitis	40(66)
Viral meningitis/encephalitis	18(30)
Tuberculous meningitis	3(4)
Medication no.(%)	
Seftriakson	21(34)
Meronem	26(43)
Vancomycin	19(31)
Linezolid	2(3)
Asiklovir	30(49)
Anti TBC	3(6)
Invasive mechanical ventilator n. (%)	35(56)
Mechanical ventilation length of stay d, median (IQR)	14(5-18)
ICU length of stay d, median (IQR)	10(4-17)
Hospital length of stay d median (IQR)	15(10-22)
Death n (%)	32(%53)

Abbreviations; APACHE II: Acute Physiology and Chronic Health Evaluation score II, CSF: Cerebrospinal fluid ICU: intensive care unit. IQR, interquartile range. GCS, Glaskow coma score. n: number SOFA: Sequential Organ Failure Assessment score, y: year.

Table 2. Comparison of bacterial meningitis patients and viral meningitis/encephalitis patients in terms of laboratory and clinical findings

Characteristics	Bacterial meningitis N:40)	Viral meningitis/encephalitis (N:18)	p
CSF WBC /ul median (IQR)	303(55-1465)	60(9-119)	0,004
Blood WBC 103/ul median (IQR)	11.490(7.580-16.100)	11.680(7.955-18.215)	0,522
CSF Glucose mg/dl median (IQR)	45(16-80)	68(51-77,75)	0,011
Blood Glucose mg/dl median (IQR)	126 (99-154)	116 (90-140)	0,393
CSF chlorine mmol/L median (IQR)	116(108-123)	119(110-123)	0,470
Blood chlorine mmol/L median (IQR)	106(99-110)	99(94,5-106)	0,032
CRP mg/L median (IQR)	59(30-164)	49(17-145)	0,196
Procalcitonin ng/ml median (IQR)	0,25(0,007-3,05)	0,19(0,008-0,31)	0,480
APACHE II median (IQR)	16(10-20)	20(6-25)	0,207
GCS median (IQR)	9(3-12)	9(3-12)	0,938
SOFA median (IQR)	3(2-4)	4(2-5)	0,632
Invasive Mechanical ventilation n.(%)	26(%65)	7(%39)	0,12
Mechanical ventilation length of stay d, median (IQR)	13(5-19)	15(8-21)	0,703
ICU length of stay median(IQR)	10(4-17)	10(4-20)	0,811
Hospital length of stay d, median(IQR)	14(11-22)	16(10-23)	0,554
Mortality n (%)	24(%60)	8(%45)	0,417

Abbreviations; APACHE II: Acute Physiology and Chronic Health Evaluation score II, CSF: Cerebrospinal fluid ICU: intensive care unit. IQR, interquartile range. GCS, Glaskow coma score. n: number SOFA: Sequential Organ Failure Assessment score,

Table 3. Laboratory and clinical characteristics of tuberculous meningitis patients

Characteristics	Patients n:3
CSF WBC /ul median(IQR	83(50- *)
Blood WBC 103/ul median(IQR)	8260(1140- *)
CSF Glucose mg/dl median(IQR)	19(10-*)
Blood Glucose mg/dl median(IQR)	128(102- *)
CSF chlorine mmol/L median(IQR)	113(112- *)
Blood chlorine mmol/L median(IQR)	105(97-*)
CRP mg/L median(IQR)	50(8,6- *)
Procalcitonin ng/ml median(IQR)	0,1(0,09-*)
APACHE II median(IQR)	19(18-*)
GCS median(IQR)	7(3-*)
Invasive Mechanical Ventilation n.(%)	3(100)
Mechanical ventilation length of stay d, median(IQR)	9(5-*)
ICU length of stay d, median(IQR)	9(7-*)
Hospital length of stay d, median(IQR)	22(21-*)
Mortality n(%)	3(100)

Abbreviations; APACHE II: Acute Physiology and Chronic Health Evaluation score II, CSF: Cerebrospinal fluid ICU: intensive care unit. IQR, interquartile range. GCS, Glaskow coma score. n: number SOFA: Sequential Organ Failure Assessment score, (* Not calculated due to lack of number of patients)

Table 4. The univariable and multivariable evaluation of factors affecting mortality of CNS-diagnosed patients

	Univariable HR	p	Multivariable HR	p
Age	1,058(1,025-1,093)	0,001	1,098(1,031-1,169)	0,003
GCS	0,785(0,682-0,907)	0,001		
Sofa	1,763(1,237-2,511)	0,002		
APACHE II	1,185(1,078-1,302)	<0,001		
Time from the onset of symptoms to hospital admission	1,244(1,034-1,496)	0,02	1,614(1,037-1,278)	0,008
Charlson Comorbidity Index	1,901(1,326-2,726)	<0,001		
Invasive Mechanical ventilation	0,107(0,033-0,343)	<0,001		
Mechanical ventilator length of stay d, median(IOR)	0,993(0,948-1,040)	0,771		
ICU length of stay	1,014(0,980-1,049)	0,419		
Hospital length of stay	0,999(0,978-1,022)	0,957		

Discussion

This study was designed to evaluate ICU patients hospitalized due to CNS infection in the last ten years. Sixty-six percent of 61 patients were diagnosed with bacterial meningitis while 30% was diagnosed with viral encephalitis and 4% was diagnosed with tuberculous meningitis. The mortality rate was 53% and the independent risk factors for mortality were age and time from the onset of symptoms to hospital admission. As the time from the onset of symptoms to hospital admission lengthens, mortality rate was higher as well.

Proulx et al.[10] reported an independently increasing relationship between the delay in using antibiotics and mortality due to acute bacterial meningitis. Similarly, there are studies reporting that the delay in using antimicrobials for viral encephalitis, especially >48 hours after hospitalization, have increased morbidity and mortality dramatically.[11,12]

Appearance typical symptoms of patients with meningitis and encephalitis like nausea, vomiting, headache, photophobia, confusion, high fever and loss of consciousness, take hours, maybe days.[13] The most common symptoms of the patients in the current study were high fever and loss of consciousness. The median time from the onset of symptoms to hospital admission was approximately 2 (1-7) days. This was an independent risk factor for mortality of the patients in the study.

CRP values, which are one of the infection parameters at hospital admission, were high while procalcitonin levels were low. There was no statistically significant difference between procalcitonin levels and CRP values considering bacterial meningitis and viral meningitis/encephalitis patients. Dashti et al.[14] stated in the study conducted to determine predictors of viral and bacterial meningitis on infants that procalcitonin values were similar in viral and bacterial meningitis, and that it is not a diagnostic predictor. There were more leucocytes, and lower glucose values in the CSF of patients with bacterial meningitis than that of those with viral meningitis/encephalitis.

Similar to many studies in the literature, the current study determined active microorganisms in the CSF of very few patients.[14-16] This is because BOS sampling was performed after antibiotic treatment not to delay the treatment or because patients have received antibiotic treatment for another reason. The antibiotic medications for gram-negative bacteria were Meronem and Seftriakson while Vancomycin and Linezolid were the medications for gram-positive bacteria. Anti-tuberculosis treatment was done for tuberculous meningitis while Asiklovir was the medication for viral encephalitis.

The mortality rate of the study was 53% and, considering the factors for mortality, age, GCS, SOFA and APACHE scores, Charlson morbidity index, time from the onset of symptoms to hospital admission and the need for IMV were effective in the univariable analysis (p<0,05).

Flores-Cordero et al.[17] reported in a study on patients with community-based bacterial meningitis that age, APACHE II score and GCS were associated with vital clinical outcomes (death and serious neurological deficits). The independent risk factor for mortality was APACHE II score in same study.

In a retrospective study done in India, it was stated that GCS, APACHE II score and SIRS findings on admission were not effective on mortality; however, the length of stay at hospital and the presence of pneumonia during admission to ICU were effective on mortality.[15]

A study conducted on tuberculous meningitis patients showed that APACHE II and GCS were reliable indicators for predicting the course of disease and in-hospital mortality.[18]

Another study on severe purulent bacterial meningitis reported that univariable logistic regression analysis revealed that age, APACHE II, SAPS, SOFA and GCS scores, length of stay in ICU and length of stay in hospital were risk factors for mortality. The multivariable of the same study analysis showed that SAPS II score, length of stay in ICU and length of stay in hospital were independent risk factors for mortality.[19] The current study showed that age and time from the onset of symptoms to hospital admission were independent risk factors for mortality.

Advanced age is considered as a risk factor for vital outcomes in CNS infections. However, very few studies have

evaluated the effect of advanced age on prognosis of critical patients with CNS infections. Advanced age was an independent risk factor on mortality in the current study. Lai et al.[20] have specifically studied on bacterial meningitis data of patients over 65 admitted to a tertiary center. They have found higher rate of meningitis incidence along with higher mortality rate (% 34,8 and % 39 respectively). Fernandes et al. have studied for seven years on 65 acute bacterial meningitis patients over 18 admitted in ICU, and found that APACHE score was 23 and in-hospital mortality rate was 40%. Advanced age was also stated as an independent risk factor in this study.[6]

Another study conducted on bacterial meningitis patients found out that mortality rate was 44%, and the authors stated that this might be associated with severity of the disease and/or with the delayed admission to ICU.[21]

We believe that the current study contributed to the data on critical CNS infection patients. In fact, we collected data about risk factors, microbiological documentation, antibiotics and results of treatments of all adult CNS infection patients admitted to ICU over a 10-year period.

It is acceptable that the current study had some limitations; relatively low number of patients, lack of standardized treatment protocols and lack of info about procedure time from the hospitalization to antibiotic use.

Consequently, the mortality rate of patients hospitalized in ICU with diagnosis of CNS infection was high. Age and time from the onset of symptoms to hospital admission were the independent risk factors on mortality.

Referances

1. Tunkel AR, Van de Beek D, Scheld WM. Acute meningitis. In: Mandell GL, Bennett JE, Dolin R, editors. Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases. 7th edn. Philadelphia: Churchill Livingstone-Elsevier; 2010.
2. Solbrig MV, Tyler KL. Infections of the nervous system: viral infections. In: Bradley WG, Daroff RB, Fenichel GM, Jankovic J, editors. Neurology in Clinical Practice, 5th edn. Philadelphia: Butterworth-Heinemann Elsevier; 2008: pp. 1457–88.
3. Solomon T, Dung NM, Kneen R et al. Japanese encephalitis. J Neurol Neurosurg Psychiatry 2000:68:405–15.
4. Kalita J, Misra UK, Pandey S et al. A comparison of clinical and radiological findings in adults and children with Japanese encephalitis. Arch Neurol 2003:60:1760–4.
5. Chou CH, Lin GM, Ku CH, Chang FY. Comparison of the APACHE II, GCS and MRC scores in predicting outcomes in patients with tuberculous meningitis. Int J Tuberc Lung Dis. 2010;14(1):86-92.
6. Fernandes D, Gonçalves-Pereira J, Janeiro S, Silvestre J, Bento L, Póvoa P. Acute bacterial meningitis in the intensive care unit and risk factors for adverse clinical outcomes: retrospective study. J Crit Care. 2014;29(3):347-350. doi:10.1016/j.jcrc.2013.12.001
7. Edberg M, Furebring M, Sjölin J, Enblad P. Neurointensive care of patients with severe community-acquired meningitis. Acta Anaesthesiol Scand. 2011;55(6):732-739. doi:10.1111/j.1399-6576.2011.02460.x
8. Trachtenberg JD, Kambugu AD, McKellar M et al. The medical management of central nervous system infections in Uganda and the potential impact of an algorithm-based approach to improve outcomes. Int J Infect Dis 2007:11:524–30.
9. Thakur KT, Motta M, Asemota AO et al. Predictors of outcome in acute encephalitis. Neurology 2013;81:793–800.
10. Proulx N, Fréchette D, Toye B, Chan J, Kravcik S. Delays in the administration of antibiotics are associated with mortality from adult acute bacterial meningitis. QJM. 2005;98(4):291-298. doi:10.1093/qjmed/hci047
11. McGrath N, Anderson NE, Croxson MC, Powell KF. Herpes simplex encephalitis treated with acyclovir: diagnosis and long term outcome. J Neurol Neurosurg Psychiatry. 1997;63(3):321-326.
12. Raschilas F, Wolff M, Delatour F, et al. Outcome of and prognostic factors for herpes simplex encephalitis in adult patients: results of a multicenter study. Clin Infect Dis. 2002;35(3):254-260. doi:10.1086/341405 doi:10.1136/jnnp.63.3.
13. Ziai WC, Lewin JJ 3rd. Update in the diagnosis and management of central nervous system infections. Neurol Clin. 2008;26(2):427-viii. doi:10.1016/j.ncl.2008.03.013)
14. Ziai WC, Lewin JJ 3rd. Update in the diagnosis and management of central nervous system infections. Neurol Clin. 2008;26(2):427-viii. doi:10.1016/j.ncl.2008.03.013)
15. Sanaei Dashti A, Alizadeh S, Karimi A, Khalifeh M, Shoja SA. Diagnostic value of lactate, procalcitonin, ferritin, serum-C-reactive protein, and other biomarkers in bacterial and viral meningitis: A cross-sectional study. Medicine (Baltimore). 2017;96(35):e7637. doi:10.1097/MD.0000000000007637.
16. Misra UK, Kalita J, Bhoi SK. Spectrum and outcome predictors of central nervous system infections in a neurological critical care unit in India: a retrospective review. Trans R Soc Trop Med Hyg. 2014;108(3):141-146. doi:10.1093/trstmh/tru008,
17. Flores-Cordero JM, Amaya-Villar R, Rincón-Ferrari MD, et al. Acute community-acquired bacterial meningitis in adults admitted to the intensive care unit: clinical manifestations, management and prognostic factors. Intensive Care Med. 2003;29(11):1967-1973. doi:10.1007/s00134-003-1935-4
18. Chou CH, Lin GM, Ku CH, Chang FY. Comparison of the APACHE II, GCS and MRC scores in predicting outcomes in patients with tuberculous meningitis. Int J Tuberc Lung Dis. 2010;14(1):86-92.
19. Pietraszek-Grzywaczewska I, Bernas S, ojko P, Piechota A, Piechota M. Predictive value of the APACHE II, SAPS II, SOFA and GCS scoring systems in patients with severe purulent bacterial meningitis. kk. 2016;48(3):175-179. doi:10.5603/AIT.a2016.0030
20. Lai WA, Chen SF, Tsai NW, et al. Clinical characteristics and prognosis of acute bacterial meningitis in elderly patients over 65: a hospital-based study. BMC Geriatr. 2011;11:91. Published 2011 Dec 28. doi:10.1186/1471-2318-11-91
21. Edberg M, Furebring M, Sjölin J, Enblad P. Neurointensive care of patients with severe community-acquired meningitis. Acta Anaesthesiol Scand. 2011;55(6):732-739. doi:10.1111/j.1399-6576.2011.02460.x

Original Articles
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Evaluation of Tracheatomies Performed by Percutaneous Dilatation Method in Adult Intensive Care Unit

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Abstract

Aim: Percutaneous dilatation tracheotomy in our clinic; It is opened using the advantages and methods of Griggs (GWDR) and Ciaglia Blue Rhino (CBR). We wanted to share our one-year experience with you.

Method: In the study that we retrospectively examined tracheotomies performed in adult intensive care in 2019-2020; Demographic data of patients, SOFA scores, intensive care, tracheotomy, intubation days, complications, mortality and morbidity were recorded.

Results: A total of 50 patients, 33 females, 17 males, were included in the study. The mean age is 65,54 ± 15,95. BMI was 26,94 ± 2,75. Ciaglia was used in 22 patients and Griggs method was used in 28 patients. Tracheotomy opening day is 10,45 ± 1,27. Griggs method; It was found to be significantly higher in terms of complications (6 minor bleeding, 1 emphysema, 1 lack of ventilation) (p = 0,001). Mortality (independent of tracheotomy method and complications) was significantly higher in the Griggs method (p = 0,005).

Conclusion: Except for minor differences, no significant difference was found between both GDWR method and CBR method in the study.

Keywords: Griggs, Ciaglia Blue Rhino®, percutaneous dilatational tracheotomy, complications

Introduction

Prolonged endotracheal intubation can lead to laryngeal damage, tracheal damage (tracheomalacia, tracheal dilatation and tracheal stenosis), vocal cord paralysis, glottic and subglottic stenosis, and infectious complications[1]. With tracheotomy, it is aimed to reduce the complications that may occur due to prolonged endotracheal intubation. Despite these advantages, tracheotomy is an invasive procedure and some complications related to the intervention may develop[2].

In 1955, Shelden et al. Applied the first percutaneous dilatation tracheotomy (PDT) technique[3]. It was developed with the Seldinger method by PDT Toye and Weinstein in 1969[4]. Sequential dilatation method was used by Ciaglia in 1985 by means of guidewires and dilators[5]. Over time, the Ciaglia Blue Rhino (Single Dilatation, CBR) method, Percutwist (Controlled Dilatation) method, Griggs (Forceps Dilatation, GWDR) method, Fantoni Translaryngeal method have been developed[6-9].

Tracheotomies opened by percutaneous dilatation method; It is frequently used in patients receiving prolonged mechanical ventilator support. In this study, we aimed to compile and present the tracheotomies opened with two different dilatation methods (Griggs (GWDR) and Ciaglia Blue Rhino (CBR)) used in our clinic.

Method

In the study that we retrospectively examined tracheotomies performed in adult intensive care in 2019-2020; The demographic data of the patients, SOFA scores, indications for intensive care hospitalization, tracheotomy opening days, complications, and mortality were recorded.

