EPAT
Emergency Physicians Association of Turkey

EAJEM

Eurasian Journal of Emergency Medicine

Citation abbreviation: Eurasian J Emerg Med

ISSN 2149-5807 • EISSN 2149-6048

Volume: 22
Issue: 1

www.eajem.com

March
2023

galenos yayınevi

Official Journal of Emergency Physicians Association of Turkey

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Printing Date: March 2023 **ISSN:** 2149-5807 **E-ISSN:** 2149-6048
International scientific journal published quarterly.

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The journal aims to publish scientifically high quality articles which can contribute to the literature and written in the emergency medicine field and other related fields. Review articles, case reports, editorial comments, letters to the editor, scientific letters, education articles, original images and articles on history and publication ethics which can contribute to readers and medical education are also published.

The journal's target audience includes Emergency Medicine experts, School members who conduct scientific studies and work in the Emergency Medicine field, researchers, experts, assistants, practicing physicians and other health sector professionals.

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Clinical Imaging/ Visual Diagnosis	400	N/A	5	No tables	3 or total of 6 images
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Publication ethics	900	N/A	10	No tables	No media

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Are statistical analyses appropriate?

Are the results presented clearly?

Does the discussion cover all of the findings?

Are the references appropriate for the manuscript?

4. Remarks to the editor

Accepted in its present form

Accepted after modest revisions

Reconsidered for acceptance after major changes

Rejected

5. Remarks to the author

What would be your recommendations to the author?

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Citation abbreviation: Eurasian J Emerg Med

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Original Article
DOI: 10.4274/eajem.galenos.2022.88155
Eurasian J Emerg Med. 2023;22(1): 1-6

Evaluation of Compatibility Between Emergency Physicians and Cardiologists in Measuring Pulmonary Artery Pressure: A Prospective, Observational Study

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Abstract

Aim: To evaluate the degree of agreement between emergency physicians (EPs) and cardiologists in measuring pulmonary arterial pressure (PAP) (measurement with simplified Bernoulli equation).

Materials and Methods: This prospective observational study was conducted between January 2020 and January 2022 in the University of Health Sciences Turkey, Antalya Training and Research Hospital, Clinic of Emergency Medicine, a tertiary hospital. Sample size calculation: According to the kappa (2 raters) - Hypothesis testing method: Assuming minimum acceptable kappa 0.6 and Expected kappa 0.85, significance level 0.05, and Power 90%, including the Expected dropout rate of 10% in the study, 117 patients were included in the study. Demographic findings, personal history, laboratory tests, and PAP values of the patients calculated by the EPs and cardiologists were recorded.

Results: The study included 117 patients who attended the emergency department with shortness of breath or chest pain complaints. While 72.6% of them are female, 27.4% are male patients. The age of the patients included in the study was a minimum of 33 and a maximum of 80. Their mean age and deviation were 59.6±10.6. A near-perfect agreement was found between the measurements of the cardiologist and the EP according to the criteria for PAP measurement ≤20 and >20 (Cohen's kappa coefficient 0.86; <0.0001).

Conclusion: We found near-perfect agreement between cardiologists and emergency room physicians trained in focused cardiac ultrasound (FoCUS) in detecting normal or increased PAP.

Keywords: Pulmonary artery pressure, chest pain, dyspnea, focused cardiac ultrasound, emergency medicine

Introduction

Patients who applied to emergency department (ED) clinics with shortness of breath and chest pain are important among all applications (1). In addition to a detailed examination, laboratory tests, and imaging techniques, ultrasound is used to correct these patients. Focused cardiac ultrasound (FoCUS) is a rapid and reliable point-of-care ultrasonography (USG) protocol recommended to evaluate symptomatic patients in ED clinics (2). FoCUS can provide a quick prediction of cardiac activity, cardiac contractility, central venous pressure and volume status, pericardial effusion or tamponade, and cardiac arrest. Additionally, the left ventricular ejection fraction (LVEF) can be determined; also, volume overload and right-sided cardiac pressure can be estimated by the caval index (3-5). One of the most important causes of high pulmonary artery pressure (PAP) is pulmonary embolism (PE), and it is a condition that should be taken care of ED clinics. Many methods are used to measure PAP (6,7). The Bernouilli equation, a technique used to measure PAP in ED clinics, is a very practical method (8).

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Cite this article as: Duyan M, Günlü S, Sarıdaş A, Ertaş E, Cander B. Evaluation of Compatibility Between Emergency Physicians and Cardiologists in Measuring Pulmonary Artery Pressure: A Prospective, Observational Study. Eurasian J Emerg Med. 2023;22(1): 1-6.

Received: 01.02.2022
Accepted: 09.03.2022

The aim of this study was to determine whether PAP measurements with the simplified Bernoulli equation by the emergency physicians are compatible with the PAP measurement calculated in the echocardiography performed by the cardiologist.

Materials and Methods

Study Design and Settings

This study is a prospective observational study conducted between January 2020 and January 2022 in the Clinic of Emergency Department, University of Health Sciences Turkey, Antalya Training and Research Hospital, a tertiary hospital. The study was approved by the Ethics Committee of University of Health Sciences Turkey, Antalya Training and Research Hospital (no: 2019-392 - decision number: 27/23, date: 26th December 2019). This study was conducted in line with the Declaration of Helsinki.

Pre-study Power Analysis

Sample size calculation: According to the kappa (2 raters) - hypothesis testing method: Assuming minimum acceptable kappa 0.6 and Expected kappa 0.85, significance level 0.05, and Power 90%, and considering the Expected dropout rate of 10% in the study, 117 patients were included in the study.

Selection of Participants

Patients over the age of 18 who gave written informed consent, applied to the ED with shortness of breath or chest pain, and performed echocardiography by the emergency physician and the cardiologist were included in the study. Pregnant patients who had chest trauma in the last three weeks and had ST-elevation acute coronary syndrome were transferred to the ED with pneumothorax, known severe tricuspid stenosis, and pulmonary hypertension (HT) excluded from the study's diagnosis.

Study Protocol

Patients who met the inclusion criteria among patients who applied to the ED with shortness of breath or chest pain were included in the study. Demographic findings, histories, and laboratory tests of the patients were recorded. PAP measurements were recorded by emergency physicians who had at least two years of experience as an emergency physician, attended an accredited ultrasound course, and achieved success. Before the study, emergency medicine physicians received two hours of didactic and two hours of practical training. In the preliminary research, it was observed that she made accurate measurements at least 20 times. Ultrasound images were transferred to a computer environment and interpreted by an experienced and independent cardiologist. Images with inaccurate measurements and poor image quality were excluded from further analysis and the study.