Written informed consent for the tracheotomy procedure was obtained from the first degree relatives of the patients. All of the cases were intubated orotracheally and received mechanical ventilation support. Percutaneous tracheotomy was performed in the intensive care unit by an intensive care specialist. Following fentanyl 1 mcg / kg, propofol 2 mg / kg, and rocuronium 0,6 mg / kg IV in patients undergoing percutaneous tracheostomy, 100% oxygen, PEEP 0 mmHg with pressure control synchronized intermittent mandatory ventilation (P-SIMV) mode mechanical ventilation done. The patients were monitored with electrocardiography, blood pressure and saturation probe. After the patient was placed in a flat supine position, the head was extended with an under-shoulder support. The area to be treated was cleaned with 2% povidone iodine and the patient was covered with a sterile condition. 1.-2 of the tracheal cartilage. or 2.-3. Local anesthesia with 2% prilocaine (4-5 mL) was applied to the area to be treated by palpating the area. After

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Table 1. Hospitalization indications of patients who underwent tracheostomy

	N	%
Serebrovasculer disease (SVD)	7	14
Respiratory System Pathology	5	10
After Cardiopulmonary Resuscitation	3	6
Sepsis	8	16
Head trauma	27	54

Table 2. Study results

	CBR (n:22)	GWDR (n:28)	P değeri
Age	67,14	64,29	,138
BMI	27,15	26,79	,808
SOFA	8,50	8,29	,601
Platelet	240,77	186,36	,308
INR	1,23	1,52	,009*
aPPT	34,03	35,94	,351
Complication	2	8	,001*
Minör bleeding	2	6	
Emphysema		1	
Lack of ventilation		1	
Mortality	10	24	,005*
Decanulation	8	9	,871

local anesthesia, 3 mL of saline solution was drawn, and the tracheal lumen was entered by aspiration from the designated area with the help of an injector with a 14G needle at the tip. When air was aspirated into the injector, the injector was detached from the needle and the guidewire passed through it was inserted into the tracheal lumen. The area was enlarged with the help of a dilator passed over the guidewire. After removing the dilator and expanding the subcutaneous and trachea with the help of Griggs forceps or Blue Rino, the size 7.5 or 8 tracheotomy cannula was passed over the guide and inserted into the trachea.

Statistical analysis was done with SPSS version 20. Nonparametric tests were applied. Frequency and average values were calculated.

Results

A total of 50 patients, 33 females, 17 males, were included in the study. The patients were admitted to the intensive care unit due to cerebrovasculer disease (SVD) 7 (14%), respiratory system pathology 5 (10%), after cardiopulmonary resuscitation 3 (6%), sepsis 8 (6%), head trauma 27 (54%). (Table 1). In our study, the most common elective percutaneous tracheotomy indication was due to 74% prolonged coma (n: 37) and 26% prolonged mechanical ventilation need (n: 13). The mean age is 65,54 ± 15,95. BMI was 26,94 ± 2,75. Tracheotomy opening day is 10,45 ± 1,27. CBR method was used in 22 patients and GWDR method was used in 28 patients. In the CBR method, minor bleeding was observed in 2 patients. The GWDR method was found to be significantly higher in terms of complications (6 minor bleeding, 1 emphysema, 1 lack of ventilation) (p = 0,001). Comparing the INR values; Values were found to be significantly higher in the GWDR method. In our study, there was no case loss due to complications of the procedure during or after the tracheostomy procedure. There were no late complications. Thirty-four patients (68%) died as a result of the natural course of the pathologies followed in the intensive care unit. Mortality (independent of the tracheotomy method and complications) was found to be significantly higher in the GWDR method (p = 0,005) (Table 2). Of the patients using the GWDR method, there were 9 patients who underwent decanulation and 8 patients in the CBR method. Complete closure of the stoma after decanulation occurred within 48-72 hours before any patient developed stenosis.

Discussion

Tracheotomy procedure is a procedure performed in intensive care units to reduce complications of endotracheal intubation and mechanical ventilation and to increase patient comfort, rather than being an emergency airway supply method. With the increase in the number of patients connected to mechanical ventilators, the tracheotomy procedure has also increased[10].

Çiçek et al.[11] determined the opening day of tracheotomy as 13,23 ± 6,29 days. Kırca et al.[12] It was found to be 8,65 ± 5,97 days. Scales et al.[13], the average time to open tracheotomy by day in the intensive care unit was found to be 34,3% within the first 10 days. In this study, the day of tracheotomy opening; It was found to be 10,45 ± 1,27.

Complications can be divided into perop, early and late complications. Perop period complications include apnea, cardiac arrest, air embolism, pneumothorax, pneumomediastinum, adjacent tissue injury, and bleeding. Early complications include cannula obstruction, cannula dislocation, tracheitis, emphysema, aspiration, and hemorrhage. Late complications include tracheoesephageal fistula, tracheoesephageal fistula, tracheomalacia, decannulation difficulty, and laryngotracheal stenosis. Subcutaneous emphysema and pneumothorax are serious complications that may develop during percutaneous tracheotomy. In our study; Subcutaneous emphysema developed in 1 patient after PDT with the GWDR method due to the increase in PEEP value to provide oxygenation. Spontaneous resorption was observed in the patient, pneumothorax did not develop. In 1 patient with low aeration, the problem was resolved with aspiration performed after the procedure. Güçyetmez et al.[14] found the most frequent bleeding (68%, n:138 patients) as an early complication in their study. In our study, one of the early

complications, minor bleeding, depending on the high INR; It was more common in the GWDR method. Minor bleeding seen in the early period; It was taken under control with a printed dressing made with the help of adrenaline gauze.

Güçyetmez et al. The most common reasons for opening a tracheostomy were prolonged mechanical ventilation need (76,9%) and prolonged coma (14,8%)[14]. In our study, the most common indication for opening an elective percutaneous tracheotomy was due to prolonged coma and the need for prolonged mechanical ventilation.

As a result; PDT methods are safe in terms of major complications. Minor bleeding seen more in the GWDR method; depends on the INR height in the group.

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Referances

1. Whited RE. A prospective study of laryngotracheal sequelae in long term intubation. Laryngoscope 1984; 94(3): 367-77.
2. Friedman Y. Percutaneous versus surgical tracheostomy: The continuing saga. Crit Care Med 2006; 34(8): 2250-1.
3. Sheldon CH, Pudenz RH, Freshwater D B. A new method for tracheostomy. Journal of Neurosurgery1955; 12: 428-431.
4. Toye FJ, Weinstein JD. A percutaneus tracheostomy device. Surgery 1969; 65: 384-389.
5. Ciaglia P, Firsching R, Syniec C. Elective percutaneous dilatational tracheostomy. A new simple bedsideprocedure; preliminary report. Chest 1985; 87: 715-719.
6. Byhahn C, Wilke HJ, Halbig S, Lischke V, Westpal K. Percutaneous tracheostomy: Ciaglia Blue Rhio versus the basic Ciaglia technique percutaneous tracheostomy. Anesth Analg 2000; 91: 882-886.
7. Frova G, Quintel M. A new simple method for percutaneous tracheostomy: Controlled rotating dilatation a preliminary reportIntensive Care Med 2002; 28: 299-303.
8. Griggs WM, Wortley LIG, Gilligan JE, et al. A simple percutaneous tracheostomy technique. Surg Gynecol Obstet 1990; 170: 543-545.
9. Fantoni A, Ripamonti D. A non-derivative,nonsurgical tracheostomy: The Translarnygeal method. Intensive Care Med 1997; 23: 386-392.
10. Erden V, Şanlı Hamzaoğlu N, Başaranoğlu G, Delatioğlu H, Erkalp K. Percu Twist Yöntemi ile Perkütan Trakeostomi. Yoğun Bakım Dergisi 2004; 4: 57-60.
11. Çiçek M, Gedik E, Yücel A. ve ark. Griggs tekniği ile açılan perkütan trakeostomi sonuçlarımız. İnönü Üniversitesi Tıp Fakültesi Dergisi 2007; 14: 17-20.
12. Kırca H, Çakın Ö, Cengiz M, Yılmaz M, Ramazanoğlu A. Yoğun Bakımda Trakeotomi: Endikasyonlar, Komplikasyonlar ve Prognoz. J Turk Soc Intens Care 2018; 16: 17-25.
13. Scales DC, Thiruchelvam D, Kiss A, Redelmeier DA. The effect of tracheostomy timing during critical illness on longterm survival. Crit Care Med 2008; 36: 2547-57.
14. Gücyetmez B, Atalan HK, Cakar N. Elective Tracheotomy Practices in Turkey. 2016;15.

Original Articles
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Evaluation of the Awareness of Chronic Kidney Disease Among Patients Receiving Hemodialysis

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Abstract

Objectives: Awareness of chronic kidney disease is important for compliance to treatment before the disease progresses to advanced stages. Low patient awareness causes the disease to advance to end-stage renal failure requiring high cost dialysis and kidney transplantation treatments.

The objective of this study is to measure the awareness of chronic kidney disease in patients receiving hemodialysis and to assess the correlation of patient awareness with quality of life and depression. Additionally, this study assessed the importance of patient monitoring.

Study design: This study is an evaluation and analysis study.

Material & Methods: A total of 213 hemodialysis patients from 7 centers in Giresun were enrolled in this study. Awareness, factors affecting awareness, quality of life (SF-36) and the Beck depression index of chronic kidney disease in patients receiving hemodialysis treatment.

Results: Of patients, 71.4% (n=152) were monitored by nephrology, 43.2% (n=92) were monitored by dieticians and 10.8% (n=23) were receiving psychological support. The awareness points of patients monitored by dieticians is significantly high compared with that of not under the control of dieticians. Also, the awareness points of patients monitored by nephrology is significantly lower compared with the patients not monitored by nephrology. There was no significant difference between awareness points of those who were receiving psychological support compared to those who were not.

Conclusions: Consultations with dieticians may provide positive support to increase the disease awareness of hemodialysis patients. Increasing disease awareness does not create a positive or negative situation in terms of depression and quality of life.

Keywords: Chronic kidney disease,Awareness, Hemodialysis, Quality of Life, Depression

Introduction

Chronic kidney disease (CKD) is a significant public health concern all over the world. Although its progression can be prevented or delayed with early diagnosis, low patient awareness and ineffective communication between patients and providers communication can impede such efforts. Awareness of CKD is important for compliance to treatment before the disease progresses to advanced stages and to improve health outcomes[1]. Unfortunately, awareness of this disease is lower among patients compared to other chronic diseases. According to studies in different parts of the world, the awareness of the disease is below 10 percent[2, 3]. Even among patients with 2-4 clinical symptoms linked to CKD, awareness rates do not exceed 10 percent[4].

In Turkey, awareness rates are even lower. According to the Chronic Renal Disease in Turkey prevalence study (CREDIT) by the Turkish Society of Nephrology, lower patient awareness of CKD in Turkey was detected (<2%)[5]. In 2010, the Renal Health Bus project run by the Turkish Society of Nephrology revealed that the awareness of the disease was 5.7% in 21 provinces of Turkey[6]. Due to low patient awareness, the disease advances to end-stage renal failure (ESRF) requiring high cost dialysis and kidney transplantation treatments. This situation causes a severe threat to patient health and health budgets.

A continuous and rapid increase has recently occurred in the number of patients undergoing renal replacement therapy in Turkey. As of the end of 2013, according to nation-wide health registry data, approximately 66700 patients were currently undergoing renal replacement therapy, with a prevalence and incidence of 870 and 138 per-million population, respectively, for end-stage renal failure[6]. The most frequent treatment modality for end stage renal failure is hemodialysis Other therapeutic modalities in this patient group include renal transplantation (14%) and peritoneal dialysis (7%)[7].

In this study, we aimed to measure the awareness, factors affecting awareness, quality of life and Beck depression index in CKD patients receiving hemodialysis (HD) treatment.

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Methods

A total of 213 HD patients from 7 centers in Giresun province were enrolled in this study. A written informed consent was obtained from each participant, and data were collected with face-to-face interviews. The study protocol was approved by the local ethics committee and the study procedures were carried out in accordance with the principles set forth by the Declaration of Helsinki.

Patients' age, educational level, income level, chronic diseases, habits, previous operations and duration of hemodialysis therapy in years, were obtained during the interview portion of the surveys. Patients were asked to answer the disease awareness questions. In addition they were asked to fill out the "Quality of Life (SF-36)[8] and "Beck Depression Inventory" (BDI)[9] with adaptation, validity and reliability studies completed for Turkish society.

The questions used to measure disease awareness of the patients were prepared by the researchers with screening the literature.

Patients were asked the following question to assess their awareness of CKD:

	DISEASE AWARENESS QUESTIONS
1	What is kidney failure?
2	What is dialysis?
3	How many types of dialysis are there?
4	Do you know the names of the types of dialysis?
5	What is the disease that you have requiring you to have dialysis?
6	What are things that you should not eat or drink?
7	Are you monitored by nephrology?
8	Have you applied to a dietician?
9	Are you receiving psychological support?

All answers were classified and given points. As the first 2 questions had subjective answers, 2 necessary answers were determined, with points given as 0 (zero) for not mentioning either, 1 (one) for mentioning one of the answers and 2 (two) for mentioning both answers. Question 5 was asked to determine whether the patient knew the disease that required them to have dialysis and points were given for knowing or not knowing. Question 6 enquired about foods and fluids that should not be eaten with patients expected to answer related to foods containing water, salt, potassium and phosphorus.

In this study for the first 6 questions aiming to assess awareness, total points were compared. The final 3 questions were to assess experts, the patient had consulted with about the disease and each question was compared separately.

Statistical Analysis

Data was analyzed using the Statistical Package for the Social Sciences (SPSS) software program (22.0 for Windows) (SPSS Inc., Chicago, IL, USA). Normality of the variables was analyzed with the Kolmogorov-Smirnov test. Statistical significance between different groups were tested with Independent sample t-test whenever both groups have normal distribution, otherwise Fisher's exact test was used. Mann-Whitney U test was used in comparison of non-normally distributed variables. $p<0.05$ values considered statistically significant.

Results

The study assessed 213 patients who volunteered to answer questions and fully answered the survey forms. Mean age was 60.73 ± 13.89 years, with female/male ratio of 89/124. Demographic data for the patients are shown in Table 1.

Table 1. Demographic features of the patients

Number of patients	213	-
Age (mean)	60.73	-
Sex (F/M)	89/124	-
Education	(%)	(n)
None	23	49
Primary	50.2	107
Middle school	10.8	23
High school	10.8	23
University	2.3	5
Income	(%)	(n)
0-300 $	36.2	77
300-600 $	48.4	102
600-900 $	6.6	14
900-1400 $	0.9	2
> 1400 $	0.9	2

The question form relating to disease awareness had total points of 11, and the mean score was found as 3.67. Of patients, 46.9% (n=100) answered the question "what is kidney failure?" incorrectly, while 92.5% (n=197) answered the question "what is dialysis?" incorrectly. Of patients, 71.4% (n=152) were monitored by nephrology, 43.2% (n=92) were monitored by dieticians and 10.8% (n=23) were receiving psychological support (Table 2). The points for SF-36, Beck Depression Index and awareness are shown on Table 3.

Table 2. Disease awareness scores of the patients

What is kidney failure?	0	46.9	100
	1	49.8	106
	2	3.3	7
What is dialysis?	0	92.5	197
	1	5.2	11
	2	2.3	5
How many types of dialysis are there?	0	38.5	82
	1	56.8	121
	2	4.7	10
Do you know the names of the types of dialysis ?	0	57.3	122
	1	8.0	17
	2	34.7	74
What is the disease that you have requiring you to have dialysis?	0	47.4	101
	1	52.6	112
What are things that you should not eat or drink?	0	50.7	108
	1	44.6	95
	2	4.7	10
Are you monitored by nephrology?	YES	71.4	152
	NO	23.0	49
Have you applied to a dietician?	YES	43.2	92
	NO	51.2	109
Are you receiving psychological support?	YES	10.8	23
	NO	83.6	178

Table 3. The points for SF-36, Beck Depression Index and awareness are shown on Table 3.

Physical Functioning	39.014 ± 31.046
Role-Physical Limitation	26.115 ± 23.532
Role Emotional	31.925 ± 22.386
Vitality	27.418 ± 22.864
Mental Health	61.390 ± 17.728
Social Functioning	78.287 ± 29.381
Bodily Pain	70.599 ± 29.948
General Healty Perception	31.362 ± 20.690
Phsical Component Summary Score	41.773 ± 18.542
Mental Component Summary Score	49.755 ± 13.386
Beck Depression Inventory Score	14.200 ± 8.250
Awareness Score	3.671 ± 2.419

The answers given by patients, demographic data, SF-36 form evaluation and Beck Depression Index results were compared with each other. While the awareness points for those who applied to a dietician were significantly higher compared to those who had not applied to a dietician ($p<0.001$), there was no significant difference between SF-36 points. The awareness points of those monitored by nephrology were significantly lower compared to those not monitored ($p<0.001$). Additionally the mental component points on SF-36 evaluation for those monitored by nephrology were observed to be significantly higher compared to those who were not monitored by nephrology ($p<0.001$), with no significant difference observed for the physical component (Table 4).

There was no significant difference between awareness points of those who were receiving psychological support compared to those who were not. Other evaluations found that those who were receiving psychological support had significantly higher social work points ($p=0.039$) and significantly lower general health perception points ($p=0.008$) with no significant difference identified between physical and mental components. There was no significant difference observed between all groups in terms of Beck Depression Index points.

Discussion

In our study, we attempted to assess our patients' awareness of CKD, quality of life and depression levels. When the sociodemographic data of our patients were examined, no significant differences were found between SF-36, Beck and awareness points in terms of age. We observed that only education had a significant contribution to physical function

Table 4. The mean scores of SF-36 according to monitoring by nephrology

			p
Physical Functioning	41.15 ± 3092	36.73 ± 31.57	0.388[a]
Role-Physical Limitation	**29.68** ± 23.23	**16.07** ± 21.35	**<0.001[a]**
Role Emotional	**36.4** ± 20.61	**16.66** ± 21.25	**<0.001[a]**
Vitality	**24.73** ± 21.92	**39.38** ± 22.95	**<0.001[b]**
Mental Health	61.5 ± 18.20	62.28 ± 17.22	0.790[a]
Social Functioning	**80.67** ± 28.80	**69.64** ± 31.15	**<0.023[a]**
Bodily Pain	**73.66** ± 29.70	**63.97** ± 27.38	**<0.042[a]**
General Healthy Perception	**30.49** ± 20.68	**38.06** ± 19.12	**<0.024[a]**
Physical Component Summary Score	43.77 ± 18.18	38.71 ± 17.96	0.398[b]
Mental Component Summary Score	50.83 ± 13.07	46.99 ± 14.3	**<0.02[b]**
Beck Depression Inventory Score	14 ± 7.88	14.18 ± 9.30	0.590[a]
Awareness Score	1.59 ± 1.41	2.3 ± 1.30	**<0.001[b]**
a) Independent Samples t-test			
b) Mann -Whitney U test			

points. We found that only income status had a significant difference on Beck Depression Index points.