Imaging 2

The emergency physician performed an FoCUS examination. In imaging, tricuspid regurgitation velocity (TR V_{max}) was measured from the apical four-chamber window, and the diameter of the inferior vena cava (IVC) was measured from the subcostal window. It was evaluated whether it collapsed with respiration. The guidelines for echocardiographic evaluation of the right heart in adults were used as the basis for cardiac images (9). FoCUS were examined with a cardiac probe in a Mindray brand USG device (Model DC-T6). Pulmonary arterial pressure calculated by the cardiologist was accepted as the reference. The systolic PAP (sPAP) was measured echocardiographically, and peak tricuspid regurgitation flow velocity (CRAD m/s) was first measured by color Doppler examination from the apical 4-chamber window. In patients without pulmonary valve stenosis, right ventricular systolic pressure was assumed to be equal to sPAP, and sPAP was calculated from TR V_{max} using Bernoulli's equation and adding the estimated right atrial pressure (RAP). RAP was calculated echocardiographically based on the diameter of the IVC and the variation in diameter during respiration (Figure 1, 2).

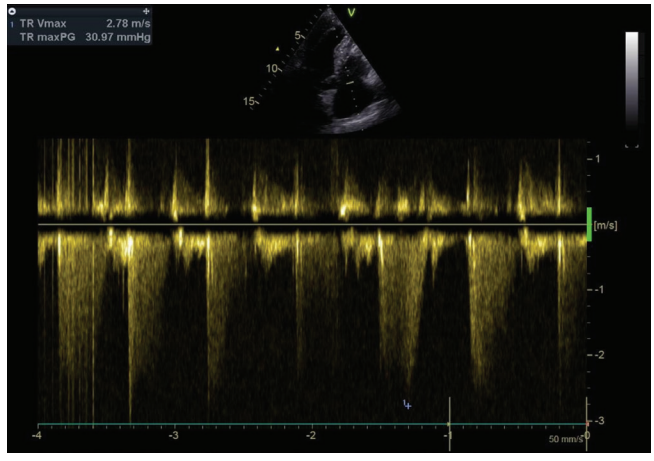

Figure 1. Peak tricuspid regurgitation flow velocity

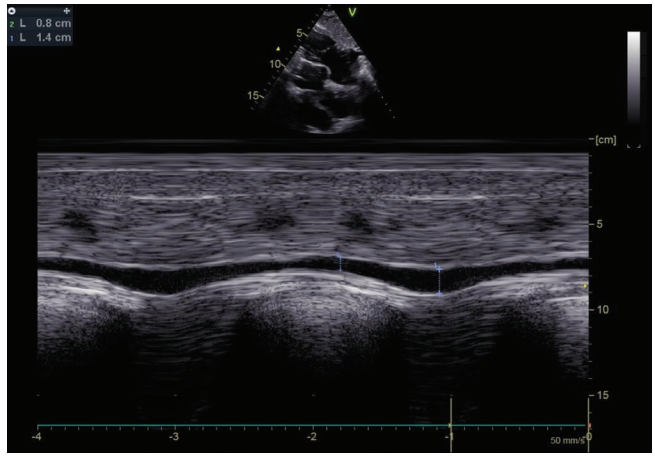

Figure 2. VCI inspiration and expiration image

In the joint guidelines of the European Society of Cardiology and Respiratory and recommended by other authors, PH was defined as the upper limit of the normal value, with mean PAP (oPAP) above 20 mmHg (10-13).

Outcome

PAP was measured by the consultant echocardiography (cardiologist) using the Bernoulli equation of the emergency physician.

Statistical Analysis

In the analysis of the data, the mean and standard deviation, minimum and maximum values of the features: Frequency, and percentage values were used to define categorical variables. The compatibility of different doctors' nominal level measurement results was evaluated with Cohen's kappa. The statistical significance level of the data was taken as $p<0.05$. www.e-picos.com New York software and MedCalc statistics for the data evaluation package program was used.

Results

The study included 117 patients who visited the ED with shortness of breath or chest pain complaints. The flow chart of the clinical study is shown in Figure 3.

The patients' socio-demographic and disease history characteristics are shown in Table 1. While 72.6% of them are female, 27.4% are male patients. The age of the patients included in the study was a minimum of 33 and a maximum of 80. Their mean age and deviation were 59.6±10.6. When their distribution according to chronic disease states is examined, 29.9% of them are HT, 28.2% are diabetes mellitus, 11% are coronary artery disease, 20.5% are chronic obstructive pulmonary diseases, 8.5% have congestive heart failure (Table 1).

In Table 2, the mean values of vital signs and laboratory parameters and minimum-maximum measurements of the patients included in the study are given, respectively (Table 2).

In Table 3, physician compliance statistics between emergency doctors and cardiologists according to PAP measurement.

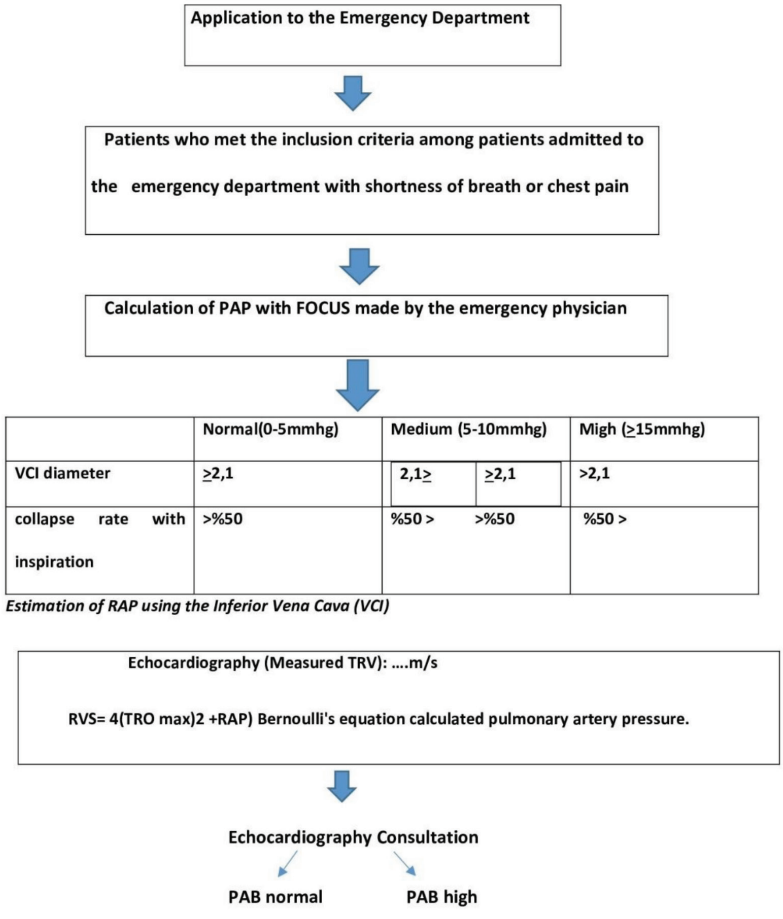

Figure 3. Patient flow in the study

RVS: Right ventricular strain, PAP: Pulmonary arterial pressure

As seen in Table 3: According to the criteria for PAP measurements of ≤20 and >20, a significant and almost perfect agreement was found between the measurements of cardiologists and emergency doctors (Cohen's kappa coefficient 0.86; <0.0001) (Table 3).

Discussion

This study suggests that emergency medicine physicians who are successful in accredited USG training can successfully detect the PAP increase with short-term training.

In many cases, emergency physicians quickly decide with targeted examination and imaging. They provide significant benefits to patients with early treatment by detecting the pathological condition that causes the disease early. The use of USG in ED clinics is increasing day by day. Many fatal diseases can be diagnosed or excluded by USG (14-17). In a consensus statement made by the American Society of Echocardiography and the American College of Emergency Physicians in 2010, a cardiac ultrasound performed by emergency physicians (EPs) is a "basic ultrasound" was accepted as a "tool" (18).

FoCUS provides important information in diagnosing and differential diagnoses of patients who applied to EDs with chest pain and shortness of breath. In addition to providing information about direct cardiac functions, it provides important information in pathologies that rapidly increase PAP, such as PE. By detecting PAP elevation and early treatment for pathology causing it, mortality or morbidity that may develop is prevented.

Table 1. Socio-demographical and disease history distribution

N=117	$\bar{X}$±SD	Min.-Max.
Age	59.6±10.6	33-80
	n	%
Gender		
Sex		
Female	85	72.6
Male	32	27.4
HT		
No	82	70.1
Yes	35	29.9
DM		
No	84	71.8
Yes	33	28.2
CHD		
No	117	100
Yes	-	-
CAH		
No	104	88,9
Yes	13	11.1
COPD		
No	93	79.5
Yes	24	20.5
CHF		
No	107	91.5
Yes	10	8.5

Values are reported as n (%) for categorical variables.
HT: Hypertension, DM: Diabetes mellitus, CVD: Cerebrovascular disease, CHD: Coronary heart disease, COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure, SD: Standard deviation, Min.: Minimum, Max.: Maximum, CAH: Congenital adrenal hyperplasia

Table 2. Distribution of vital findings and laboratory measurements

N=117	$\bar{X}$±SD	Min.-Max.
Systolic blood pressure (mmHg)	140.51±12.24	110-180
Diastolic blood pressure (mmHg)	85.94±8.98	60-110
Pulse (beat/min.)	99.1±21.49	55-120
Respiration rate (per min.)	22.3±2.9	16-30
O_2 saturation (%)	95.4±3.6	65-99
Glucose (mg/dL)	151.38±60.62	72-400
Creatinine (mg/dL)	0.91±0.2	0.56-1.78
Na (mmol/L)	139.27±3.38	124-147
K (mmol/L)	4.17±0.39	3.04-5
HGB (g/dL)	14.43±1.41	9.2-17.11
HCT (%)	42.96±4.08	30.1-51.71
AST (U/L)	27.92±18.88	10-114
ALT (U/L)	20.79±16.44	5-147
WBC ($10^3/mm^3$)	12.68±3.85	6.05-25.41
PLT ($10^3/mm^3$)	275.48±67.03	149-577.1
INR	1.17±0.08	0.98-1.45
Troponin T (ng\L)	36.16±34.5	3-110

Values are reported as mean±SD for continuous variables.
Na: Sodium, K: Potassium, HGB: Hemoglobin, HTC: Hematocrit, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, WBC: White blood cells, PLT: Platelets, INR: International normalized ratio, SD: Standard deviation, Min.: Minimum, Max.: Maximum

Table 3. Inter-physician compliance evaluation according to PAP measurement

n=117		Cardiology			
PAB		**≤20**	**>20**	**Cohen's kappa**	**p value**
Emergency physicians	≤20	78	4	0.86	<0.0001
	>20	3	32		
	Total	81	36		

*Significant at the p<0.05 level (Cohen's kappa coefficient).
PAP: Pulmonary artery pressure

Right heart catheterization should be performed to diagnose increased PAP (19). Right heart catheterization cannot always be performed under emergency conditions. For this reason, it can be used briefly and practically in echocardiography to measure the effect of excessive pressure overload on the right ventricle to detect the increase in PAP. We investigated FoCUS-trained emergency physicians whether there was an acceptable agreement between cardiologists and PAP measurements according to the simplified Bernouilli equation.

According to the results of our study, significant and almost perfect compatibility was found between the measurements of Cardiologists and Emergency Doctors, according to the criteria of ≤20 and >20 in PAP measurement with the simplified Bernouilli equation (Cohen's kappa coefficient 0.86; <0.0001).

There are many studies in which a concordance was found between emergency physicians who received FoCUS training and cardiology specialists in the literature. Randazzo et al. (20) evaluated the LVEF and central venous pressure of USG-trained emergency physicians similar to cardiologists using echocardiography. Echocardiography interpretations from a clinical study compared with a cardiologist for right ventricular strain (RVS) showed excellent agreement with kappa values between 0.89 and 0.96 (21). In another study for RVS, a moderate agreement (k=0.44) was found with limited echocardiography performed by emergency physicians compared with consultation echocardiography (22). In a study comparing emergency physicians and cardiologists in terms of LVEF evaluation, a significant correlation ($r=0.73$, $p<0.001$) was found (23). Rasooli et al. (24) found that the echocardiography results of the emergency physician to be equivalent to the results of cardiologists in their patients with acute coronary syndrome. In the meta-analysis of Albaroudi et al. (25), it was found that there was a concordance in the evaluation of echocardiography use between emergency physicians and cardiologists with USG training.

Emergency physicians who received USG training in PAP measurement significantly contributed to the literature by determining measurements compatible with cardiologists. We think this will be beneficial to the clinical decisions of emergency physicians.

Study Limitations

Our study had some limitations. Since the study aimed to evaluate the ability of the emergency physician to measure PAP, the exact diagnoses of the patients were not followed. Laboratory values increased in PE, such as D-dimer, were excluded from the evaluation because all patients did not demand them. FoCUS could not be performed in cases suspected or diagnosed with coronavirus diseases-2019 (COVID-19) infection during the COVID-19 pandemic period. Therefore, some patients could not be included in the study. Our current findings may provide insight into larger clinical studies in the future.

Conclusion

We found near-perfect agreement between cardiologists and emergency room physicians trained in FoCUS in detecting normal or increased PAP. We believe this will benefit the emergency physician in clinical decision-making for patients presenting to ED clinics with shortness of breath or chest pain complaints.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of University of Health Sciences Turkey, Antalya Training and Research Hospital (no: 2019-392, decision number: 27/23, date: 26th December 2019). This study was conducted in line with the Declaration of Helsinki.

Informed Consent: Informed consent was obtained.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.D., Concept: M.D., Design: M.D., Data Collection and Processing: M.D., S.G., A.S., E.E., B.C., Analysis and Interpretation: M.D., S.G., A.S., E.E., B.C., Literature Search: M.D., S.G., A.S., E.E., B.C., Writing: M.D., S.G., A.S., E.E., B.C.

Conflict of Interest: No conflicts of interest was declared by the authors.

Financial Disclosure: The authors declare that this study received no financial support.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2022.90582
Eurasian J Emerg Med. 2023;22(1): 7-13

True Bacteremia or Contamination? Predictive Factors for Contamination in Blood Cultures Obtained in the Pediatric Emergency Room

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Abstract

Aim: This study aimed to investigate the factors affecting bacteremia and contamination in patients admitted to the pediatric emergency room.