The important information for us was related to the awareness levels of patients about their disease, the level of support they were receiving and how much these had benefited the patients. As a result, we attempted to determine how much knowledge they had about dialysis and CKD through questions asked to the patients, whether they received psychological and dietician support and whether they were monitored by nephrology, apart from the dialysis clinician. Then we assessed the correlations between these factors with SF-36 and Beck Depression Index points for the patients.

There is no standard method among the studies investigating CKD awareness of the patients. This has caused different results in the literature. Therefore, making an exact comparison is difficult.

In a study on awareness of diabetic disease, it was observed that 74% of patients gave incorrect answers to the question "what is diabetes?" The same study found that 53% of patients gave wrong answers to the question "what should starving and satiated blood sugar levels be?"[10]. Though our study does not relate to the same disease, a comparison was made as both studies examined awareness of diseases with chronic progression requiring continuous treatment. In our study 46.9% of patients answered the question "what is kidney failure?" incorrectly, while 92.5% answered the question "what is dialysis?" incorrectly.

Before beginning our study, we considered that patients with high awareness of the disease would expend more effort and would receive greater levels of support from dieticians, psychologists and nephrology departments. However, when our results are assessed, we found that only patients receiving dietician support had high disease awareness. Contrary to this, patients receiving nephrology support had lower awareness and there was no difference in the awareness levels of the patients receiving psychological support and those who were not. We thought that consulting with a dietician may provide positive support to increase the disease awareness of patients receiving hemodialysis treatment. It appears that nephrology monitoring was not a significant factor in awareness; however we thought the high percentage of patients consulting with nephrology (71.4%) may be due to the patients who have to consult due to the natural progression of the disease. In our patient group the number of patients receiving psychological support was very low (10.8%) and we did not observe any positive or negative contribution of disease awareness about this topic. We did not observe any significant correlation between Beck Depression points and SF-36 points with disease awareness.

In a study by Tuot et al. related to dialysis groups, CKD awareness was assessed in 1852 adults with an estimated GFR of 60 ml/min per 1.73 m2 using 1999 to 2008 National Health and Nutrition Examination Survey data[4]. CKD awareness was a "yes" answer to "Have you ever been told you have weak or failing kidneys?" Participants were grouped by distribution of the following abnormal markers of CKD: hyperkalemia, acidosis, hyperphosphatemia, elevated blood urea nitrogen, anemia, albuminuria, and uncontrolled hypertension. The results of the study found that 90% of individuals with two to four markers of CKD and 84% of individuals with 5 markers of CKD were unaware of their disease[11]. A study by Alsadhan et al. assessed the awareness of dialysis patients about diet and asked patients whether sodium, potassium, fluid intake, calcium/phosphorus and lipids were dangerous. They found awareness points between 86.5% (lipids) and 71.3% (fluid intake). In the study they showed a positive effect of dietician visits on awareness points[12].

In a study by Oluyombo et al. from Nigeria, awareness and knowledge about chronic kidney disease was investigated in the general population. Only 33.7% of the patients had heard of CKD, 10.6% could mention at least one function of

the kidneys, and majority of the patients (67.0%) could not know the correct localization of the kidneys in the body[13]. In another study by Shirazian et al. with 2500 patients with CKD, awareness of CKD was found as 6.4%. Awareness of CKD was found to be significantly associated with depressive symptoms.

In our study, we did not observe a significant difference in the Beck Depression points of the patients receiving dietician support or nephrology follow-up compared to those who were not. Interestingly, the Beck Depression Index points were significantly higher for the patients receiving psychological support compared to those who were not. When this situation is assessed together with the lack of significant difference in disease awareness between the patients receiving psychological support and those not receiving it, it leads to the consideration that consultation with psychologists was linked to the necessity rather than awareness.

We did not show any effect of receiving dietician support on SF-36 points. We observed that the patients receiving psychological support had significantly higher social work points and significantly lower general health perception points. The physical role, emotional role, social work, pain and mental component points of the patients receiving nephrology follow-up were high, while general health perception and energy points were significantly lower.

As our study encompassed a whole province, we think our results are valuable. However, there is a need for broader scale studies as there are insufficient studies on disease awareness among hemodialysis patients in the literature.

In conclusion; we found that chronic kidney disease awareness of the patients receiving hemodialysis was found low. The awareness was higher among the patients who were receiving support from a dietitian. Consultations with dieticians may provide positive support to increase the disease awareness of hemodialysis patients.

Correct perceptions of disease and accessing accurate information about the disease have a significant effect on correct management of disease by individuals.

References

1. Bodenheimer T, Lorig K, Holman H, Grumbach. Patient self-management of chronic disease in primary care. K JAMA. 2002 Nov 20; 288(19):2469-75.
2. Plantinga LC, Boulware LE, Coresh J, et al. Patient awareness of chronic kidney disease. Trends and Predictors. Arch Intern Med 2008; 168: 2268-75.
3. Bridges, Torrel R., "Awareness, Education, and Prevention of Chronic Kidney Disease in the Older Adult" (2014).Honors Theses.Paper 253.
4. Tuot DS, Plantinga LC, Hsu C, et al. Chronic kidney disease awareness among individuals with clinical markers of kidney dysfunction. Clin J Am Soc Nephrol 2011; 6: 1838-44.
5. Süleymanlar G, Utaş C, Arinsoy T, et al. A population based survey of chronic renal disease in Turkey - The CREDIT study. Nephrol Dial Transplant 2011; 26: 1862-71.
6. http://www.nefroloji.org.tr/pdf/Turkiye_Bobrek_Hastaliklari_Onleme_ve_Kontrol_Programi.pdf
7. Seyahi N, Altiparmak MR, Ates K, Trabulus S, Suleymanlar G. Current Status of Renal Replacement Therapy in Turkey: A Summary of Turkish Society of Nephrology 2014 Annual Registry Report. Turk Neph Dial Transpl 2015;24(1): 10-16.
8. Kocyigit H, Aydemir O, Fisek G, Olmez N, Memis A. The reliability and validity of the short form-36(SF-36) Turkish version. Drug and Treatment Journal 1999;12:102-6.
9. Hisli N. The reliability and validity of the Beck Depresion Inventory for university students. Psychology Journal 1989;7:13.
10. Usta Atmaca H, Akbas F, Sak T, Uysal Sak D, Acar S, Niyazoglu M. Consciousness Level and Disease Awareness among Patients with Diabetese. İstanbul Med J 2015; 16:101-4
11. Delphine S. Tuot, Laura C. Plantinga, Chi-yuan Hsu, Regina Jordan, Nilka Ríos Burrows, Elizabeth Hedgeman, Jerry Yee, Rajiv Saran, and Neil R. Powe, for the Centers for Disease Control Chronic Kidney Disease Surveillance Team. Chronic Kidney Disease Awareness Among Individuals with Clinical Markers of Kidney Dysfunction. Clin J Am Soc Nephrol 6: 1838–1844, August, 2011.
12. AlSadhan AA, Hejaili F, Bin Salih S, Level of Dietary Awareness among Saudi Dialysis Patients and the Influence of Various Factors. Saudi J Kidney Dis Transpl 2015;26(3):544-548
13. Oluyombo R, Ayodele OE, Akinwusi PO, Okunola OO, Gbadegesin BA et al. Awareness, knowledge and perception of chronic kidney disease in a rural community of South-West Nigeria. Niger J Clin Pract. 2016 Mar-Apr;19(2):161-9.

Original Articles
Eurasian Journal of Critical Care

Neutrophil-Lymphocyte Ratio as a Mortality Predictive Paramater In Patıents Wıth Out-of-Hospital Cardiac Arrest

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Abstract

Introduction: Cases of gunshot injuries among trauma patients admitted in the emergency room are fatal cases in Turkey as much as all over the world. It is perhaps the most complex group among trauma patients. Because the route of the bullet fragment, how much damage it causes on its way and which organ or organs will be harmed cannot be understood immediately so long-term follow-up may be required.

Case report: A 48-year-old civilian male patient brought to our hospital after gunshot injury. It was found that he was injured with pellets in many parts of his body. He was not operated on to prevent possible bleeding and to remove the pellets. Instead, vital signs were followed.

Results and Conclusion: Most of the patients who are injured by guns die. The most important reason for this is acute and large amount of bleeding. In this article, we will present a patient who has been exposed to multiple pellet shots but survived.

Key words: Emergency Service,Gunshot injury, multiple injury, trauma

Introduction

The rates of out-of-hospital cardiac arrests (OHCA) increase every passing day[1], while the corresponding survival rates display regional differences. The survival rate is around 10% percent in Europe, 6% percent in North America, 11% percent in Australia and 2% in Asia[2]. In patients with return of spontaneous circulation (ROSC), the systemic ischemia/reperfusion injury leads to development of a systemic inflammatory response and thereby, a sepsis-like condition[1,3], which is called post-cardiac arrest syndrome (PCAS) ensues.

PCAS is composed of 4 major components including post-cardiac cerebral injury, myocardial injury, systemic ischemia reperfusion response and persistent precipitating pathology[4]. Despite all the improvements in care after cardiac arrest, the majority of mortalities occur in the first 24-hours after the cardiac arrest[5]. Unfortunately, the prognostic factors, which can be utilized in this critical period, are not well defined[1] .

According to the studies performed in recent years, prominent changes have been found to occur in the white blood cell (WBC) subtypes following stress. Galus reported that lymphocytopenia can develop in infectious conditions[6] and Jilma *et al.* determined increases in neutrophil counts and decreases in lymphocyte and monocyte counts following inflammation[7].

Zahorec proposed a new parameter, which he called "neutrophil to lymphocyte stress factor". It was indicated that the ratio of the peripheral neutrophils to lymphocytes (NLR) was a better indicator of prognosis in comparison to the total WBC counts[8]. In recent years, studies performed on acute coronary syndrome, acute decompansed heart failure and pulmonary embolism revealed that NLR was associated with mortality[9-12]. In this current study, we also aimed to investigate the association of NLR with early mortality in OHCA patients with return of spontaneous circulation (ROSC).

Methods

Study Setting

This retrospective study was conducted in an emergency department of a regional academic hospital in Konya providing services with 1096 beds. This emergency department provides services to an approximate 300,000 patients per year. All the OHCA patients with ROSC between January 1st and 31st of December were included in the study. Resuscitations were performed on all patients according to the recommendations of the American Heart Association Cardiopulmonary Resuscitation Guideline of 2010.

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Table 1. Demographics and laboratory findings of the study population.

Age, years, median (IQR)	73(19)
Sex, no(%)	
Male	44(48.4)
Female	47(51.6)
Presence of witness, n (%)	
Witnessed	65 (71)
Bystander CPR, n(%)	
Done	3 (3.2)
Arrest rhythm, n(%)	
Asystole	52(57.1)
PEA	29(31.9)
VT/VF	10(11)
Cause of arrest, n(%)	
Cardiac	37 (40.6)
Noncardiac	54 (59.4)
Hemoglobin,gr/dl, median (IQR)	12.7(3.6)
Neutrophil, K/UL, median (IQR)	8.6(8.3)
Lymphocyte, K/UL, median(IQR)	2.8(5.2)
NLR, median(IQR)	3.05(9.8)
Platelet, K/UL, median(IQR)	208.000(128.500)
Urea, mg/dl, median(IQR)	65(55)
Creatinine, mg/dl, median(IQR)	1.37(1.51)
Arterial lactate, mmol/L, median(IQR)	6.2(3.9)
24-h mortality, n (%)	51 (56.1)
14-day mortality, n(%)	75(82.4)

IQR: Interquartile range, CPR: cardiopulmonary resuscitation, PEA: pulseless electrical activity, VF: ventricular fibrillation, VT: ventricular fibrillation, NLR: neutrophil lymphocyte ratio

Prehospital patient data were obtained from the records of the 112-Emergency Medical System, which is the nationwide official emergency service in Turkey. All the laboratory data were acquired by the survey of the laboratory findings, which were obtained from the blood specimens obtained on patient admission.

Participitants and The Data Collection

The study population was defined as OHCA patients with ROSC. The exclusion criteria comprised patient age of under 18, a medical history of hematological disease, cancer and cirrhosis and traumatic and toxicological causes of OHCA. The age, gender, the presence of witness, bystander CPR and the arrest rhythms of the patients were recorded.

Among the laboratory data, the WBC, hemoglobin, neutrophil, lymphocyte counts, lactate and creatinine values were recorded. NLR values were calculated and the 24-hour and the 14-day mortalities of the patients were recorded. Local ethics committee approval was obtained for the study and is compatible with the Helsinki declaration.

Statistical analysis

Statistical analysis was performed using the SPSS v.15.0 for Windows. Both visual (histogram and probability graphs) and analytical (Kolmogorov-Smirnov and Shapiro-Wilk tests) methods were used to determine if the data was normally distributed. Descriptive variables were expressed as mean ± SD for data that were normally distributed, and as median and interquartile range (IQR) for variables that were not normally distributed. The chi-square or Fisher's exact test was used to compare the categorical values.

The clinical and laboratory characteristics of the deceased and surviving patients in the first 24-hours were compared with the Mann Whitney U-test. The cause of arrest was classified as cardiac and non-cardiac arrest according to the etiology. These two groups were also compared by the Mann-Whitney U-test. Two groups were formed according to the median values of the NLR and their clinical and laboratory features were compared with the Mann Whitney U-test and the Fisher's exact test.

The effect of the NLR median values on the survival of the ROSC patients was evaluated with the log rank test.

Table 2. Analysis of factors associated with 24-h mortality

	Death within 24-h (n=51)	24–h survivors (n=40)	p
Age,years, median(IQR)	72 (21)	76.5 (15)	0.31
Sex			0.26
Male, n (%)	22(43.1)	22(55)	
Female, n (%)	29(56.9)	18(45)	
Arrest rhythm, n(%)			0.06
Asystole	34(66.7)	18(45)	
PEA	13 (25.5)	16(40)	
VT/VF	4(7.8)	6(15)	
Cause of arrest, n(%)			0.16
Cardiac	24(47.1)	13 (32.5)	
Noncardiac	27 (52.9)	27 (67.5)	
Hemoglobin,gr/dl, median (IQR)	12.3(3.4)	13.1(5)	0.47
Neutrophyl, K/UL, median (IQR)	7.1 (5.7)	11.2(7.1)	0.004
Lymphocyte, K/UL, median(IQR)	4.1(5.4)	2.0(3.8)	0.1
NLR, median(IQR)	1.27 (3.8)	5.6(12.8)	0.004
Platelet, K/UL, median(IQR)	205.000 (119.000)	203.000(146.000)	0.76
Urea, mg/dl, median(IQR)	57.5 (75.5)	65.5 (46.7)	0.69
Creatinine, mg/dl, median(IQR)	1.37 (1.3)	1.37 (1.7)	0.98
Arterial Lactate, mmol/L, median(IQR)	6.3 (3.8)	4.6 (4.8)	0.04

IQR: Interquartile range, PEA: pulseless electrical activity, VF: ventricular fibrillation, VT: ventricular fibrillation, NLR: neutrophil lymphocyte ratio

The Kaplan-Meier survival estimates were calculated. The univariate and the multivariate Cox regression models were utilized to evaluate the independent associations of the NLR values with the 24-hour mortality. Age, sex, arrest rhythm on admission, lactate and creatinine were included in this model. Utility of the NLR in 24-hour mortality in ROSC patients was evaluated via receiver operating characteristic (ROC) curves: the cut-off value was determined using the Youden's index. A p value of < 0.05 was considered statistically significant.

Results

Between the 1st of January and 31st of December in 2013, 191 OHCA cases were surveyed. It was determined that 115 (60.2% percent) of these patients returned to spontaneous circulation. 24 patients from this group were excluded by the exclusion criteria and a total of 91 patients were included in the study. The median (interquartile range) age of the patients was 73 (19), and 44 (48,4% percent) of the patients were males. The basal characteristics of the patients have been presented in Table-1.

Hypothermia never been applied to a patient. 34% percent (31) of the patients administered percutaneous coronary intervention. 43.9% percent (40) of the patients survived for more than 24 hours, and in the group who survived less than 24 hours, significant differences were found in neutrophil counts, NLR, lactate levels and arrest rhythm on admission ($p<0,05$). (Table-2). No significant differences were detected with regard to age, gender, neutrophil, lymphocyte, platelet counts and levels of hemoglobin, lactate and creatinine

Table 3. Performance parameters of neutrophil / lymphocyte ratio as a predictor of mortality

Performance parameters	95 % Confidence interval
Sensitivity	52.0 (37,4 - 66,3)
Specificity	80.0 (64,4 - 90,9)
Positive predictive value	76.5 (64.2-86.1)
Negative predictive value	56.1 (41.9-74.2)
Positive likelihood ratio	2.60 (1,3 - 5,1)
Negative likelihood ratio	0.60 (0,4 - 0,8)
Receiver operator characteristic curve area	0.68 (0.57-0.77)

between the cases of arrest due to cardiac and non-cardiac causes (p>0,05). The performance characteristics of the NLR to predict the 24-hour mortality were calculated (Table-3). The cut-off value of the mortality obtained by the ROC curve was ≤ 1,55. (Sensitivity: specificity: AUC 0.68 CI% 0.57-0.77, p=0.02) (Figure 1).

Two groups were formed according to the NLR median values lower and higher than 3.05. Significant differences were found with regard to the 24-hour and 14-day survivals, platelet counts and urea levels between these two groups (p<0,05) (Table-4). In the 1. group with lower NLR, the survival rate calculated with the Kaplan Meier curve was significantly lower (Log Rank 5.07 p=0.02) (Figure 2). It was determined with the multivariable Cox regression model, that the NLR being lower than 3.05 was a predictive parameter of the 24-hour mortality independent of age, gender, lactate levels, creatinine and the arrest rhythm on admission (Hazard Ratio: 0.34 (0.15-0.79), p=0.01).

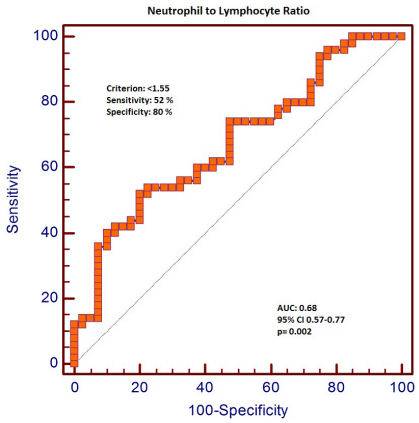
Discussion

This was a retrospective study evaluating the prognostic value of the NLR in OHCA patients with ROSC. According to the data which we obtained from this study and opposite to the previous observations, a low NLR level was found as an indicator of 24-hour mortality independent of the age, gender, arrest rythm on admission, lactate and creatinine levels.

The beginning phase of the inflammation is called SIRS (Systemic Inflammatory Response Syndrome), which could be either caused by a pathogen or by the tissue degradation products[13-14]. Besides the infectious causes, SIRS can develop following sepsis, trauma, surgery and resuscitation. The main role of SIRS is played by the WBC[8]. Jilma *et al.* investigated the changes in WBC subtypes following inflammation and they revealed a 300% increase in neutrophils, 96% decrease in monocytes and 85% decrease in lymphocytes in 4 to 6-hours after inflammation[7]. Zahorec reported that neutrophilia and lymphocytopenia developed in 90 oncological patients who required intensive care treatment, but also underlined that the neutrophil to lymphocyte ratio was a more predictive parameter. He mentioned that this ratio was a reliable parameter with regard to reflecting the intensity of the stress and for evaluating and monitoring the systemic inflammatory response[8]. In studies performed in recent years, high NLR levels were found to be associated with mortality in acute decompensated heart failure, acute coronary syndrome and pulmonary embolism[9-12].

The compensatory anti-inflammatory response syndrome (CARS) defined in 1996 was described as a loss of systemic efficacy of the immune system by its re-organization from an inflammatory stage to haematopoesis[15]. Conquy has defended the hypothesis that the CARS is an adaptation mechanism to suppress the excessive inflammatory response[13]. CARS occurs in immunocompromised patients or during the endotoxin intolerance phase of the SIRS or sepsis[13-14]. Endotoxin intolerance is defined as an attenuated responsiveness to lipopolysaccharides following the first exposure to endotoxin[16]. This has been reported to be a protective mechanism against the destructive effects of pro-inflammatory processes, yet it is also mentioned that it is associated with nosocomial infections and mortality by causing immunosuppression[16-18]. In this process, the aim is to avoid the detrimental effects of the neutrophils and monocytes against the host via receptor-based changes in monocytes, neutrophils and lymphocytes. It has been reported that the apoptosis rates are increased in leukocytes in endotoxin intolerance leading to leukopenia[14,16,17]. It has also been underlined that the survival lengths of the neutrophils and their sensitivity to apoptosis are important factors in determining the severity of the inflammatory response[19]. The likely cause of the endotoxemia in post-resuscitative patients is the increase in permeability in the intestinal mucosa following ischemia/reperfusion injury and the subsequent translocation of bacteria and endotoxins[18].

In PCAS, the systemic ischemia reperfusion response is characterized with systemic inflammatory immune respons-



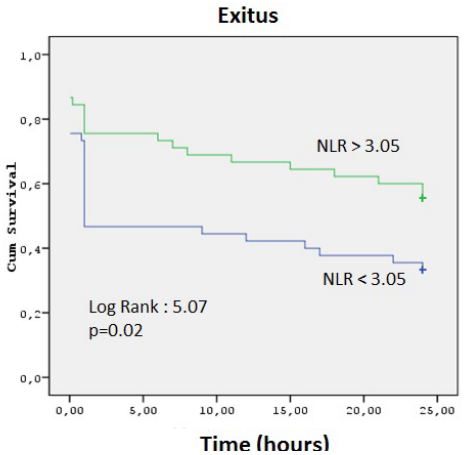


Table 4. Patients characteristics according to median of neutrophil / lymphocyte ratio

	NLR<3.05 (n=46)	NLR≥3.05 (n=45)	p
Age, years, median (IQR)	72(19)	75(15)	0.09
Sex, n (%)			0.34
Male	20 (43.5)	24 (53.3)	
Female	26 (56.5)	21 (46.7)	
Arrest rhythm, n(%)			0.43
Asystole	28 (60.9)	24 (53.3)	
PEA	13 (28.2)	16 (35.6)	
VT/VF	5 (10.9)	5 (11.1)	
Cause of arrest, n(%)			0.07
Cardiac	23 (%50)	14 (31.1)	
Noncardiac	23 (%50)	31 (68.9)	
Hemoglobin, median (IQR)	12.7 (3.2)	12.7 (3.8)	0.80
Platelet, K/UL, median (IQR)	172.000 (149.800)	243.000 (108.000)	0.008
Urea, mg/dl, median (IQR)	52.5 (48.5)	73 (83)	0.009
Creatinine, mg/dl, median (IQR)	2.0 (1.75)	3.0 (2.0)	0.09
Arterial lactate, mmol/L, median (IQR)	3.5 (0.75)	3.1 (1.0)	0.13
24-h mortality	31 (67.4)	20 (44.4)	0.02
14-day mortality	42 (91.3)	33 (73.3)	0.02

NLR: neutrophil lymphocyte ratio, IQR: Interquartile range, PEA: pulseless electrical activity, VF: ventricular fibrillation, VT: ventricular fibrillation

es, perturbed vasoregulation, increased coagulation, adrenal suppression and immunosuppression[20].

The mainstay of these results was obtained by the study of Adrie *et al.* performed in 2002. According to the results of this study, increase in plasma cytokines, presence of plasma endotoxins in 50% percent of cases, and dysregulation of cytokine synthesis were determined in patients resuscitated successfully, and it was also stated that these features were also seen in severe sepsis, and thus, the PCAS may be a sepsis-like syndrome[17-18].

In our results, we found the NLR to be lower in OHCA patients with ROSC, contrary to the usual responses in SIRS. We think that this result may be a consequence of the endotoxin intolerance or CARS subsequent to an immunodepression with as yet an unknown pathophysiology. According to our view, this result may reflect the severity of immune-paralysis and the inflammation occuring in PCAS. Low NLR level is an independent indicator of the 24-hour mortality independent of the important prognostic markers such as lactate, creatinine, age, gender and the arrest rhythm on admission.

The majority of the mortalities in PCAS patients occur in the first 24-hours and the prognostic factors which can be utilized in this period are not well known[1]. At this point, it may be possible to use NLR as a marker, which may also lead to the development of different treatment choices. For instance, Vasileiou *et al.* demonstrated that the erythropoietin improves survival following cardiac arrest in their experimental study, and proposed that the likely causes of their results may be explained by the erythropoietin-reduction of ischemia reperfusion injury, apoptosis and inflammation[21].

In previous studies, CRP and procalcitonin levels were found to be elevated due to the systemic inflammation subsequent to ischemia reperfusion response in PCAS, and they were also found to be associated with short and long-term mortality[22-23]. In comparison to these markers, NLR can be obtained cheaper and faster in daily practice and it is a parameter with easier accesibility.

Limitations

This study has some limitations. First of all, this study is a single-center retrospective study performed by the survey of hospital records. Some biases are unavoidable to the retrospective character of the study. Secondly, Bystander CPR was only done in %3. 69.2% (45) of the witnesses of the arrest has witnessed an emergency call system. Therefore bystander CPR ratio is low. Third, due to the low number of cases and due to low survival rates, the associations of the NLR with long term mortality and neurological sequelae were not investigated. Prospective studies with higher numbers of cases are needed.

Conclusion

A low NLR level is an independent indicator of the 24-hour mortality in PCAS, indepedent of the age, gender, creatinine, lactate and arrest rhythms on admission. It is a labo-

ratory parameter, which can be obtained cheaply and easily, and it may help for development of novel treatment choices in cardiopulmonary resuscitation and postresuscitation care.

REFERANCES

1. Kim J., Kim K., Lee JH., Jo YH, Rhee JE, Kim TY et al. Red blood cell distribution width as an independent predictor of all-cause mortality in out of hospital cardiac arrest. Resuscitation 2012;83: 1248–52
2. Szymanski F.M., Karpinski G., Filipiak K.J., Platek A.E., Hrynkiewicz-Szymanska A., Kotkowski M., et al. Usefulness of the D-Dimer Concentration as a Predictor of Mortality in Patients With Out-of-Hospital Cardiac Arrest. Am J Cardiol 2013;112:467-71
3. Kilgannon JH, Roberts BW, Reihl LR, Chansky ME, Jones AE, Dellinger RP et al. Early arterial hypotension is common in the post-cardiac arrest syndrome and associated with increased in-hospital mortality. Resuscitation 2008;79:410–6,
4. Nolan JP, Neumar RW, Adrie C, Aibiki M, Berg RA, Böttiger BW, et al. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication. A ScientificStatement from the International Liaison Committee on Resuscitation; theAmerican Heart Association Emergency Cardiovascular Care Committee;the Council on Cardiovascular Surgery and Anesthesia; the Council onCardiopulmonary, Perioperative, and Critical Care; the Council on Clin-ical Cardiology; the Council on Stroke. Resuscitation 2008;79:350–79,
5. Peberdy MA, Callaway CW, Neumar RW, Geocadin RG, Zimmerman JL, Donnino M, et al. Part 9: post-cardiac arrest care:2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010;122:S768-S786
6. Galus MA, Stern J. Extreme lymphocytopenia associated with toxic shock syndrome. J Intern Med 1998;244:351-54
7. Jılma B., Blann A., Pernerstorfer T, Stohlawetz P, Eichler HG, Vondrovec B, et al. Regülation of adhesion molecules during human endotoxemia. Amer J Resp Crit Care Med. 1999;159:857-863
8. Zahorec. Ratio neutrophil to lymphocyte counts-rapid and simple parameter of systemic inflamtion and stres in critically ill. Bratisl Lek Listy 2001;102:5-14
9. 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;102:653-7
10. Azab B, Zaher M, Weiserbs K, Estelle T. Usefulness of neutrophil to lymphocyte ratio in predicting short and long term mortality after Non-ST elevation myocardial infarction. Am J Cardiol 2010;106:470-6
11. Uthamalingam S, Patvardhan EA, Subramanian S Ahmed W, Martin W, Daley M, et al. Utility of the neutrophil to lymphocyte ratio in predicting long-term outcomes in acute decompensated heart failure. Am J Cardiol 2011;107:433-8
12. Kayrak M, Erdoğan Hİ, Solak Y, Akilli H, Gül EE, Yildirim O et al. Prognostic value of neutrophil to lymphocyte ratio in patients with acute pulmonary embolism: A redrospective Study. Heart, Lung and Circulation 2014;23:56-62
13. Conquy MA, Cavaillon JM. Compensatory anti-inflammatory response syndrome. Thromb Haemost 2009; 101: 36–47
14. Biswas SK, Lopez-Collazo E. Endotoxin tolerance: new mechanisms, molecules and clinical significance. Trends in Immunology 2009;30: 475-87
15. Bone RC, Grodzin CJ, Balk RA. A New Hypothesis for Pathogenesis of the Disease Process. Chest 1997; 112:235-43
16. Cavaillon JM, Adrie C, Fitting C, Conquy MA. Endotoxin tolerance: is there a clinical relevance? J Endotoxin Res 2003;9:101-7
17. Adrie C, Adib-Conquy M, Laurent I, Monchi M, Vinsonneau C, Fitting C, et al. Successful cardiopulmonary resuscitation after cardiac arrest as a ''sepsis-like'' syndrome. Circulation 2002;106:562—8.
18. Adrie C, Laurent I, Monchi M, Cariou A, Dhainaou JF, Spaulding C. Postresuscitation disease after cardiac arrest: a sepsis-like syndrome? Curr Opin Crit Care 2004;10:208-12.
19. Sauneufa B, Bouffarda C, Cornet E, Daubin C, Desmeulles I, Masson R et al. Communication Immature/total granulocyte ratio: A promising tool to assess theseverity and the outcome of post-cardiac arrest syndrome. Resuscitation. 2014 ;85:1115-9
20. Stub D, Bernard S, Duffy SJ, Kaye DM. Post Cardiac Arrest Syndrome: A Review of Therapeutic Strategies Circulation 2011;123:1428-1435
21. Vasileiou PVS, Xanthos T, Barouxis D, Pantazopoulos C, Papalois AE, Lelovas P et al. Erythropoietin administration facilitates return of spontaneous circulation and improves survival in a pig model of cardiac arrest. Am J Emerg Med. 2014;32:871-7
22. Dell'anna AM, Vinotti JB, Beumier M, Orbegozo-Cortes D, Donadello K, Scolletta S et al. C-reactive protein levels after cardiac arrest in patients treated with therapeutic hypothermia. Resuscitation. 2014 ;85:932-8.
23. Annborna M, Dankiewicza J, Erlinge D, Hertel S, Rundgren M, Smith JG, et al. Procalcitonin after cardiac arrest – An indicator of severity of illness, ischemia-reperfusion injury and outcome. Resuscitation 2013;84:782–87.

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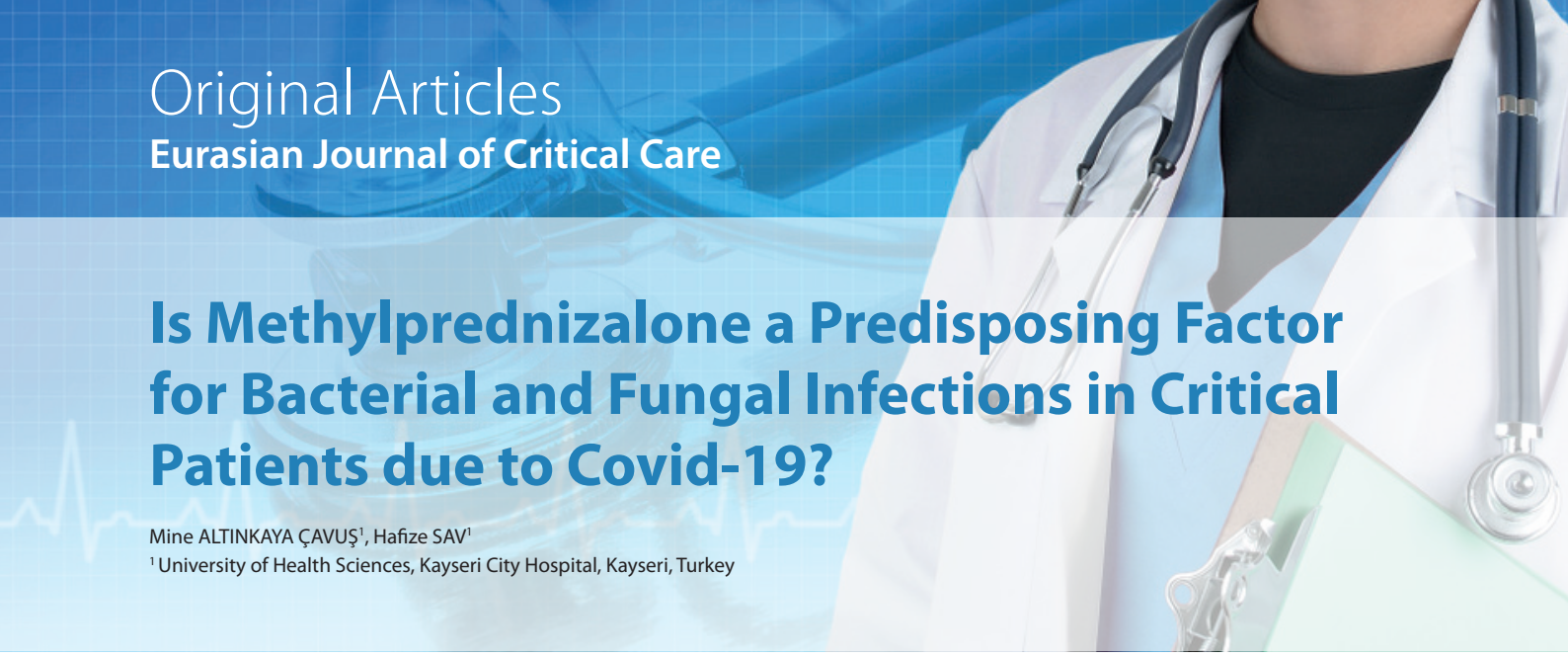

Is Methylprednizalone a Predisposing Factor for Bacterial and Fungal Infections in Critical Patients due to Covid-19?

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Abstract

Aim: The COVID -19 outbreak was first seen in Wuhan, China\'s Hubei province. Lung infections caused by COVID-19; It can progress to severe ARDS (acute respiratory distress syndrome) with a high mortality.For ARDS patients, methylprednisolone (1-2 mg / kg per day) is recommended to be as short as possible

Methods: All patients with a diagnosis of covid-19 over the age of 18 who were hospitalized in the pandemic intensive care unit between March 2020 and September 2020 were retrospectively screened.Patients; demographic data, hospitalization APACHE II scores, length of stay in hospital and intensive care, laboratory values (d-dimer, creatinine, CRP (C reactive protein)), culture results, mortality and morbidity, mechanical ventilator needs. On the first day of intensive care admissions, methylprednizalone was added to the treatment intravenously at 0.5 mg/kg/day for 5 days.

Results: A total of 201 patients hospitalized in adult level 3 intensive care were included in the study. All patients were PCR positive. 44.8% of the patients were female (n: 90), 55.2% were male (n: 111). Blood, urine and ETA cultures; there was no statistically significant relationship between gender, IMV need, mortality and prednol use.

Conclusion: COVID-19 is a viral infectious disease that manifests mainly as fever and pneumonia. Corticosteroid therapy; in addition, it includes the following risks: hyperglycemia, poor wound healing, psychosis, pancreatitis, and prolonged muscle weakness in impaired functional status in a meta-analysis published in 2012, nine randomized controlled trials, 1001 patients were included. Consequently, the use of corticosteroids did not decrease mortality.