Materials and Methods: This retrospective study focused on patients 1 month to 18 years of age who underwent blood culture tests at the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital from 2013 to 2017. We performed a history and physical examination and noted the presence of fever, pediatric assessment triangle findings on admission, laboratory characteristics, and outcomes associated with true bacteremia and contamination. Patients with no growth in blood culture were excluded from the study. Statistical analysis consisted of the χ^2 test, Mann-Whitney U test, receiver operating characteristic analysis, calculations of sensitivity and specificity, and the multivariable logistic regression model.

Results: Blood culture growth was detected in 514 (12.2%) of 4,200 culture samples assessed during the study period. A total of 449 patients were included in the study. Culture results of 165 patients (36.7%) were defined as indicative of true bacteremia and those of 284 patients (63.2%) as contamination. Patients with true bacteremia were more likely to have fever (81.4% vs. 64.5%, p<0.001), underlying risk factors (61.9% vs. 23.5%, p<0.001), and longer hospital stays (11 days vs. 7 days, p<0.001). Normal pediatric assessment findings on admission were observed between the contamination group and the true bacteremia group (p<0.001). Patients with bacteremia had higher white blood cell counts (13,900 vs. 11,300, p<0.001), C-reactive protein (CRP) (38.5 vs. 6.3, p<0.001), and procalcitonin (1.04 vs. 0.18, p<0.001). The area under the curve was 0.712 for the CRP level. The cut-off value for CRP (mg/L) was 11.75 (sensitivity, 72.6%; specificity, 62.4%). In the multivariable logistic regression analysis, fever on admission [odds ratio (OR), 2.4; 95% confidence interval (CI), 1,037-5,524; p=0.041], male sex (OR, 2.2; 95% CI, 1,066-4,716; p=0.033), and CRP (OR, 1.0; 95% CI, 1,003-1,017; p=0.005) were significantly associated with true bacteremia.

Conclusion: The presence of fever on admission and high CRP levels may be good indicators of which patients require BCs.

Keywords: Bacteremia, blood culture, contaminant, pediatrics

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Cite this article as: Berksoy E, Karadağ Öncel E, Bardak Ş, Demir Ş, Bozkaya Yılmaz S, Demir G, Çiçek A, Yılmaz N, Gökalp G, Anıl M, Yılmaz Çiftdoğan D. True Bacteremia or Contamination? Predictive Factors for Contamination in Blood Cultures Obtained in the Pediatric Emergency Room. Eurasian J Emerg Med. 2023;22(1): 7-13.

Received: 18.02.2022
Accepted: 11.04.2022

Introduction

Bacteremia is a severe invasive infection defined by the presence of bacteria in the blood and is associated with high morbidity and mortality rates. Blood culture (BC) is one of the most used microbiological tests in pediatric emergency services as the gold standard method for the diagnosis of bacteremia because the detection of causative microorganisms allows for appropriate antibiotic selection. However, obtaining BCs remains controversial in emergency settings.

Although the risk of bacteremia in children under 3 years of age is less than 1%, BCs are still commonly obtained, resulting in 2-5-fold more false-positive BC results (1,2). False-positive, negative, or contaminated BC results are increasing in pediatric emergency rooms. Previous studies have reported contamination rates of BCs obtained for cellulitis and fever in children between 0.7% and 8% (3-5). This results in wasted resources, financial burden, antibiotic side effects, and a prolonged hospital stay (3). At this time, there are no guidelines for distinguishing between true and false bacteremia in children. Previous studies have explored C-reactive protein (CRP) levels, white blood cell (WBC) counts, and the duration of fever before pneumococcal vaccine (6). Therefore, there is a need to identify predictive factors of contamination that may be used for clinical decision-making upon admission to the pediatric emergency room (7). In this study, we explored the true prevalence of bacteremia in children who underwent BCs in the pediatric emergency room and identified factors affecting true bacteremia and contamination rates.

Materials and Methods

This study was conducted as a retrospective, cross-sectional study. Files from patients aged between 1 month and 18 years admitted to the Pediatric Emergency Department (ED) of the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital between 2013 and 2017 who had BCs drawn for any reason were examined. The patients included in this study were identified from the BC reports requested from the pediatric emergency room by the microbiology laboratory of our hospital. Patients with no growth in BCs were excluded from the study. Patients with positive BCs were divided into two groups-namely, those with "true bacteremia" and those with "contamination". Typical pathogens (*Escherichia coli, Streptococcus pneumonia, Staphylococcus aureus, Salmonella, Klebsiella, Group B Streptococcus, Neisseria*) grown in BCs indicate true bacteremia. Organisms considered contaminants include coagulase-negative staphylococci (*CoNS*), *Corynebacterium* species, *Bacillus* species other than *Bacillus anthracis*, and *Propionibacterium acnes*. If the potential pathogenicity of one of the isolated species was unclear, especially *CoNS,* the pediatric infectious specialist treating disease reviewed the case to determine whether the corresponding BC as should be included in the study as positive for bacteremia. Independent variables (age, sex, nationality, vaccination status, physical examination findings, pediatric assessment triangle (PAT) findings, WBC counts, CRP, procalcitonin, microorganism growth in the BC, other accompanying organ infections, the presence of risk factors, and length of hospital stay) were recorded for both groups. The presence of any abnormalities, including respiratory and pulse rates; any pulmonary or cardiovascular auscultation findings (such as rails, rhonchus, wheezing, murmur, or gallop, cyanosis, respiratory distress findings; prolonged capillary refill time; presence of petechia, purpura, ecchymosis, meningeal irritation findings, or abdominal tenderness; and findings of arthritis, soft tissue infections, lymphadenitis, cellulitis, pharyngeal hyperemia, or otitis were defined as positive physical examination findings. Immunosuppression (chronic renal failure, malignancies, patients undergoing organ transplant, sickle-cell anemia, or hereditary spherocytosis), the presence of intravascular and dialysis catheters or a ventriculoperitoneal shunt, history of invasive diagnostic procedures, hospitalization up to 15 days before admission, and the presence of chronic systemic diseases were identified as risk factors for bacteremia.

PAT is a tool developed by the American Academy of Pediatrics that allows for rapid assessment of children in the field of triage. It consists of evaluating the child based on respiratory status, circulation status, and appearance (state of consciousness) without physically examining the child. If one of these parameters is abnormal, the patient is considered unstable (8). The laboratory values and first BC results of the patients at the time of admission to the pediatric emergency room were recorded and included in the study. We defined "complete" or "incomplete" vaccinations considering whether the vaccine was available in the National Immunization Programme during the children's immunization period.

All blood samples for BCs were taken by nurses in our ED. Blood samples were incubated in a BacT/ALERT 3D (bioMérieux, France) automated BC system. Samples with positive signals in the BC system were examined using the Gram-staining method and simultaneously cultivated on blood agar, eosin methylene blue agar, and chocolate agar media. Identification and antibiotic susceptibility testing of the isolated bacterial strains were performed using the Vitek 2 compact (bioMérieux) and Phoenix (BD, USA) automated systems.

Statistical Analysis

The data were analyzed using IBM Statistical Package for the Social Sciences Statistics (Windows, version 20.0. IBM Corp., USACo).

The χ^2 test was used to compare categorical variables between groups. The Kolmogorov-Smirnov test was used to evaluate the normal distribution assumption for numerical variables. Differences between the two groups were examined using the independent samples t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. Differences among more than two groups were examined using ANOVA and the Kruskal-Wallis test for normally and non-normally distributed variables, respectively. The discriminatory performance of each variable was determined based on the area under the receiver operating characteristic curve, and the best cut-off values were calculated using the Youden index. A p value of <0.05 was considered indicative of statistical significance.

Ethics

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and approved by the Institutional Ethics Committee of the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital (approval number: 2020/13-12, date: 16.11.2020).

Results

The study was conducted at the hospital of the University of Health Sciences Turkey, İzmir Tepecik Training and Research Hospital in the city of İzmir, Turkey. The pediatric ED of this hospital is the only pediatric trauma and emergency center in a public hospital serving the population of the western region of Turkey. It is a busy pediatric ED admitting approximately 165,000 children per year, aged 1 month to 18 years.

During the 4-year study period, we had 675,000 pediatric ED admissions for which 4,200 BCs were taken. BC growth was detected in 514 (12.2%) of the 4,200 culture samples. A total of 449 patients were included in the study after patients with incomplete data and repeated BCs were removed. The culture results of 165 patients (36.7%) were defined as indicative of true bacteremia and those of 284 patients (63.2%) as contamination (Figure 1).

The median age of the bacteremia group (9 months) was significantly higher than that of the contamination group (3 months) (p<0.001). When the patients were examined in four different age groups: 1-3 months (n=44 with bacteremia; n=136 with contamination), 4-12 months (n=47 with bacteremia; n=66 with contamination), 2-5 years (n=47 with bacteremia; n=56 with contamination), and over 5 years (n=27 with bacteremia; n=26 with contamination), a significant difference was found between the bacteremia and contamination groups (p<0.001, Table 1). When comparing subjects with bacteremia or contamination, there were no significant differences according to sex or race. Concerning clinical and medical history, there were no significant differences in vaccination status, the use of antibiotics before admission, and the presence of abnormal physical findings. There was a significant difference in PAT findings (p<0.001, Table 1), with fewer patients with normal PAT findings with

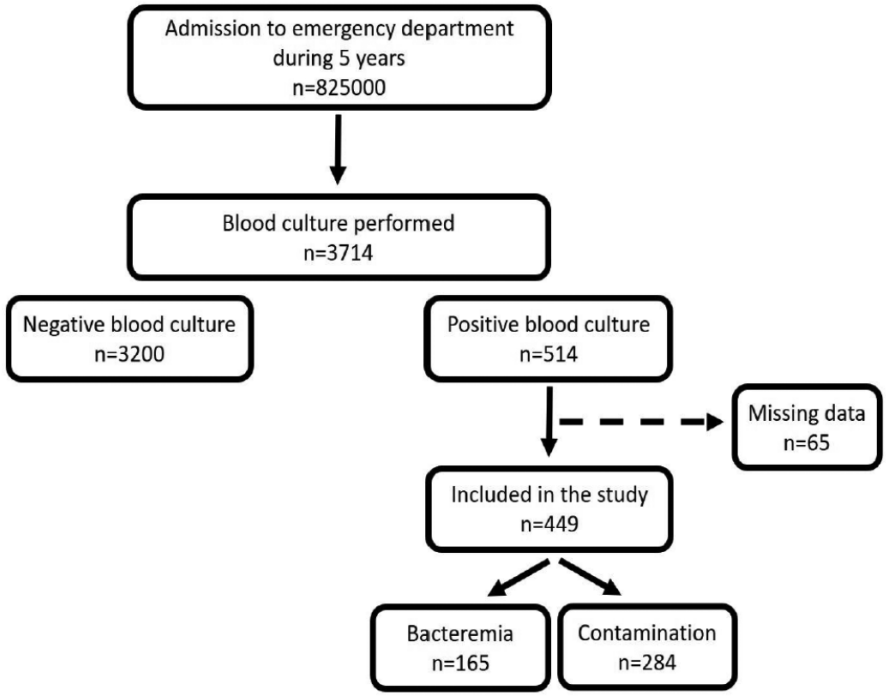

Figure 1. Flow chart of the study population

bacteremia compared with those with contamination. Those with bacteremia were more likely to have fever (81.4% vs. 64.5%, p<0.001), underlying risk factors (61.9% vs. 23.5%, p<0.001), and longer hospital stays (11 days vs. 7 days, p<0.001) (Table 1).

When examining the laboratory results, the bacteremia and contamination groups differed in terms of WBC counts, levels of CRP and procalcitonin, and the number of microorganisms according to Gram staining. Patients with bacteremia had higher WBC counts (13,900 vs. 11,300, p<0.001) and higher levels of CRP (38.5 vs. 6.3, p<0.001) and procalcitonin (1.04 vs. 0.18, p<0.001). The mean WBC, CRP, and procalcitonin levels of the subjects are shown in Table 2.

As shown in Table 3, the most common pathogen in the bacteremia group was *CoNS* (30.9%), followed by *Streptococcus* spp. (20.6%), *E. coli* (13.3%), *Klebsiella* spp. (7.8%), *Staphylococcus aureus* (5.4%), *Streptococcus pneumoniae* (5.4%), *Pseudomonas* spp. (4.2%9, *Acinetobacter* spp. (3.6%), *Stenotrophomonas maltophilia* (2.4%), and others (6.1%).

As shown in Figure 2, the area under the curve (AUC) was 0.712 for the CRP level. The cut-off value for CRP level (mg/L) based on the AUC was 11.75 (sensitivity, 72.6%; specificity, 62.4%). We performed logistic regression analysis after controlling for potential confounding factors and found that male sex [odds ratio (OR), 2,242, p=0.033], high fever (OR, 2,392, p=0.041),

Table 1. Demographical and clinical characteristics of patients with bacteremia and contamination

Characteristics	Bacteremia (n=165)	Contamination (n=284)	p value
Age, months[a]	9 (2-34.5)	3 (1-16)	<0.001
Age groups[b]			<0.001
1-3 months	44 (26.6)	136 (47.8)	
3-12 months	47 (28.4)	66 (23.2)	
1-5 years	47 (28.4)	56 (19.7)	
>5 years	27 (16.3)	26 (9.1)	
Gender (male)[b]	98 (59.4)	151 (53.1)	0.201
Race (Turkish)[b]	141 (85.4)	242 (85.2)	0.944
Use of antibiotics prior to admission[b] (n=327)	30/127 (23.6)	34/200 (17)	0.141
Incomplete/no vaccination[b] (n=333)	15/126 (11.9)	10/207 (4.8)	0.018
Underlying risk factors[b]	61 (36.9)	67 (23.5)	0.002
Normal pediatric assessment triangle[b] (n=445)	67/165 (40.6)	183/280 (65.3)	<0.001
Abnormal physical examination[b] (n=443)	94/164 (57.3)	148/279 (53)	0.383
Presence of fever[b] (n=433)	132/162 (81.4)	175/271 (64.5)	<0.001
Outcome[b] (n=442)			<0.001
Discharged from the emergency	21/161 (13)	88/281 (31.3)	
Admission to pediatric services	105/161 (65.2)	167/281 (59.4)	
Admission to pediatric intensive care unit	29/161 (18)	20/281 (7.1)	
Day of hospitalization[a] (n=321)	11 (6-16)	7 (5-11)	<0.001