Keywords: Methylprednisolone, bacterial and fungal infections, COVID-19

Introduction

Coronavirus disease 2019 (COVID-19) severe acute respiratory syndrome coronavirus 2 (SARS-CO-V-2) is a member of the betacoronavirus. The COVID -19 outbreak was first seen in Wuhan, China's Hubei province. It quickly spread to over 50 cities in December 2019[1]. It quickly spread to more than 100 countries around the world. The disease is primarily spread by inhalation with droplets, but the possibility of other transmission routes (feces and urine) cannot be excluded[2]. The course of the disease can range from mild self-limiting flu-like illness to fulminant pneumonia and death. Report of the World Health Organization dated March 5, 2020; 3.4% of 95,333 confirmed COVID-19 cases result in death[3]. However, a lower mortality rate of 1.4%; Analysis of data from 1099 patients with laboratory-confirmed COVID-19 came from 552 hospitals in mainland China[4]. This disease is mild to severe; fever (88%), cough (67%) and fatigue (34%) are the most common symptoms. COVID-19 patients; 3 creates a picture similar to infection caused by other respiratory viruses (Influenza A / B, respiratory syncytial virus and rhinovirus)[5]. Considering that the number of unreported and unconfirmed cases is higher than the reported cases, it can be predicted that the actual mortality may be similar (less than 1%) to seasonal influenza[6]. It has been found that the virus is transmitted from person to person[7].

Lung infections caused by COVID-19; It can progress to severe ARDS (acute respiratory distress syndrome) with a high mortality. Treatment strategies are not based on precise data, but the evidence is increasing day by day. Today, systemic glucocorticoids are used empirically to prevent serious complications[8]. However, there is no evidence from randomized clinical trials to support glucocorticoid therapy for COVID-19. For ARDS patients, methylprednisolone (1-2 mg / kg per day) is recommended to be as short as possible[9].

Coronavirus disease 2019 (Covidien-19) are associated with infections of bacteria and fungi is poorly understood. Isolated COVID-19 associated viral infection and possible bacterial and/or fungal infection are clinically challenging. 15% of the Covidien-19 case in Wuhan hospitalized reported secondary bacterial infections[10] and survival group was observed at a higher ratio than in survivors (50% vs. 1%).

The aim of this study; to investigate the effect of methylprednisolone on secondary infection rates in critically ill patients.

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Material and method

All patients with a diagnosis of covid-19 over the age of 18 who were hospitalized in the pandemic intensive care unit between March 2020 and September 2020 were retrospectively screened. A total of 1458 patients; According to pcr (polymerase chain reaction), antibody (ab), or CT (computed tomography) results, they were hospitalized in the intensive care unit due to covid-19-induced pneumonia.

Intensive care unit hospitalization indications; respiratory rate ≥ 30, signs of dyspnea and respiratory distress, SPO2 <90% (room air), PO2 <80 mmhg, PO2 / fio2 <300, Lactate> 4 mmol / L, bilateral infiltrations or multi-lobar involvement on chest radiography or tomography, organ dysfunction such as hypotension (systolic blood pressure <90 mmhg, mean arterial pressure <65 mmhg), skin perfusion disorder, renal function test, liver function test disorder, thrombocytopenia, confusion, presence of immunosuppressive disease, presence of multiple uncontrolled comorbidity, increased troponin was identified as arrhythmia.

Among these patients, those who had pcr +, ab + and developed ARDS were included in the study. Patients were divided into 2 groups as methylprednisolone and those not.

Patients; demographic data, hospitalization APACHE II scores, length of stay in hospital and intensive care, laboratory values (d-dimer, creatinine, CRP (C reactive protein)), culture results, mortality and morbidity, mechanical ventilator needs. It was recorded whether they took prednol or not. Laboratory values saved last day of hospitalization. On the first day of intensive care admissions, methylprednizalone was added to the treatment intravenously at 0.5 mg/kg/day for 5 days.

Inclusion criteria in the study; level 3 intensive care patients over 18 years of age with covid-19 positive and non-invasive and / or needing non-invasive mechanical ventilation.

Exclusion criteria are those under the age of 18, trauma and cancer patients, covid-19 negative patients.

Statistical analysis

In the statistical analysis made with Spss version 20; The distribution of the groups was determined by the Kolmogorov-Smirnov test. Assym sig. Values greater than 0.05 were considered as normal distribution, small values as abnormal distribution.

While parametric tests (T test) were applied to data with normal distribution, non-parametric tests were applied to data with a number of cases greater than 30 and not showing a normal distribution (Mann Whitney U). Pearson correlations were used in parametric data and spearman correlations were used in non-parametric data.

In the analysis of all statistical data, values with a p value less than 0.05 were considered statistically significant.

Statistical analysis was performed and the findings were discussed with tables and graphs in the light of the data.

Table I. Results of the study

	Yes (n)	%	No (n)	%
Gender (female)	90	44,8	111	55,2
IMV needs	99	49,3	102	50,7
Mortality	101	50,2	100	49,8
Methyprednizalone	94	46,8	107	53,2
Blood Culture	99	46,3	102	50,7
Staphylococcus	84	41,8		
Enterococcus	10	5		
Candida Albicans	2	1		
Klebsiella	2	1		
Psoudomonas Aeruginosa	1	0,5		
Acinetobacter	1	0,5		
Urine Culture	34	16,9	167	83,1
E.Coli	5	2,5		
Candida Albicans	22	10,9		
Enterococcus	2	1		
Klebsiella	1	0,5		
Psoudomonas Aeruginosa	1	0,5		
Acinetobacter	2	1		
ETA culture	8	4	193	96
Acinetobacter	4	2		
Staphylococcus	1	0,5		
Candida Albicans	3	1,5		

Table II. Methylprednizalone

	Mp0	Mp1	Total	P value	
Age	67,7±14,9	66,7±12,9	67,3±14	,102	NS
Hospital day	16,1±11,2	15,1±9,4	15,6±10,4	,637	NS
ICU day	9,4±8,8	8,9±6	9,1±7,6	,069	NS
CRP	100,4±119,4	96,5±115	98,6±117,1	,488	NS
D-dimer	3173,9±3703,2	4945,2±5157,4	3946±4468,9	,013*	S
Kreatinine	1,9±2,9	1,5±1,4	1,7±2,3	,033*	S
APACHE II score	27,5(19-32)	26,5(20-33)	27(19-33)	,42	NS

Mp 1: Group using methylprednizalone, Mp 0: Group without methylprednizalone, NS:Not Statistically Significant, S: Statistically Significant, APACHE: Acute Physiology and Chronic Health Evaluation

Table III. Length of stay according to culture results

	-culture	**+culture**	**P value**	
Blood				
Hospital day	13,5±8	17,9±11,9	,029	S
ICU day	7,4±5,4	10,9±9,1	,028	S
Urine				
Hospital day	14,3±9	22,4±13,9	,003	S
ICU day	7,9±5,7	15,3±11,9	,000	S

S: Statistically Significant, ICU: Intensive care unit

Results

A total of 201 patients hospitalized in adult level 3 intensive care were included in the study. All patients were PCR positive. 44.8% of the patients were female (n: 90), 55.2% were male (n: 111). 102 (50.7%) patients received invasive mechanical ventilation (IMV) support. 101 patients died (50.2%). 46.8% of the patients were those using methylprednizalone (n: 94). Growth was detected in the blood culture in 49.3% of the patients, in the urine culture in 16.9%, in the endotracheal aspiration (ETA) culture in 4%. The mean age was calculated as 67.3 ± 14 years. The length of stay in the hospital was 15.6 ± 10.4. The mean intensive care hospitalization was found to be 9.18 ± 7.6 (Table I).

When the patients were divided into two groups as methylprednisone and those not; between groups; No significant differentiation was observed in terms of IMV need, mortality, age, APACHE II score, length of hospital and intensive care stay, blood, urine and ETA cultures. However, creatinine and d-dimer values were significantly different from the laboratory values obtained on the last day of hospitalization (p value <0.05) (Table II).

Blood, urine and ETA cultures; There was no statistically significant relationship between gender, IMV need, mortality and prednol use. Hospital and intensive care unit stay of patients with positive blood and urine cultures were found to be higher than those without growth (p value <0.05) (Table III).

Discussion

COVID-19 is a viral infectious disease that manifests mainly as fever and pneumonia. Anti-viral and respiratory supportive therapies are the main part of treatments for severe cases. The course of infections with COVID-19 is different for each patient. The disease may progress from mild clinical findings to severe ARDS, even resulting in death. Anti-inflammatory therapy can be applied in critically ill patients with ARDS and multiple organ damage.

Corticosteroid therapy; in addition, it includes the following risks: hyperglycemia, poor wound healing, psychosis, pancreatitis, and prolonged muscle weakness in impaired functional status[11]. In this study, infection rates and complications due to methylprednisolone use were not examined.

In their multicenter randomized controlled study, Confalonieri et al. Found that hydrocortisone treatment significantly reduced mortality in severe pneumonia[12]. In a retrospective study by Garcia-Vidal et al., Mortality decreased in patients who were given systemic steroids in addition to antibiotics in severe pneumonia[13]. Studies have been published showing that it reduces hospital mortality, length of stay in intensive care, duration of hospitalization, incidence of shock, and chest radiography findings[14].

In a meta-analysis published in 2012, nine randomized controlled trials, 1001 patients were included. Consequently, the use of corticosteroids did not decrease mortality. In the

subgroup analysis, prolonged survival was found in cases of severe pneumonia. It was determined that the use of corticosteroids for a period exceeding 5 days decreased mortality. Hyperglycemia was detected as a side effect. There was no risk of superinfection or gastrointestinal (GIS) bleeding[15].

As a result, the use of steroids in ARDS is a controversial issue. Studies supporting the use of low doses of steroids stand out in the literature findings. In this study; There was no effect of metiprednisone on mortality, infection rates and length of stay in intensive care patients due to COVID-19. Significant decrease in creatinine values suggested that prednisolone may have nephroprotective effects. Hospital and intensive care stay were longer, as expected, in patients with culture positive.

Referances

1. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020; 395(10224):565-74.
2. Del Rio C, Malani PN. COVID-19-New insights on a rapidly changing epidemic. J Am Med Assoc. 2020:28.
3. Coronavirus disease 2019 (COVID-19) situation report e 45. https://www.who.int/publications-detail/infection-prevention-and-control-during-health-care-when-novel-coronavirus-(ncov)-infection-is-suspected-20200125
4. Guan WJ, Ni ZY, Hu Y et al. China medical treatment expert group for covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020.
5. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of 2019 novel coronavirus disease in China. N Engl J Med. 2020.
6. Fauci AS, Lane HC, Redfield RR. Covid-19 navigating the uncharted. N Engl J Med, 2020.
7. Kumar A, Liang B, Aarthy M, et al. Hydroxychloroquine Inhibits Zika Virus NS2B-NS3 Protease, ACS Omega3. Journal Pre-proof. 2018;18132-41.
8. Yao XH, Li TY, He ZC, et al. A pathological report of three COVID-19 cases by minimally invasive autopsies, Chinese Journal of Pathology. 2020;49:9.
9. Pairu J, Triveni GS, Manohar A. The study of serum calcium and serum magnesium in pregnancy induced hypertension and normal pregnancy. Int J Reprod Contracept Obstet Gynecol. 2015;4:30-4.
10. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Inten Care Med. 2020;46:846-8.
11. Herridge MS, Cheung AM, Tansey CM, et al. One-year outcomes in survivors of the acute respiratory distress syndrome. N Engl J Med. 2003;348:683-93
12. Confalonieri M, Urbino R, Potena A, Piattella M, Parigi P, Puccio G. Hydrocortisone infusion for severe community-acquired pneumonia: a preliminary randomized study. Am J Respir Crit Care Med. 2005;171:242-8.
13. Garcia-Vidal, Calbo E, Pascual V, Ferrer C, Quintana S, Garau J. Effects of systemic steroids in patients with severe community-acquired pneumonia. Eur Respir J. 2007;30:951-6.
14. Shafiq M, Mansoor MS, Khan AA, Sohail MR, Murad MH. Adjuvant steroid therapy in community-acquired pneumonia: a systematic review and meta-analysis. J Hosp Med. 2013; 8:68-75.
15. Nie W, Zhang Y, Cheng J, Xiu Q. Corticosteroids in the Treatment of Community-Acquire Pneumonia in Adults: A Meta-Analysis. PLoS One. 2012;7.

Original Articles
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Evaluation of The Relationship Between the Frequency of Attacksand Vitamin Levels in Patients Admitted to The Emergency Department With Migraine Headache

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Abstract

Introduction: Migraine is a common multifactorial, neurovascular primary headache disorder that develops due to the increased excitability of the central nervous system (CNS) and causes limitations in the quality of life of individuals. In this study, it was aimed to evaluate the relationship between the frequency of attacks and vitamin levels of patients who had migraine attacks and presented to the emergency department with a migraine attack. Method: The study is a retrospective cross-sectional study. 54 patients who were diagnosed with migraine headache according to the International Headache classification between January 1, 2019, and January 1, 2020, in the Emergency Medicine clinic of Yozgat Bozok University (Group 1). There was no history of systemic diseases such as diabetes mellitus, hypertension, heart disease, or goiter. The control group consisted of individuals who were examined for a general medical examination during the same period, whose migraine history was not in their anamnesis and history, and who did not receive vitamin supplements (Group 2). Mann-Whitney U test was used in statistical evaluations according to the status of the statistically nonparametric variables and the correlated variables were categorical (nominal or ordinal) and numerical independent group. Spearman rank correlation method was used in nonparametric data for correlations between data. The results were evaluated for a significance level of p <0.05. Results: A total of 51.4% (n = 54) migraine patients (Group 1) and 48.6% (n = 51) healthy control group (Group 2) were included in the study. Of group 1 patients, 85.7% (n = 46) were female and 14.3% (n = 8) were male. Vitamin B12, Folate and Vitamin D levels were significantly lower in Group 2 (<0.05). While there was a moderate negative correlation with vitamin D level, there was a weak negative correlation with vitamin B12 and Folate parameters (<0.05). Vitamin D level was found to be significantly lower in migraine patients with aura in the migraine patient group (<0.05). Conclusion: Especially vitamin D, vitamin B12, and folate levels have an important place among the causes of migraine headaches. Besides, we think that low Vitamin D level is important in migraine-type with aura. Therefore, prospective studies are needed, especially on vitamin D and migraine subgroups.

Key words: vitamin D,vitamin B12, Migraine, emergency department

Introduction

Migraine is a common multifactorial, neurovascular primary headache disorder that develops due to the increased excitability of the central nervous system (CNS) and causes limitations in the quality of life of individuals[1]. Although the pathogenesis of migraine remains uncertain, basically; It is a result of a complex neurovascular imbalance with stimulation of central pain pathways[2]. Nausea, vomiting, and headache accompanied by light sensitivity are more common in females[3]. In approximately 25% of migraine patients, temporary visual, sensory or speech-related neurological dysfunction findings, called the aura, appear before the onset of pain [4,5].

Although drugs such as anticonvulsants and beta-blockers have been used in the treatment of migraine so far, magnesium and vitamin groups have also been used as prophylactic treatments[6]. It is emphasized that vitamin D deficiency is associated with many painful disorders including headaches[7]. In the literature, vitamin B12 used in migraine disease is effective in pain transmission, hyperalgesia, chronic pain, inflammation, central sensitizing pathways caused by nitric oxide (NO). It is emphasized that it is a NO scavenger[8]. Although vitamin levels are considered separately in the treatment of migraine disease, studies investigating the frequency of migraine and vitamin levels are limited in the literature.

In this study, it was aimed to evaluate the relationship between the frequency of attacks and vitamin levels of patients who had migraine attacks and presented to the emergency department with a migraine attack.

Method

GPower 3.1 software (Universität Kiel, Kiel, Germany) was used to clarify the adequacy of the sample size in all calculations for this study before data collection. Type 1 was determined as 51 people for both groups (healthy control and patient group) with α 0.05 error and 85% power analysis. The

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Table 1. Vitamin level analysis between groups

Group	Calcium	Magnesium	Phosphorus	Folate	B12 vitamin	vitamin D
Group 1(mean±sd)	9,51±,43	1,92±,14	3,37±,60	5,44±1,7	322,1±123,2	11,99±7,74
Group 2(mean±sd)	9,49±,37	1,95±,19	3,39±,57	8,18±4,4	439,1±152,7	16,47±5,6
P value	0,814	0,447	0,883	0,012*	0,003*	0,010*

As statistical analysis, Mann-Whitney U test was used. * sign =p<0.05 was considered significant.

study is a retrospective cross-sectional study. 54 patients who were diagnosed with migraine headache according to the International Headache classification between January 1, 2019, and January 1, 2020, in the Emergency Medicine clinic of Yozgat Bozok University (Group 1). There was no history of systemic diseases such as diabetes mellitus, hypertension, heart disease, or goiter. The control group consisted of individuals who were examined for a general medical examination during the same period, whose migraine history was not in their anamnesis and history, and who did not receive vitamin supplements (Group 2). The study was approved by the local ethics committee.

Statistical analysis

In statistical analysis; We analyzed our data using the SPSS® 17.0 package program. Kolmogorov-Smirnov test was used for the compatibility of the data to normal distribution. When evaluating the data in the study, if it was qualitative, the Chi-Square test was used. While evaluating the study data, numerical values were expressed as mean ± standard deviation. Mann-Whitney U test was used in statistical evaluations according to the status of the statistically nonparametric variables and the correlated variables were categorical (nominal or ordinal) and numerical independent group. Spearman rank correlation method was used in nonparametric data for correlations between data. The results were evaluated for a significance level of p <0.05.

Results

A total of 51.4% (n = 54) migraine patients (Group 1) and 48.6% (n = 51) healthy control group (Group 2) were included in the study. Of group 1 patients, 85.7% (n = 46) were female and 14.3% (n = 8) were male. The healthy control group was 72.5% (n = 37) women and 27.5% (n = 14) men. The mean age of the patients in group 1 was 32.5 ± 11, and the mean age of the healthy group was 39.2 ± 12. There was no statistically significant difference between the groups in terms of age factor (p = 0.507). While 61.4% (n = 33) of the patients described migraine without aura, 38.6% (n = 21) had migraine with aura. The mean frequency of the patients applying to the emergency department was 2.3 ± 4.5 days.