[a]Values are given median and IQR (25-75%), [b]Values are given as percentage.
IQR: Interquartile range

Table 2. Laboratory characteristics of patients with bacteremia and contamination

	Bacteremia (n=165)	Contamination (n=284)	p value
White blood cell count, /μL[a] (n=443)	13900 (9000-19800)	11300 (8500-14800)	<0.001
C-reactive protein, mg/L[a] (n=448)	38.5 (6.5-133.3)	6.3 (1.7-21.0)	<0.001
Procalcitonin, ng/mL[a] (n=280)	1.04 (0.18-10.48)	0.18 (0.11-0.29)	<0.001
Microorganism according to gram staining[b]			<0.001
Positive	107 (64.8)	284 (100)	
Negative	58 (35.1)	-	

[a]Values are given median and IQR (25-75%), [b]Values are given as percentage.
IQR: Interquartile range

and high CRP levels (OR, 1,010, p=0.005) were risk factors for bacteremia (Table 4).

Discussion

In this study, we found that the rate of true bacteremia was 4.4% and the overall contamination rate was 7.6% in the 1-month- to 18-year-old pediatric patients. These results conflict with those of previous studies conducted in emergency services, which reported a bacteremia rate of 0.25% to 2.1% (9-11). However, most previous reports included children under 3 years of age febrile illness or occult bacteremia. The reasons for the high rate of true bacteremia in our study may be that we included not only infants with occult bacteremia or febrile infants, but children in all age groups with focal or systemic infections and bacteremia risk factors (such as children with an indwelling catheter, etc.). We also included isolated growth of *CoNS*, which were identified as true pathogens by pediatric infectious specialists that contribute to bacteremia. Although previous reports (12,13) showed that contamination rates vary significantly among institutions, from 6% to 11%, acceptable rates were reported as lower than 2-3% (14). The reason for our high contamination rate is that we have a broad population with a younger age who typically have a higher rate of contamination (2 of 3 BCs of 180 infants aged 1-3 months were contaminated) because obtaining BCs from very uncooperative infants significantly increases the risk for contamination (14). As expected, we found that the median age of the contamination group was significantly lower than that of the bacteremia group in our study. Additionally, variation in taking and collecting BC samples (e.g., blood collected during night shifts, nursing skills, busy ED, etc.) in our ED might have resulted in a higher contamination rate. Furthermore, the significant differences among age groups in terms of bacteremia (highest rate in children younger than 1 year) were consistent with the study by Chiu et al. (15). They found that both bacteremia and contamination rates increased with a younger age (the highest true bacteremia rate was found in the group younger than 1 year) and reported an overall contamination rate of 3%. Similar to a previous report (15-17), although there was no significant difference between the groups in terms of sex, there were more males than females in both groups. However, we showed that the risk of true bacteremia was 2.2-fold higher in males based on regression analysis.

We also explored vaccine history, physical exam findings, underlying risk factors, the presence of fever (≥38 °C axillar) upon admission, and PAT evaluation findings in the triage room that could be used to differentiate bacteremia from contamination. In our analysis, the use of antibiotics before admission, incomplete vaccinations, and any abnormal physical examination findings

Table 3. List of microorganisms causing bacteremia in patients

Microorganisms	Bacteremia (n=165)
CoNS	51 (30.9)
Streptococcus spp. (including *Streptococcus pyogenes*)	34 (20.6)
Escherichia coli	22 (13.3)
Klebsiella spp.	13 (7.8)
Staphylococcus aureus	9 (5.4)
Streptococcus pneumoniae	9 (5.4)
Pseudomonas spp.	7 (4.2)
Acinetobacter spp.	6 (3.6)
Stenotrophomonas maltophilia	4 (2.4)
Others	10 (6.1)

CoNS: Coagulase negative staphylococci

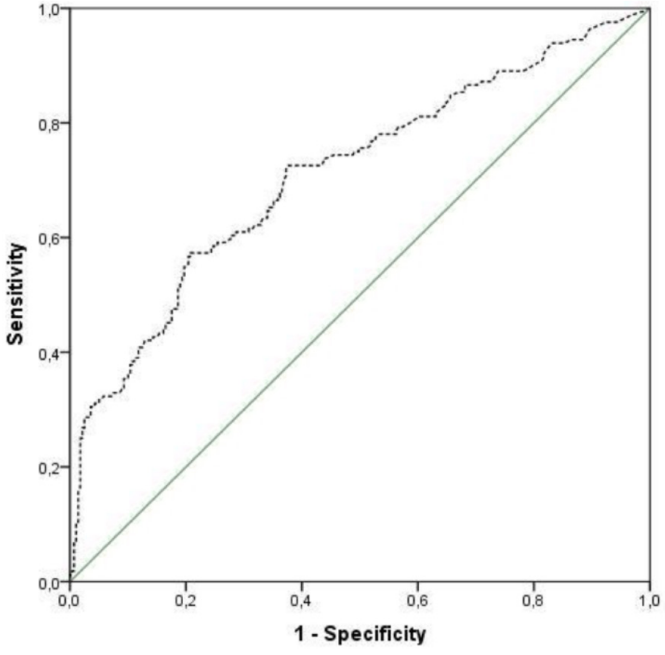

Figure 2. Reciever operating curve for C-reactive protein

Table 4. Multivariate analysis for effect on bacteremia

Variables	Odds ratio (95% CI)	p value
Age	0.998 (0.989-1.008)	0.754
Gender (male)	**2.242 (1.066-4.716)**	**0.033**
Incomplete/no vaccination	1.794 (0.513-6.278)	0.360
Abnormal PAT	0.493 (0.237-1.04)	0.058
Fever	**2.392 (1.037-5.524)**	**0.041**
Underlying risk factors	0.941 (0.411-2.154)	0.086
White blood cell count	1.01 (1-1)	0.802
C-reactive protein, mg/L	**1.010 (1.003-1.017)**	**0.005**
Procalcitonin, ng/mL	1.046 (0.906-1.099)	0.073

CI: Confidence interval, PAT: Pediatric assessment triangle

were not differentiating factors between bacteremia and contamination. We found that true bacteremia was only significantly associated with the presence of fever at admission, underlying risk factors, and abnormal PAT findings in the triage room. In our country, a pneumococcal conjugate vaccine was introduced in 2007. Therefore, the study population included older children who had missed the vaccination schedule during the study period. Although we did not find statistical significance, children with incomplete vaccination were more likely to be in the bacteremia group. We found significant differences between the bacteremia and contamination groups in terms of the presence of fever and underlying risk factors, which agrees with the pattern of septicemia and previous adult studies including immunosuppressed patients (18).

In this study, prehospital oral antibiotic use had no significant effect on bacteremia. This finding is interesting and similar to that of Nannan Panday et al. (19), who performed their study in adults. This may be because most patients in our study had used narrow spectrum oral antibiotics at insufficient doses. Our study showed that more than half of the children (almost 60%) in the bacteremia group were classified as having abnormal PAT findings at the triage. Moreover, up to 65% of the children in the contamination group were stable and appeared "well" in the initial PAT assessment. However, upon multivariable regression analysis, we did not find any association between abnormal PAT findings and bacteremia. Our findings in terms of abnormal PAT outcomes in the bacteremia group conflicts with that of the multicenter prospective study of Gomez et al. (20) involving 15 EDs. They reported that 65.7% of patients with positive BCs had normal PAT findings upon arrival to the ED. As a result, although PAT is an empirical tool for predicting the severity of the clinical condition of the patients, it may not be predictive of true bacteremia. When we compared the length of hospital stay between the two groups, the bacteremia group had longer hospitalizations due to their antibiotic use, as expected.

Our study showed that although considered a contaminant, *CoNS* (which were considered true pathogens after review by pediatric infectious doctors and clinical evaluation) was the dominant isolated pathogens among those contributing to bacteremia. Although they exhibit low virulence, *CoNS* can cause bacteremia (especially in malignancy, immunocompromised patients, and patients with catheters) (21,22). In a study evaluating 76,331 BCs from 13,519 pediatric patients over an 11-year period, *CoNS* was the most common cause of bacteremia, and the true pathogen rate was reported to be 23.8% (23). Because our study focused on identifying the predictive factors of true bacteremia, we did not examine the variables and outcomes associated with pathogens or contaminants.

For laboratory markers, this study also showed that CRP has a better predictive ability than WBCs, which is similar to a previous study by Chiu et al. (15). Despite numerous studies that demonstrate the superiority of procalcitonin over CRP in diagnosing bacteremia (24-28), we found that among the biomarkers, CRP had a one-fold effect on bacteremia based on multivariable regression analysis. Moreover, in this study, the CRP AUC value was 0.712 for differentiating true bacteremia from contamination. When a cut-off value of 11.75 mg/dL was used for CRP, the sensitivity and specificity were 72.6% and 62.4%, respectively. If the CRP cut-off value (≥11.75 mg/dL) is used, approximately 28% of true bacteremia patients would be missed.

Study Limitations

A limitation of this study is that we could not include patients with no growth in BCs. Another limitation of this study is that it is a retrospective design with chart review for clinical and history data from a single center. The third limitation is that due to the lack of clear guidelines for indications for obtaining BCs in pediatric EDs, patients with true bacteremia might not have had samples taken for BCs and therefore were excluded from the study. Additionally, we could not evaluate the reason BCs were drawn or the disease diagnosis (such as urinary tract infections, pneumonia, occult bacteremia, and/or any other specific local infections). Despite these limitations, our study highlights the need for future investigation into factors of BC contamination to generate guidelines and prevent unnecessary BCs.

Conclusion

Based on the results of this study, to reduce the BC samples in pediatric EDs, it is important to evaluate the vaccination status, underlying risk factors (especially for *CoNS* as a true pathogen), fever, and PAT findings at admission. Additionally, among the wide variety of clinical features, the presence of fever and elevated CRP values may support and improve the efficiency of BC in EDs.

Acknowledgment

The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: http://www.textcheck.com/certificate/GOdF7U

Ethics

Ethics Committee Approval: The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and approved by the Institutional Ethics Committee of the University of Health Sciences Turkey, İzmir Tepecik

Training and Research Hospital (approval number: 2020/13-12, date: 16.11.2020).

Informed Consent: This study was conducted as a retrospective, cross-sectional study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.B., S.B.Y., G.G., M.A., Design: E.B., E.K.Ö., S.B.Y., M.A., D.Y.Ç., Data Collection and Processing: E.B., Ş.B., Ş.D., G.D., A.Ç., Analysis and Interpretation: E.B., E.K.Ö., A.Ç., N.Y., Literature Search: E.B., S.B.Y., Writing: E.B., E.K.Ö., N.Y., M.A., D.Y.Ç.

Conflict of Interest: No conflicts of interest was declared by the authors.

Financial Disclosure: The authors declare that this study received no financial support.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2022.38358
Eurasian J Emerg Med. 2023;22(1): 14-7

Demographic and Cost Analysis of Intoxication Cases Admitted to University Hospital Emergency Service Within a Year

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Abstract

Aim: We described the demographic and etiological characteristics of drug-induced intoxication cases who were admitted to the adult emergency department of our hospital between 01.01.2017 and 31.12.2017 and how much they cost to the Social Security Institution.

Materials and Methods: This was descriptive research, and the records of the patients who were admitted to the adult emergency service and diagnosed with drug intoxication between January 01, 2017 and December 31, 2017 were obtained from the automation system and analyzed retrospectively.

Results: The data of 83 patients were evaluated in our study. 63.9% (n=53) of the patients were female and 36.1% (n=30) were male. Intoxications were most common in the 18-24 age group (48.2%; n=40). 92.8% (n=77) of the patients took the drug to commit suicide, and the majority of the intakes (60.2%; n=50) were due to single drug intake. The most common used drugs are antidepressants. The treatment costs increased significantly in the cases of suicidal intake (p=0.038) and multiple drug intake (p=0.035).

Conclusion: Most of the drug-induced intoxications occurred because of suicidal intake. An important part of the drugs used for this purpose are psychiatric drugs. Therefore, the presence of psychiatric symptoms should be investigated in patients diagnosed with drug intoxication, and psychological support should be provided when necessary.

Keywords: Drug intoxication, social security costs, toxins, suicidal intake, and accidental intake

Introduction

Any chemical, physical, or organic substance that is digested, inhaled, absorbed, or injected can damage structures and impair functions due to its chemical effects. When taken in small amounts is called a toxin, and exposure to this substance is called intoxication (1). Intoxication cases are among the most common medical emergencies. Intoxication may occur due to accidental or suicidal intake, occupational exposure, or the effects of a drug that should be regularly used medically (2). While accidental intoxications are observed more frequently under the age of six, suicidal intoxications are more common in the puberty period when mental changes are becoming evident (3). Among emergency service admissions, intoxication is the most common cause of non-traumatic coma in patients younger than 35 (4). It was reported that the intoxication cases that applied to the emergency service only constitute 0.46-1.57% of all emergency service admissions. The causes of intoxication vary based on geographical region, socio-cultural, and economic status. Pharmaceuticals, foods, and industrial and agricultural toxic substances are the most common causes of intoxication (4). In the study Özayar et al. (5) conducted, 87% of the cases were suicidal intoxication; 70.2% occurred due to multiple drug intake, and 29.8% to single drug intake. It was found that multiple drug intake happens primarily due to antidepressant combinations.