Vitamin levels between groups are shown in Table 1. According to this; Vitamin B12, Folate and Vitamin D levels were significantly lower in Group 2 (<0.05). No statistically significant difference was found between the groups in the laboratory parameters of calcium, magnesium, phosphorus (> 0.05). When the relationship between migraine headache and vitamin levels was evaluated; While there was a moderate negative correlation with vitamin D level, there was a weak negative correlation with vitamin B12 and Folate parameters (<0.05) (Table 2).

Vitamin D level was found to be significantly lower in migraine patients with aura in the migraine patient group (<0.05). However, there was no significant difference in other laboratory parameters between migraine with and without aura groups (> 0.05) (Table 3). When the relationship between vitamin levels according to the type of migraine is evaluated; A moderate negative correlation with vitamin D was found (rs: 0.418; p = 0.045).

When the frequency of presentation according to the gender of the patients who applied to the emergency service with migraine headache symptoms; There was no significant difference in the frequency of admission between the groups (> 0.05). When the frequency of admission was evaluated according to the type of migraine, no statistically significant difference was found between the groups (> 0.05).

Discussion

According to the results we evaluated in our study; It was seen that migraine headache and vitamin levels were affect-

Table 2. Correlation analysis between migraine headache and vitamin levels

Laboratory Parameters	*Corr.Coef.(r_s)*	*P value*
Vitamin D	-0.415	0.012
B12 vitamin	0.374	0.004
Folate	-0.275	0.040

Spearman Correlation Method was used. The level of significance was considered p< 0.05 in all comparisons.

Table 3. Vitamin levels according to aura and non-aura type Migraine groups

Group	Calcium	Magnesium	Phosphorus	Folate	B12 vitamin	vitamin D
Migraine with aura (mean±sd)	9,5±0,45	1,92±0,15	3,2±,58	5.3±1.7	303.5±107	10±7.4
Migraine without aura (mean±sd)	9,4±0,4	1,93±0,12	3,48±,65	5,5±3,6	349.4±142.8	14.8±6.8
P value	0,945	0,795	0,508	0,682	0,293	0,06*

As statistical analysis, Mann-Whitney U test was used. * sign =p<0.05 was considered significant

ed by vitamin B12, folate, and vitamin D. It was also associated with the level of vitamin D in the aura type in migraine disease.

Migraine is a heterogeneous disease caused by the interaction of many genetic and environmental risk factors[14]. Studies on abnormal vitamin D levels, inflammatory agent production around neurons and cerebrospinal fluid, low serotonin levels, homocysteine , and nitric oxide (NO) have been studied to elucidate the pathogenesis of migraine[15].

Gazerani et al. Emphasized that the use of vitamin D is effective in migraine patients. Besides, they state that it can be used in the treatment where it is effective in periods with aura[9]. Significantly low levels of vitamin D in our study, especially in the type of migraine with aura, support the literature. In our study, vitamin levels were lower than normal limits in both the control group and the patient group, and this lowness was significant in migraine patients. In a study in the literature, it was reported that 40% of migraine patients had vitamin D deficiency[10]. However, in another study, it was emphasized that migraine attacks were triggered especially in the winter and spring months. Although our country is exposed to sunlight in latitude and longitude, we think that vitamin D is low due to the low utilization of sunlight as a society. Some studies emphasize that low vitamin D increases migraine attacks[11]. This literature information supports our study.

Vitamin D is effective against anti-inflammatory cytokines or relieving muscle pain[12]. Reducing the pain symptom due to vitamin D use has also been directed to the study of vitamin D in many studies in migraine cases[13]. In our study, magnesium and calcium levels were not found to be significant except for vitamin D. In the literature, it is reported that Magnesium and Calcium are effective in migraine cases like vitamin D in the treatment of migraine. Unlike these studies, we believe that the low vitamin D level associated with our study is one of the main factors, and the Ca and Mg used during the treatment is supportive of vitamin D.

Although the pathophysiological causes that trigger migraine attacks are not fully understood, among the mechanisms that are thought to trigger migraine attacks include increased nitric oxide (NO), neurogenic inflammation, trigeminovascular system activation, vascular dysfunction, nitric oxide (NO) release, and hyperhomocysteinemia[15]. Vitamin B12 and folate levels were lower than the healthy control group. Considering that vitamin B12 somewhat lowers the homocysteine level, low B12 causes high homocysteine , and high NO and migraine attack. However, in our study, the frequency of attacks and in migraine with aura was not associated with B12 and Folate. In our study, although the vitamin levels of the control group and migraine patients were different, there was no correlation with the admission to the emergency service due to the frequency of attacks.

One of the major limitations of our study is that it is retrospective and has a small sample. Consequently, the attacks of the patients could not be evaluated except for emergency service applications.

Conclusions

Especially vitamin D, vitamin B12, and folate levels have an important place among the causes of migraine headaches. Besides, we think that low Vitamin D level is important in migraine-type with aura. Therefore, prospective studies are needed, especially on vitamin D and migraine subgroups.

References

1. Graham JR, Wolff HG. Mechanism of migraine headache and action of ergotamine tartrate. Arch Neurol Psychiatry. 1938;39(4):737-63.
2. Chen ZY, Chen XY, Liu MQ, et al. Altered functional connectivity of amygdala underlying the neuromechanism of migraine pathogenesis. J Headache Pain 2017;18:1-8
3. Charles A. The evolution of a migraine attack – a review of recent evidence. Headache 2013;53:413-19
4. Vetvik KG, MacGregor EA. Sex differences in the epidemiology, clinical features, and pathophysiology of migraine. Lancet Neurol 2017;16:76-87.
5. Uggetti C, Squarza S, Longaretti F, et al. Migraine with aura and white matter lesions: an MRI study. Neurol Sci 2017;38:11-13.
6. Adams J, Barbery G, Lui CW. Complementary and alternative medicine use for headache and migraine: a critical review of the literature. Headache 2013;53:459-73.
7. Prakash S, Kumar M, Belani P, et al. Interrelationships between chronic tension-type headache, musculoskeletal pain, and vitamin D deficiency: is osteomalacia responsible for both headache and musculoskeletal pain? Ann Indian Acad Neurol 2013;16:650-8.

8. Thomsen LL, Iversen HK, Brinck TA et al (1993) Arterial supersensitivity to nitric oxide (nitroglycerin) in migraine sufferers. Cephalalgia 13(6):395–399.
9. Gazerani P, Fuglsang R, Pedersen JG, Sørensen J, Kjeldsen JL, Yassin H, Nedergaard BS. A randomized, double-blinded, placebo-controlled, parallel trial of vitamin D_3 supplementation in adult patients with migraine. Curr Med Res Opin. 2019 Apr;35(4):715-723. doi: 10.1080/03007995.2018.1519503. Epub 2018 Sep 28. PMID: 30182753.
10. Wheeler S. Vitamin D Deficiency in Chronic Migraine: S33. Headache. 2008;48.
11. Şarkı TJ, Chu MK, Sohn JH, Ahn HY, Lee SH, Cho SJ. D Vitamini Eksikliğinin Migrende Baş Ağrısı Sıklığına Etkisi. *J Clin Neurol* . 2018; 14 (3): 366-373. doi: 10.3988 / jcn.2018.14.3.366
12. Song TJ, Chu MK, Sohn JH, Ahn HY, Lee SH, Cho SJ. Effect of Vitamin D Deficiency on the Frequency of Headaches in Migraine. *J Clin Neurol*. 2018;14(3):366-373. doi:10.3988/jcn.2018.14.3.366
13. Motaghi M, Haghjooy Javanmard S, Haghdoost F, Tajadini M, Saadatnia M, Rafiee L, et al. Relationship between vitamin D receptor gene polymorphisms and migraine without aura in an Iranian population. BioMed research international. 2013;2013: 351942
14. Aydin H, Bucak IH, Geyik M. Vitamin B12 and folic acid levels in pediatric migraine patients. Acta Neurol Belg. 2020 Sep 21. doi: 10.1007/s13760-020-01491-3. Epub ahead of print. PMID: 32955709.
15. Kaiser EA, Russo AF. CGRP and migraine: could PACAP play a role too? Neuropeptides. 2013;47(6):451-61. doi: 10.1016/j.npep.2013.10.010.

Original Articles
Eurasian Journal of Critical Care

Does Passive Leg Raising Affect Intracranial Pressure in Healthy Volunteers?

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Abstract

Background: Ultrasonographic optic nerve sheath diameter (ONSD) measurements taken at the bedside are used to estimate intracranial pressure. Passive leg raising (PLR) is a maneuver that can test whether intravascular volume expansion can improve cardiac output in the presence of circulatory failure. In this study, we investigated whether the PLR maneuver has an effect on ONSD in healthy adults.

Materials and Methods: This prospective study consisted of 32 healthy volunteers. ONSD measurements were taken in three consecutive steps. In the first, patients were placed in a supine position on a flat stretcher. In the second stage, patients were brought to the semi-recumbent position by lifting the stretcher head by 45°. In the third stage, patients were raised in a position with their legs 45° above their trunk.

Results: The ONSD measurements of the subjects for the right eye were 4.75 (0.22) mm for the first position, 4.74 (0.35) mm for the second position and 4.76 (0.21) mm for the third position. The ONSD measurements of the subjects for the left eye were 4.75 (0.27) mm for the first position, 4.75 (0.16) mm for the second position and 4.76 (0.25) mm for the third position. There was no significant difference in ONSD measurements for either of the eyes in any of the three positions.

Conclusion: ONSD values measured at the bedside in the supine position were similar to those of the positions obtained with the PLR maneuver in healthy adults.

Keywords: Optic nerve sheath diameter; Passive Leg Raising; Intracranial pressure,

Introduction

Passive leg raising (PLR) is a maneuver that can be used to test whether intravascular volume expansion improves cardiac output in the presence of circulatory failure[1,2]. PLR causes this by increasing the preload of the right and left ventricles by causing blood translocation among body compartments[3,4]. The most important advantage of PLR is that it does not require any intravenous fluid administration and therefore does not expose the patient to excessive volume load due to reversible hemodynamic effects[2,4].

Although PLR[3,5] offers a prediction of hemodynamic fluid resuscitation for clinicians in critically ill patients, it is difficult to say the same for cerebral brain perfusion. Fluid resuscitation may play a key role in providing optimal cerebral brain perfusion in clinical situations with increased intracranial pressure (ICP) such as traumatic brain injury (TBI), stroke, and intracranial hemorrhage. The reason is that in cases with increased ICP, excessive fluid resuscitation may disrupt cerebral perfusion and cause ischemia[6–8]. Performing a test that can predict intracranial pressure with PLR can be useful in the management of fluid resuscitation in cases where intracranial pressure is suspected.

Optic nerve sheath diameter (ONSD), which can be measured ultrasonographically at the bedside, is a simple, accessible, noninvasive method used to estimate intracranial pressure[9–11]. In patients for whom hemodynamics and cerebral perfusion are critical, the measurement of ONSD with PLR before fluid resuscitation may facilitate decision making for clinicians in terms of providing a clinical clue in predicting potential damages due to excessive volume load. However, there is no data in the literature regarding the effects of the PLR maneuver on ONSD. Therefore, it makes sense to consider the effects in the first stage. In this study, we investigated the effects of the PLR maneuver on ONSD in hemodynamically healthy adults.

Materials and Methods

This prospective cross-over type design study was conducted from November 15, 2019 through February 15, 2020 in the Emergency Department of a tertiary hospital. The principles of the Declaration of Helsinki were adhered to through-

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Table 1. ONSD changes after supine position and PLR maneuver

	1. Position	2. Position	3. Position	pvalue
R-ONSD	4.75 (0.22)	4.74 (0.35)	4.76 (0.21)	0.261
L-ONSD	4.75 (0.27)	4.75 (0.16)	4.76 (0.25)	0.209

R-ONSD: Right Optic Nerve Sheath Diameter, L-ONSD: Left Optic Nerve Sheath Diameter
1.Position: Supine, 2. Position: Semirecumbent, 3. Position: Trunk was placed in the supine position, the legs were raised 45 ° above.
Data were expressed as median (interquartile range).

out the study and written informed consent was obtained from all participants. The study was approved by the University Ethics Committee (protocol number: 2017-KAEK-189_2019.10.30_20).

Study Population

Thirty-two healthy adults (males and females) were included in this study. The subjects were between the ages of 18 and 45. Those younger than 18 who had previously been diagnosed with a cardiovascular disease such as hypertension, coronary artery disease, arrhythmia, and/or an intracranial pathology such as an intracranial mass, hydrocephalus, stroke, and/or ophthalmological disease (trauma, tumor, infectious, etc.) were excluded. Those who had medication that would affect cerebrospinal fluid pressure were also excluded. Additionally, participants with glaucoma and/or those who were taking medications that might have affected intraocular pressure, along with those who had vasculitic or rheumatologic disease and/or were using drugs for any reason were excluded from the study.

Study Design

ONSD measurements were taken in three consecutive steps (Figure 1). In the first, patients were placed in a supine position on a flat stretcher. ONSD measurements of both eyes were taken while patients were kept in the supine position for one minute. In the second stage, patients were brought to the semi-recumbent position by lifting the stretcher head by 45°; they remained in that position for one minute and ONSD measurements were obtained for both eyes. In the third stage, patients were placed in a position with their legs 45° above their trunk. They were placed in the supine position for one minute and ONSD measurements were taken of both eyes.

Ultrasonographic Measurement Method

The HM70A with the Plus ultrasound system (Samsung Medison Co., Ltd., Seoul, Korea) model and a 7-16 Mhz linear probe were used for ultrasonographic examination. Before this, each patient's head was placed on a stretcher in a comfortable position and their eyes were closed. Their eyeballs were filled with a conductive gel. Eye structures were imaged while asking subjects to look forward with their eyes closed to align their optic nerve directly opposite the probe. Bilateral ONSD measurements were made on images recorded 3 mm behind the optic disc (Figure 2). Three measurements were taken for each eye; the average of the measurements was recorded.

Statistical Analyses

Statistical analyses were performed using SPSS software programme (IBM SPSS Statistics 22; IBM Corp.; Armonk, New York USA).The variables were investigated using analytical methods (Kolmogorov-Smirnov) to determine whether or not they are normally distributed. Descriptive analyzes were given using median and interquartile ranges for non-normally distributed variables. The effect of the PLR maneuver on the change in ONSD over time was investigated using the Friedman test as it did not match to the parametric test assumptions. An overall %5 type -1 error level was used to infer statistical significance.

Results

The mean age of the subjects was 31.25 ± 7.1 years, and 15 of the subjects were female. The mean systolic blood pressure of the subjects was 115.8 ± 6.86 mmhg, the mean diastolic blood pressure was 72.84 ± 5 mmhg, and the mean arterial pressure was 87.13 ± 4.84 mmhg. The mean body mass index of the patients was 23.8 ±2 .44 kg/m2.

The mean ONSD diameters of both eyes of the subjects in the supine position and that resulting from the PLR maneuver are shown in Table 1. No significant difference was found between the positions in ONSD measurements for the eyes (Friedman test *p* value; 0.261for the right eye and 0.209 for the left).

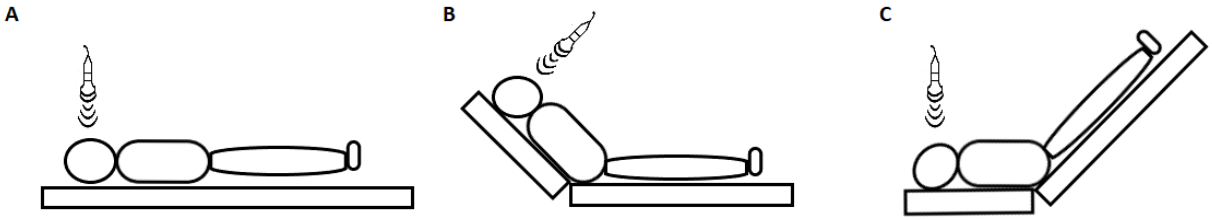

Figure 1. Demonstration of patient positions during ONSD measurements. A.) Supine position. B.) Semirecumbent position. C.) Trunk was placed in the supine position, the legs were raised 45 ° above.

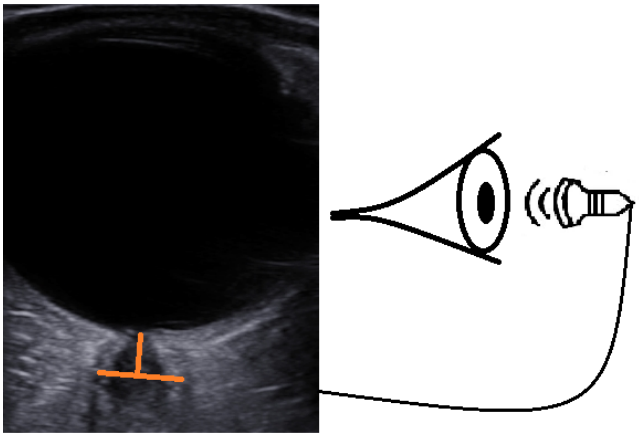

Figure 2. Demonstration of ultrasonographic measurement of ONSD measurement.

Discussion

The results indicate that the PLR maneuver does not affect ONSD measurements in hemodynamically stable healthy volunteers. This may indicate that the effect of hemodynamic change caused by the PLR maneuver on ICP in healthy adults is compensated.

Mean arterial pressure and ICP are two important major components in maintaining optimal cerebral perfusion pressure[7,12–14]. Excessive intravascular volume may lead to an increase in ICP, while lack may cause a decrease in mean arterial pressure[7,14]. In this situation, proper fluid resuscitation may play a key role in maintaining cerebral perfusion in neuro-critical patients[15]. For example, it is possible to say that a patient with a TBI injury who stays in a hypotensive state may suffer secondary ischemic brain damage[15,16]. In addition, excessive or inappropriate fluid resuscitation is also likely to reduce cerebral perfusion pressure by causing an increase in ICP[7]. Accordingly, estimating the effects of intravascular volume regulation on hemodynamics and cerebral perfusion may guide clinicians in the decision-making process of the next step.

Increasing cardiac ouput is the basis of intravenous fluid delivery to a patient[1,17]. It is known that PLR provides approximately 300 cc of venous blood return from the lower extremities[1,18,19]. Thus, the increased cardiac output obtained with PLR predicts the fluid need of the patient. It has been previously shown in the literature that PLR predicts fluid need[1,3–5,18,19]. In addition, the authors of previous studies have demonstrated the correlation of ONSD measurements to ICP in the supine position[9–11,20–22]. In our study, there was no change in ONSD measurements before or after the PLR maneuver. This situation may indicate that the bolus expansion effect in the intravascular area provided by PLR in hemodynamically stable, healthy adults can be quickly compensated for without causing a change in ICP.

Limitation

Our study had some limitations. The small number of our subjects and the fact that the subjects consisted of completely healthy adults were the major limitations of the study. Secondly, based on the subjects' basal vital signs and past medical histories, we considered their ICPs and volume status as normal. Before enrolling the subjects, we did not verify their ICP and volume status with more objective methods such as lumbar puncture, arterial pressure wave form, or stroke volume.

Conclusion

The ONSD measured after the PLR maneuver relative to the position before the PLR maneuver allows for evaluation of ICP under a volume load in an attempt to increase ICP. In our study, similar ONSD values measured before and after PLR were associated with normal physiological responses in hemodynamically stable, healthy adults. Although more research is needed to support a definitive judgment, we assert that based on these results, ONSD values measured as increased after PLR versus normal ONSD values before PLR may predict an intracranial pathology that may lead to a possible increase in ICP in the patient. However, to clarify this issue, the response of patients with increased ICP associated with the PLR maneuver should be investigated.

References

1. Mesquida J, Gruartmoner G, Ferrer R. Passive leg raising for assessment of volume responsiveness: a review. Curr Opin Crit Care. 2017 Jun;23(3):237–43.
2. Beurton A, Teboul J-L, Gavelli F, Gonzalez FA, Girotto V, Galarza L, et al. The effects of passive leg raising may be detected by the plethysmographic oxygen saturation signal in critically ill patients. Crit Care. 2019 Jan 18;23(1):19.
3. Boulain T, Achard J-M, Teboul J-L, Richard C, Perrotin D, Ginies G. Changes in BP Induced by Passive Leg Raising Predict Response to Fluid Loading in Critically Ill Patients. Chest. 2002 Apr 1;121(4):1245–52.
4. Monnet X, Teboul J-L. Passive leg raising: five rules, not a drop of fluid! Crit Care. 2015 Jan 14;19(1):18.
5. Thiel SW, Kollef MH, Isakow W. Non-invasive stroke volume measurement and passive leg raising predict volume responsiveness in medical ICU patients: an observational cohort study. Crit Care. 2009 Jul 8;13(4):R111.
6. Hariri RJ, Firlick AD, Shepard SR, Cohen DS, Barie PS, Emery JM, et al. Traumatic brain injury, hemorrhagic shock, and fluid resuscitation: effects on intracranial pressure and brain compliance. J Neurosurg. 1993 Sep 1;79(3):421–7.
7. Shackford SR. Effect of Small-volume Resuscitation on Intracranial Pressure and Related Cerebral Variables. J Trauma Acute Care Surg. 1997 May;42(5S):48S.
8. Grände P-O, Asgeirsson B, Nordström C-H. Volume-targeted therapy of increased intracranial pressure: the Lund concept unifies surgical and non-surgical treatments. Acta Anaesthesiol Scand. 2002;46(8):929–41.
9. Dubourg J, Javouhey E, Geeraerts T, Messerer M, Kassai B. Ultrasonography of optic nerve sheath diameter for detection of raised intracranial pressure: a systematic review and meta-analysis. Intensive Care Med. 2011 Jul 1;37(7):1059–68.
10. Lochner P, Czosnyka M, Naldi A, Lyros E, Pelosi P, Mathur S, et al. Optic nerve sheath diameter: present and future perspectives for neurologists and critical care physicians. Neurol Sci. 2019 Dec 1;40(12):2447–57.
11. Raffiz M, Abdullah JM. Optic nerve sheath diameter measurement: a means of detecting raised ICP in adult traumatic and non-traumatic neurosurgical patients. Am J Emerg Med. 2017 Jan 1;35(1):150–3.
12. Oswal A, Toma AK. Intracranial pressure and cerebral haemodynamics. Anaesth Intensive Care Med. 2017 May 1;18(5):259–63.
13. Wang AY-C, Hsieh P-C, Chen C-C, Chin S-C, Wu Y-M, Chen C-T, et al. Effect of Intracranial Pressure Control on Improvement of Cerebral Perfusion After Acute Subarachnoid Hemorrhage: A Comparative Angiography Study Based on Temporal Changes of Intracranial Pressure and Systemic Pressure. World Neurosurg. 2018 Dec 1;120:e290–6.
14. Rangel-Castillo L, Gopinath S, Robertson CS. Management of Intracranial Hypertension. Neurol Clin. 2008 May 1;26(2):521–41.
15. Marmarou A, Anderson RL, Ward JD, Choi SC, Young HF, Eisenberg HM, et al. Impact of ICP instability and hypotension on outcome in patients with severe head trauma. J Neurosurg. 1991 Nov 1;75(Supplement):S59–66.
16. Rossi S, Picetti E, Zoerle T, Carbonara M, Zanier ER, Stocchetti N. Fluid Management in Acute Brain Injury. Curr Neurol Neurosci Rep. 2018 Sep 11;18(11):74.
17. Cooke K, Sharvill R, Sondergaard S, Aneman A. Volume responsiveness assessed by passive leg raising and a fluid challenge: a critical review focused on mean systemic filling pressure. Anaesthesia. 2018;73(3):313–22.
18. Monnet X, Teboul J-L. Passive leg raising. Intensive Care Med. 2008 Apr;34(4):659–63.
19. Jabot J, Teboul J-L, Richard C, Monnet X. Passive leg raising for predicting fluid responsiveness: importance of the postural change. Intensive Care Med. 2009 Jan;35(1):85–90.
20. Gökcen E, Caltekin İ, Savrun A, Korkmaz H, Savrun ŞT, Yıldırım G. Alterations in optic nerve sheath diameter according to cerebrovascular disease sub-groups. Am J Emerg Med. 2017 Nov;35(11):1607–11.
21. Wang L, Chen L, Chen Y, Bao L, Zheng N, Wang Y, et al. Ultrasonography Assessments of Optic Nerve Sheath Diameter as a Noninvasive and Dynamic Method of Detecting Changes in Intracranial Pressure. JAMA Ophthalmol. 2018 Mar 1;136(3):250–6.
22. Wang L, Yao Y, Feng L, Wang Y, Zheng N, Feng J, et al. Noninvasive and quantitative intracranial pressure estimation using ultrasonographic measurement of optic nerve sheath diameter. Sci Rep. 2017 Feb 7;7(1):42063.

Case Report
Eurasian Journal of Critical Care

Role of Radiology in Pica Syndrome: A Case Report

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Abstract

Pica syndrome is a mental disorder defined as eating non-food and not-nutritive substances at least for 1 month. The diagnosis of pica syndrome is based on severe anemia which is not compatible with the developmental level, intestinal obstructions, or several conditions depending on content of the substance intaken such as lead poisoning etc. The diagnosis of pica syndrome requires active involvement of pediatrics, psychiatrists, radiologists and patients/family members. In this report, we present a 50-year-old female patient who presented to the emergency department with abdominal pain and radiologically diagnosed with pica syndrome. Patient's physical and laboratory investigations were normal, while all abdominal tomography revealed hyper-density areas. It was found in the detailed history of the patient that she was receiving psychiatric therapy and had habit of eating cigarette ashes. Upon this, cigarette ashes soaked in water were radiologically examined, similar hyper-density areas were found, and the diagnosis of pica syndrome was established. This case is the third case of eating cigarette ashes pica presented in the literature, and the first case diagnosed radiologically.

Keywords: Pica syndrome, computed tomography, radiology, eating disorders

Introduction

Pica syndrome is defined as eating non-nutritive and non-food substances in a developmentally and culturally inappropriate way at least for 1 month[1]. Pica syndrome is commonly seen in children and pregnant women, although it can be developed in each age, gender, and population[2].

Current knowledge suggests that pica is a multicausal disorder. The most commonly adopted theories for the mechanism of pica are malnutrition and psychosocial factors[3]. In addition, mental disorders such as obsessive-compulsive disorder or schizophrenia have also been associated with pica. There are studies in the literature linking pica to stress, depression, and anxiety[3, 4].

The incidence of pica syndrome is not exactly known. The diagnosis of pica syndrome is based on severe anemia which is not compatible with the developmental level, intestinal obstructions, or several conditions depending on content of the substance intaken such as lead poisoning etc[5]. The diagnosis of pica syndrome requires active involvement of pediatrics, psychiatrists, radiologists and patients/family members. Radiographic examination plays an important role in the diagnosis of pica. In this report, a patient who presented to the emergency department with abdominal pain and who was found to eat cigarette ashes with radiologic examination was presented. This case is the third case of eating cigarette ashes pica presented in the literature, and the first case diagnosed radiologically.

Case

A 50-year-old female patient presented to the emergency department of our hospital with the complaint of abdominal pain. In the physical examination, patient was pale and had nausea and vomiting. Otherwise the examination was unremarkable. Respiratory rate, heart rate, blood pressure and oxygen saturation of the patient were normal. Biochemical blood and urine analysis parameters were within the normal range. In the laboratory analysis; creatinine was found as 0.81 mg/dL, ALT 15.3 U/L, AST 12.9 U/L, urea 26 mg/dL, WBC 8.56 and RBC 4.51.

It was learned from history of the patient that she was using psychiatric drugs and receiving depression therapy. Upon abdominal pain of the patient was not relieved with hydration, all abdominal unenhanced tomography was ordered. Computed tomography performed as IV oral unenhanced revealed patchy radiopaque hyper-density areas in the stomach and small intestine (Image 1A, B, C). Thereupon, the patient was questioned about whether she underwent contrast enhanced examination within the last few day and it was learned that that patient was not administered any investigation.

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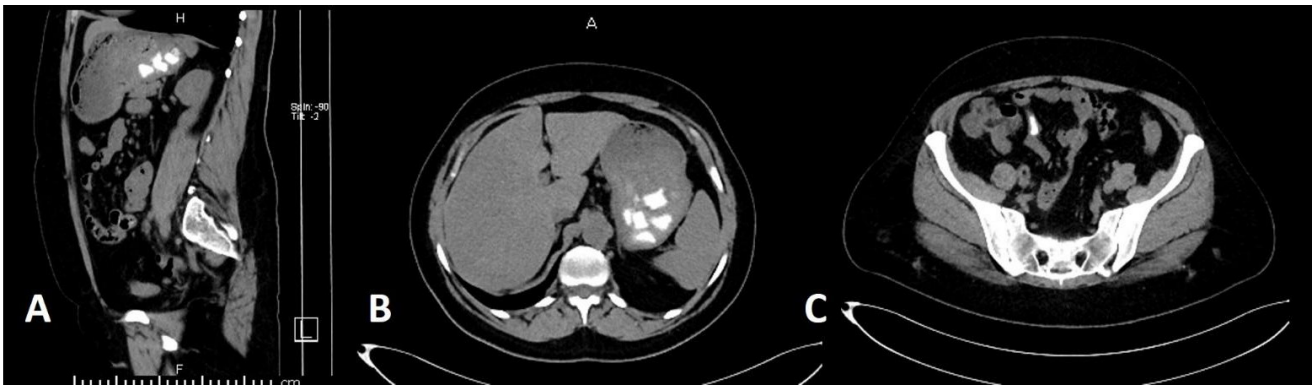

Image 1a, b: Unenhanced abdominal tomography images of the patient

In order to investigate the source of hyper-density areas in the stomach and loops, clinical questioning was deepened and it was learned that the patient was receiving not only antidepressants, but also antipsychotic drugs. Upon the psychiatric problem of the patient that was understood; considering that pica syndrome may be seen in these patients, and a probability of eating some abnormal things was taken into account. Hereon the anamnesis was deepened, and the patient reported that she was eating ashes of 2-3 cigarettes a day for a while, but she ate ashes of about 10 cigarettes on the day she arrived to the hospital, and presented to the emergency department due to abdominal pain.

Some cigarette ashes were collected and radiologically examined because of the hyper-density areas seen on the abdominal tomography. However, no bright white areas were observed on the radiograph as in our patient. It was thought that this might be caused by mixing of the ashes with sputum and gastric secretions, and some ashes were soaked in water. On the radiograph taken, a hyper-density area was observed similar to the tomography image of the patient (Image 2). The patient was diagnosed with pica syndrome.

The patient whose abdominal pain was relieved with serum, was advised for psychiatric consultation. However, the patients stated that she was already receiving psychiatric therapy, rejected the consultation, and discharged.

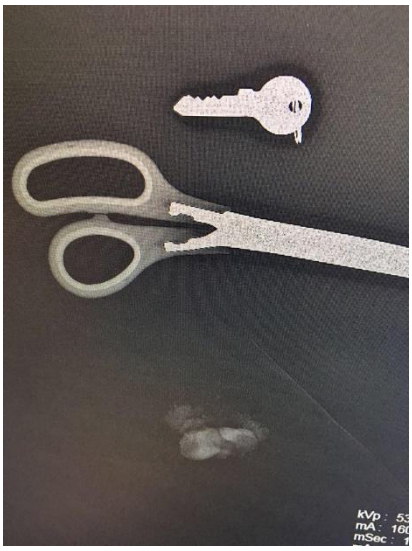

Image 2: Radiologic image of cigarette ashes soaked in water

Discussion

Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria defined pica syndrome as eating non-nutritive and non-food substances at least for 1 month. Our patient was a 50-year-old women without pregnancy. Pica syndrome has also been reported with mental retardation, schizophrenia and autistic disorder (6). In addition, this syndrome is seen in individuals with normal intelligence, and diagnosed with obsessive-compulsive disorder, pathologic anxiety, schizophrenia, emotional disorder, and depression[7]. Our patient was receiving depression therapy and using antipsychotic drugs.

Pica may lead to infections and parasitic infestation. Pica may be prolonged in persons with mental disorders.Physicians sometimes have difficulty in receiving history from pica patients. These problems are mostly resulted from the patient. The diagnosis is often established in the presence of anemia, lead poisoning, intestinal obstructions and other medical conditions. Pica diagnosis usually requires admit of the patient, because clinical findings are non-specific. In our patient also there was no pica behaviour in the first received history. However, upon the source of hyper-density areas in the abdomen could not be understood, anamnesis was deepened and the patient admitted his pica behaviour in form of eating cigarette ashes.

Although various pica syndrome case have been reported in the literature, to our knowledge only two cigarette ashes pica cases were published. First was a 33-year-old Puerto Rican woman described by DeSilva in 1975 (8). The second case was a 55-year-old woman with chronic renal failure who was described by Aoyagi et al. from Japan in 2000[9]. However, unlike these cases cigarette ashes pica was diagnosed in our patient with radiology for the first time in the literature.

In our patient, computed tomography images were found suspected, it was thought that the patient might ate a non-food thing, and it was decided to deepen her history. In the history taken for a second time, the patient was stated that she was receiving antipsychotic drugs in addition to antidepressants. Considering psychologic status and suspected attitude of the patient, a new anamnesis was received with the suspicion of pica syndrome. Upon information given by the patient, cigarette ashes collected in the outer environment was prepared and radiologically examined, and opacities similar with abdominal tomography images of the patient were obtained. Thus, definitive diagnosis of pica syndrome was established.

In conclusion; in case of opacities on abdominal tomography of patients especially those receiving psychiatric therapy, in the absence of other clinical findings these patients should be questioned for pica syndrome. For this purpose, history of patients should be carefully received and radiologic evaluation should be performed in a multi-directional way.

References

1. Rohde J , Claussen MC , Kuechenhoff B , Seifritz E , Schuepbach D. Combined symptomatology of psychosis, pica syndrome, and hippocampal sclerosis: a case report. The International Journal of Eating Disorders [03 Oct 2012, 46(1):89-91.
2. Ledford JR, Barton EE, Rigor MN, Stankiewicz KC, Chazin KT et al. Functional Analysis and Treatment of Pica on a Preschool Playground. Journal ListBehav Anal Practv.12(1); 2019 Mar. PMID: 30918781
3. Bhatia MS and Kaur N. Pagophagia – A Common but Rarely Reported Form of Pica.J Clin Diagn Res. 2014 Jan; 8(1): 195–196.
4. Stroman D, Young C, Rubano AR, Pinkhasov A. Adult-Onset Pica Leading to Acute Intestinal Obstruction. Psychosomatics. 2011 Jul-Aug;52(4):393-4.
5. Asma S, Erdogan AF, Abaci K. An iron deficiency anemia and a different pica substance: a case report. Türk Aile Hek Derg 2009; 13(3): 159-161.
6. Grewal P, Fitzgerald B. Pica with learning disability. J R Soc Med. 2002 Jan;95(1):39-40. PMID: 11773354
7. Jawed SH, Krishnan VH, Prasher VP, Corbett JA. Worsening of pica as a symptom of depressive illness in a person with severe mental handicap. Br J Psychiatry. 1993 Jun;162:835-7. PMID: 8330116
8. Desilva R. Eating Cigarette Ashes in Anemia. Ann Intern Med. 1974;80(1):115-116.
9. Aoyagi T, Hayakawa H, Matsumoto M, Ishikawa H.Eating Cigarette Ashes Pica in a Patient with Chronic Renal Failure. Japanese Journal of Clinical Urology. 2000 54(5):334-335.

Case Report
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L-Carnitine Treatment in a Child With Valproic Acid Intoxication

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Abstract

With its growing application in neurological and psychiatric diseases, valproic acid overdose due to acute and chronic use has been causing emergency admission. Asymptomatic cases of hyperammonemia may be found in valproic acid poisoning ranging from central nervous system depression to coma. While supportive therapy is adequate, in most cases active charcoal, levocarnitine supplementation, and treatment with naloxane and hemodialysis, when needed, can also be used. In the case study reported in this paper, we aimed to focus at bringing awareness to the use of levocarnitine in asymptomatic patients with valproic acid poisoning accompanied by hyperammonemia.

Keywords: hyperammonemia, intoxication, L-carnitine, valproic acid

Introduction

Valproic acid (VPA) is an antiepileptic drug frequently used for pediatric epilepsy. Due to its narrow therapeutic range, its use might result in intoxication or overdose. The clinical feature of acute and chronic VPA intoxication is usually idiosyncratic; most cases have hyperammonemia without hepatic failure, leucopenia, pancreatitis, alopecia, and thrombocytopenia[1]. The most common symptom of acute poisoning is central nervous system depression, which can progress to loss of consciousness. Mild cases might present with coma, hemodynamic instability, cerebral swelling, bone marrow depression, multiple organ dysfunction, and death [1-3]. Levocarnitine (L-carnitine) can decrease the production of the toxic metabolites of VPA, and early infusion of L-carnitine may prevent severe complications related to VPA intoxication[4-5]. In this paper, we discuss a case report of a child with VPA intoxication, presenting with asymptomatic hyperammonemia at admission and treated with L-carnitine.

Case Report

A 3-year-old boy with a 2-year history of epilepsy was admitted to our pediatric emergency department due to accidental exposure to VPA suspension (approximately 100 cc). During the initial evaluation, his vital signs were normal, his blood gas analysis pH was 7.35, pCO2 was 35.6 mm/Hg, pO2 was 32.5 mm/Hg, HCO3 was 19.2 mEq/L, and lactate level was 2.4 mmol/L. The biochemistry and complete blood count results were within the normal limits six hours after admission to the emergency department. The patient was lethargic and his Glasgow Coma Scale (GCS) was 13. Activated charcoal was given at a dose of 0.5 mg/kg through the nasogastric tube. The patient was transferred to the pediatric intensive care unit. The serum VPA level was 235.1 mcg/mL (50–100 mcg/mL), which is a toxic level. The serum ammonia level was 103 mcg/dL. Intravenous L-carnitine infusion was started at a dose of 100 mg/kg/ day until the patient was conscious. We observed that the serum level of VPA ammonia started to decrease after 48 hours of L-carnitine treatment. Six hours after starting the L-carnitine infusion, the patient's GCS was 15 and the ammonia level decreased to 93.4 mcg/dL. However, 12 hours after the first infusion of L-carnitine, the ammonia level increased from 93.4 mcg/dL to 151 mcg/d. Thus, we continued the L-carnitine treatment, which was terminated 60 hours later when the ammonia level was normal. On the 3rd day of hospitalization, the patient was discharged from the intensive care unit and discharged form the hospital on the 5th day of hospitalization.

Discussion

VPA is an antiepileptic drug that is widely used to treat a variety of neurological and psychological conditions. The

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range for a VPA therapeutic dose is narrow and the drug is commonly used for epilepsy treatment in children; however, some metabolic diseases can increase the efficacy of VPA doses worsening a patient's clinical symptoms[2]. In the case reported in this paper, the patient's medical history showed that he had been followed up for 2 years with a diagnosis of epilepsy, although he did not have a metabolic disease. VPA produces metabolites by mitochondrial B oxidation and cytosolic omega oxidation[3]. Some side effects of VPA are not dose-dependent; toxic effects can be observed at a daily VPA dose >1800 mg and blood levels >100 µg/mL[6]. VPA is metabolized in the liver via beta-oxidation, omega oxidation, and glucuronic acid conjugation[4]. VPA inhibits carbamoyl synthetase 1 enzyme, which impacts the ammonia urea cycle; in contrast, L-carnitine activates this enzyme. It decreases the ammonia level in plasma[5]. In the case presented in this paper, after admission to the emergency department clinic, the patient was asymptomatic but had a high serial serum VPA and hyperammonemia. Six hours later, the patient's lethargy and Glasgow Coma Scale (GCS) had decreased. Even if a patient is asymptomatic, the serial serum VPA level should be obtained. Ingels et al.[7] reported that 15% of patients who eventually developed toxic levels of VPA had a normal VPA level upon hospital admission. We used an L-carnitine infusion early on in the treatment process. The patient's ammonia concentration decreased to a normal level 60 hours later. These early treatments may prevent hepatotoxicity and VPA-induced hyperammonemia. If a significant VPA serum level is observed, L-carnitine may also be given to patients with asymptomatic hyperammonemia, since no randomized studies have evaluated the L-carnitine treatment dose, especially children. In this patient, 100 mg/kg L-carnitine infusion was administered until the ammonia levels were normal.

According to some clinical studies reporting cases of VPA-related severe hepatotoxicity, survival increased with early intravenous L-carnitine supplementation[4-5]. In the literature, L-carnitine supplementation has been reported to be effective in returning metabolic abnormalities and lowering hyperammonemia[6]. Although most VPA intoxication cases progress asymptomatically, it can result in multiorgan involvement, especially cerebral edema and central nervous system and respiratory depression, which can advance to coma. VPA intoxication can also result hypotension, tachycardia, and hyperthermia, and laboratory changes, such as hyperammonemia, high anion aperture metabolic acidosis, hypernatremia, and hypocalcemia. In our case, ammonia was 103.1 µg/dL (27.2–102 µg/dL) and VPA level 235.1 µg/ml (50–100 µg/ml); no abnormalities were detected in other laboratory tests.

Serum VPA level is not always correlated with toxicity. Cases of coma with normal serum VPA levels have been reported, possibly due to hyperammonemia or VPA metabolites that cannot be measured in serum[3]. In our case, the patient was evaluated asymptomatically and after a six-hour follow-up lethargy was observed; thus, we started an L-carnitine infusion. Complications due to L-carnitine treatment were prevented, as no similar symptoms were observed during follow-up. The majority of VPA is taken orally and absorbed from the gastrointestinal tract, reaching the plasma peak concentration within six hours. Although VPA is highly bound to plasma proteins, this rate decreases as the blood level exceeds 300mg/L[2]. Ghannoum et al.[8] reported high plasma VPA levels, shock table, cerebral edema, and respiratory depression development, and high gas anion gap metabolic acidosis was indicated as a hemodialysis indication VPA intoxication. in Since we did not observe these in our case, hemodialysis was not performed. In symptomatic cases, L-carnitine can be loaded in 30 minutes with a maximum dose of 6 mg at a dose of 100 mg/kg intravenously. After loading, maintenance therapy should be started at15 mg/kg, 4–6 times/day. Oral L-carnitine is administered in asymptomatic cases[9]. In our case, although the patient was initially asymptomatic, after six hours, lethargy developed so intravenous L-carnitine treatment was given due to the increase in ammonia values, and consciousness was restored with the L-carnitine treatment. The patient's VPA and ammonia levels tended to decrease. While high ammonia values were detected again 12 hours after starting L-carnitine treatment, they were in the normal range 60 hours later. If hyperammonemia is observed in pediatric patients who are asymptomatic upon admission and showing mild clinical symptoms of VPA intoxication, serious complications can be prevented by early L-carnitine infusion. Although VPA intoxications are usually asymptomatic, serious clinical results may occur. Early intervention reduces mortality and morbidity and protects against the need for interventional procedures, such as hemodialysis. Although hemodialysis is a successful treatment option, L-carnitine may be an alternative or supportive treatment approach in these patients.

Conclusion

Hyperammonemia is observed in pediatric patients who are asymptomatic upon admission and showing mild clinical symptoms of VPA intoxication. Serious complications can be prevented using an early treatment of L-carnitine infusion.

References

1. Sztajnkrycer MD. Valproic acid toxicity: overview and management. J Toxicol Clin Toxicol. 2002; 40(6): 789-801.
2. Andersen GO, Ritland S. Life threatening intoxication with sodium valproate. J Toxicol Clin Toxicol. 1995; 33(3): 279-284.
3. Nau H, Loscher W. Valproic acid and metabolites: pharmacological and toxicological studies. Epilepsia. 1984; 25 Suppl 1:S14-22.

4. Lheureux PE, Penaloza A, Zahir S, Gris M. Science review: carnitine in the treatment of valproic acid-induced toxicity - what is the evidence? Crit Care. 2005; 9(5): 431-40.
5. Lheureux PE, Hantson P. Carnitine in the treatment of valproic acid-induced toxicity. Clin Toxicol (Phila). 2009; 47(2): 101-11.
6. Katiyar A, Aaron C. Case files of the Children's Hospital of Michigan Regional Poison Control Center: the use of carnitine for the management of acute valproic acid toxicity. J Med Toxicol. 2007; 3(3): 129-38.
7. Ingels M, Beauchamp J, Clark RF, Williams SR. Delayed valproic acid toxicity: a retrospective case series. Ann Emerg Med. 2002;39(6): 616-21
8. Ghannoum M, Laliberté M, Nolin TD, MacTier R, Lavergne V, Hoffman RS, Gosselin S; EXTRIP Workgroup. Extracorporeal treatment for valproic acid poisoning: systematic review and recommendations from the EXTRIP workgroup. Clin Toxicol (Phila). 2015; 53(5): 454-65.
9. Ishikura H, Matsuo N, Matsubara M, Ishihara T, Takeyama N, Tanaka T. Valproic acid overdose and L-carnitine therapy. J Anal Toxicol. 1996; 20(1): 55-8.

Case Report
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A Case of the Surviving From Gunshot Injury Without Operation

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Abstract

Introduction: Cases of gunshot injuries among trauma patients admitted in the emergency room are fatal cases in Turkey as much as all over the world. It is perhaps the most complex group among trauma patients. Because the route of the bullet fragment, how much damage it causes on its way and which organ or organs will be harmed cannot be understood immediately so long-term follow-up may be required.

Case report: A 48-year-old civilian male patient brought to our hospital after gunshot injury. It was found that he was injured with pellets in many parts of his body. He was not operated on to prevent possible bleeding and to remove the pellets. Instead, vital signs were followed.

Results and Conclusion: Most of the patients who are injured by guns die. The most important reason for this is acute and large amount of bleeding. In this article, we will present a patient who has been exposed to multiple pellet shots but survived.

Key words: Emergency Service,Gunshot injury, multiple injury, trauma

Introduction

Cases of gunshot injuries among trauma patients admitted in the emergency room are fatal cases in Turkey as much as all over the world. It is perhaps the most complex group among trauma patients. Because the route of the bullet fragment, how much damage it causes on its way and which organ or organs will be harmed cannot be understood immediately so long-term follow-up may be required. In this article, we will present a patient who has been exposed to multiple pellet shots but survived.

Case Presentation

A 48-year-old civilian male patient was brought to our emergency department by ambulance after exposure to firearm injury. In the first examination, multiple pellet entry holes were found on the right side of the thorax and abdomen. Patient's GCS was 15, he was orientated and cooperative.He had spontaneous respiration, 15-18/minute, sPO2:96, right lung examination hadral and right abdomen tenderness. Blood pressure was 170/120 mm/Hg, pulse 92/minute. Two veins were opened for blood test and hydration. We started antibiotic treatment and tetanus vaccine.

Multipl pellet was seen on the x-ray taken (Figure-1). Thorax and abdomen tomography were reported as 'pellet fragments were seen on right and left thorax subcutaneous skin, intercostal area,in right atrium, atrioventricular septum, mediastinum right paracardiac area, axillary, left liver and portal hilus around, near gall bladder (Figure-2a-b), right upper kidney (Figure-3a), right intestine-mesentery (Figure-3b), right abdomen skin, pelvis right side, femur upper right side skin and muscle.'It has also determinedthat minimal pneumothorax and hemothorax in the right lung, sixth cot fracture, minimal laceration on the liver (Figure-2b), minimal liquid in the morrison pouch, minimal hemorrhage in the right rectus muscle, expansion of the right inguinal canal (hernia?). The patient was admitted to the intensive care unit, no operation planned.

Orthopedics, General Surgery, Cardiology, Cardiovascular Surgery have examinedthe patient during his follow-up at the intensive care unit.

Figure-1. Multiple pellets in X-ray

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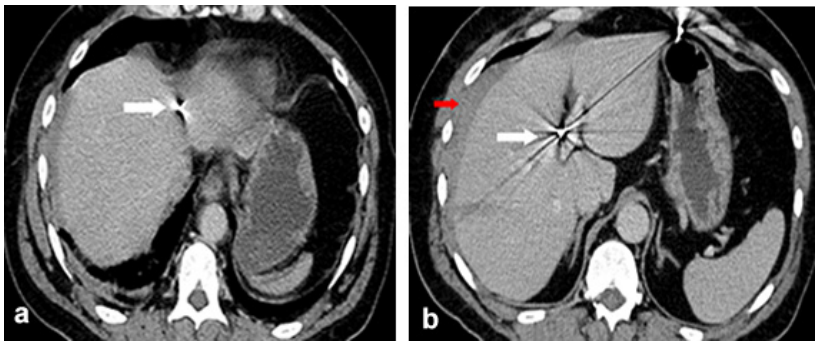

Figure-2a. Bullet in the liver (white arrow), b: Bullet in the biliary tract (white arrow), hemorrhage around the liver (red arrow)

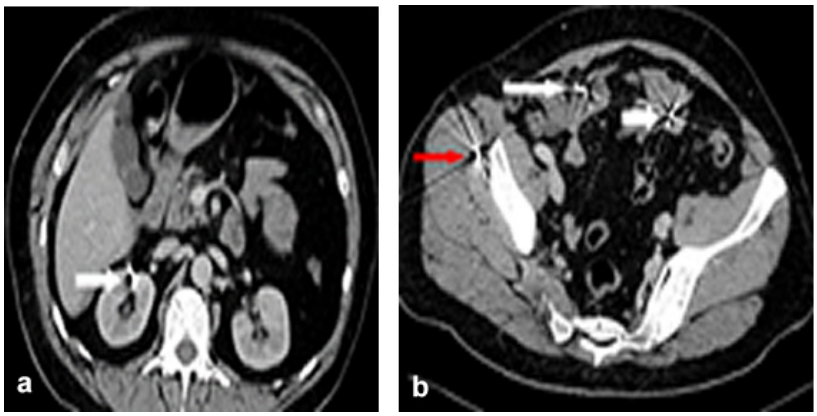

Figure-3a. Bullet on the upper pole of the right kidney (white arrow), b: Bullets in the inside small intestine (white arrows) and right thigh (red arrow)

Echocardiography reported; EF: %65, there were neither pellet particles in the heart, nor vascular injury and complication (probably seen under the heart tissue)

Orthopedic intervention not considered.

Patient with non-life-threatening transferred to the general surgery service. General surgeon decided to follow up without surgery. Hemogram follow-ups for 3 days, didn't show any problem(first/last hemoglobin-hematocrit:14,7-42,6/12,7-37,4). Patient has been discharged from hospital and recommended to come to polyclinic.

Discussion

The wounding power of the weapons depends on the kinetic energy of the bullet during impact and its propagation in tissues. The critical variable at this point is the velocity of the bullet. In slow-speed bullets, the transition track is irregular and variable, sometimes there is no relation between the lead and the exit hole and complications may develop differently than expected. On the contrary, high-speed bullets fired by military class weapons cut soft tissue smoothly and break the bones in the passageway or injure organs. It might even hit the bone and change its direction. Even if the bullet does not damage the organ in which it is stuck, it may cause damage to tissues around due to the explosion. Another important variable is distance. For example, shotguns and pistols can produce more kinetic energy than high speed guns in close range shots, even though they are low speed guns[1]. In our case, despite the exposure to close-range firing, bullet fragments were dispersed as pellet and their energy decreased.Thus,they have remained on the surface of the organsand neither bleeding nor vital organ injury occurred.

Gunshot injuries usually damage multiple organs, either directly or indirectly. In our patient, almost all of the organs on the right side of his body were damaged (even inguinal hernia due to trauma occurred). However, there was no long-term life-threatening development because there were neither self-limiting bleeding nor tissue damage. The greatest chance of our patient was that he was injured with pellets. These fragments remained in place and did not cause any new bleeding.

Statistically, there are not enough studies about gunshot injury in our country. As a result of retrospective examination of the Forensic Medicine reports, a study which is conducted in Eskişehir revealed that deaths due to gunshotinjuries was 312 patients in the autopsy data between 1997and2016. Most of them was male patients (241 (77,4%)) and these

data show us the importance of gender-based violence[2]. Our patient is also compatible with the literature.

In the study conducted by Avraham et al., 282,542 of 101,966,038 patients who applied to the emergency department due to trauma in the USA between 2009 and 2012 came with firearm injuries.At least 41.5% of the patients were between 18-44 years of age, 59% of these cases died in emergency services and 41% died in other services (total 7.8% patients). It will be inevitable that this patient population will increase as the population increases along with acquisition of gunsbecomes easier. In the same study, it was emphasized that the risk of injury by firearm was related to low socio-economic level[3].

In cases of gunshot wounds where bullets cannot be detected, emergency physicians should review the possible bullet path. In these cases, the use of imaging methods covering a large area along withrepetitive physical examination will guide the physicians in determining the serious injuries that may occur.

Conclusion

The armament problem is a social problem as well as a health problem. The number of such injuries will increase as the access to weapons becomes easier and there is a tendency to violence, even if the level of economic development increases.

In such trauma cases, emergency physicians should be careful to predict possible complications, injuries that may result in life-threatening or loss of work force in the future. Therefore, they should work with other physicians from different branchesasa team.

The management of gunshot injuries is difficult for every physician. It is necessary to compete with time. In order to understand the organs damaged by the bullet, an operation is often performed. In this article, we aimed to emphasize that the unnecessary examination and treatment should not be performed if the physiology does not deteriorate, therefore, the importance of reducing the bleeding risk of the patient.

References

1. Uzun L, et al. Baş-boyunateşlisilahyaralanması: Sıradışıbirkurşuntrasesi. KBB-Forum 2004;3(2)
2. Şimşek Ü, Karbeyaz K. (2019). Gunshot Deaths in Eskisehir, Turkey 1997 to 2016. AdıyamanÜniversitesiSağlıkBilimleriDergisi. 5 (1), 1325-1334. doi: 10.30569/adiyamansaglik.529916
3. Avraham JB, Frangos SG, DiMaggio CJ. The epidemiology of firearm injuries managed in US emergency departments. *InjEpidemiol*. 2018;5(1):38. Published 2018 Oct 15. doi:10.1186/s40621-018-0168-5