Considering this information, we described the demographic and etiological characteristics of drug-induced intoxication cases admitted to our hospital's adult emergency department between

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Cite this article as: Koşargelir M, Hakkoymaz H, İbrahim A. Demographic and Cost Analysis of Intoxication Cases Admitted to University Hospital Emergency Service Within a Year. Eurasian J Emerg Med. 2023;22(1): 14-7.

Received: 11.04.2022
Accepted: 07.10.2022

01.01.2017 and 31.12.2017 and how much they cost to the Social Security Institution.

Materials and Methods

The Type of Research and Participants

The study was planned as descriptive research, and the records of the patients who were admitted to the adult emergency service of Kahramanmaraş Sütçü İmam University Faculty of Medicine Hospital and diagnosed with drug intoxication between Jan 1, 2017, and Dec 31, 2017, were obtained from the automation system and analyzed retrospectively. The demographic characteristics of the patients, such as age, gender, the time of admission to and duration of stay in the emergency service, how the intoxication occurred, the reason why the substance was taken, the drugs, and the groups of drugs that caused the intoxication, whether the intoxication occurred due to the intake of a single type of drug or that of different drugs at the same time (multiple intakes), and the patient's clinical symptoms, prognosis, and total costs were examined.

Inclusion and Exclusion Criteria

All patients aged 18 years and above who applied to the emergency service due to drug intoxication and had no missing demographic, and clinical data in their records were included in the study. Patients under 18 years of age, those with incomplete data in their records, and those with symptoms of another intoxication accompanying the drug intoxication were excluded from the study.

Statistical Analysis

The demographic data of the patients, the type, and the injury clinic were summarized through numbers and percentages. Whether the data conformed to the normal distribution was evaluated by running the Shapiro-Wilk test. Kruskal-Wallis and Mann-Whitney U tests were used for statistical analysis of the mean scores, and Spearman correlation analysis was conducted to determine the correlation. The Statistical Package for the Social Sciences 16.0 package program was used for the analysis. The value of $p<0.05$ was considered statistically significant.

Ethics Committee

The study was performed following the Declaration of Helsinki, and the confidentiality of the patients included in the study was ensured. The Kahramanmaraş Sütçü İmam University Faculty of Medicine of Local Ethics Committee approved this study (decision no: 13, date: 21.03.2018).

Results

The data of 83 patients who were admitted to the adult emergency service due to drug-induced intoxication were evaluated in our study. 63.9% (n=53) of the patients were female and 36.1% (n=30) were male. When the patients were examined according to their age groups, it was observed that the intoxications were most common in the 18-24 age group (48.2%; n=40). It was found that 92.8% (n=77) of the patients took the drug, causing intoxication to die by suicide, and the majority of the intakes (60.2%; n=50) were due to a single drug intake. The demographic data for the patients are summarized in Table 1.

It was revealed that a significant portion of the drugs taken were psychiatric drugs, and among them, antidepressants (33.7%; n=28) constituted the drug group that caused the intoxication most frequently. Analgesics were the second most common drug group that caused intoxication. These drug groups that caused intoxication are summarized in Table 2.

When the patients were evaluated in terms of their treatment costs, it was observed that they increased significantly in the cases of suicidal intake (p=0.038) and multiple drug intake (p=0.035) (Table 3).

It was found that age group, gender, single, or multiple drug intake, and whether the drug intake was suicidal did not significantly affect the duration of hospitalization. It was observed that the mean time of arrival to the hospital after the drug intake was 60 min (minimum=15 - maximum=780), and the wider the time gap between the drug intake and the arrival to the hospital was, the longer the hospital stay was (p=0.008, r=0.289) and the more the treatment cost (p=0.029, r=0.240).

Table 1. Demographic characteristics of the patients

Demographic characteristics	Number	Percentage
Age (year)		
18-24	40	48.2
25-34	22	26.5
35 and higher	21	25.3
Gender		
Male	30	36.1
Female	53	63.9
Type of exposure		
Accidental	6	7.2
Suicidal	77	92.8
Single or multiple intakes		
Single	50	60.2
Multiple	33	39.8

Discussion

Intoxication cases are increasing worldwide day by day (6). this study, conducted with a retrospective design in a university hospital's emergency department, examined the patient's demographic characteristics and costs to the healthcare system. In many studies conducted in our country, drugs are the most common cause of acute intoxication (1). In studies conducted in our country, it is seen that the female gender is more common in poisoning cases, and the mean age is 25 years and below (1,7,8). Our study has revealed similar findings in line with the previous literature. Previous studies have shown that suicide attempts by drug intake in women are significantly more severe than for men in our country (1,9,10). In our study, cases of poisoning were more common in women, and the most common cause of poisoning was suicide attempts. These findings are similar to previous studies.

Table 2. Subgroups of drugs causing intoxication

Subgroups of drugs	Number	Percentage
Analgesic	29	34.9
Antidepressant	28	33.7
Antipsychotic	8	9.6
Narcotic	8	9.6
Antihypertensive	9	10.8
Antiviral	8	9.6
Antiepileptic	7	8.4
Antibiotic	12	14.5
Others	22	26.5

Since multiple drug intake exists, the total rate exceeds 100%

Table 3. Cost analysis of patients

Demographic characteristics	Cost [median (min-max)]	p
Age (year)		
18-24	962.35 (15.50-3907-17)	0.076[a]
25-34	587.27 (75.13-2057.36)	
35 and higher	198.75 (102.36-1828.64)	
Gender		
Male	716.39 (15.50-2497.91)	0.443[b]
Female	532.30 (75.13- 3907.17)	
Type of exposure		
Accidental	130.17 (25.04-1356.36)	0,038[b]
Suicidal	760.79 (15.50-3907.17)	
Single or multiple intakes		
Single	401.35 (15.50-3907.17)	0.035[b]
Multiple	891.12 (104.80-3015.18)	

[a]: It was found through the Kruskal-Wallis test.
[b]: It was found through the Mann-Whitney U test.
min-max: Minimum-maximum

Some studies describe the cost analysis and the influential factors on the cost of intoxication cases in our country, but these studies were not specific to drug-induced intoxication (11,12). To the best of our knowledge, our study is first describing the effect of single- or multi-drug intoxication among only drug intoxication cases admitted to the emergency department. In a previous study, Hakkoymaz et al. (12) found no statistically significant difference in costs according to age groups, gender, and type of medicine in intoxications with a single medicine intake. On the other hand, it is determined that the costs are higher for suicidal poisonings, medicine-induced intoxications, and cases that require intensive care are needed. In addition, it was found that multiple drug intake poisonings were more costly when compared to single drug intake poisonings (12).

While explaining the demographic characteristics and costs of the intoxication cases, we raised awareness in the related literature through the cases with statistical significance. Our study observed that the costs of admissions due to intoxication do not significantly differ in age groups and gender ($p>0.05$). However, we found that the type of exposure and single or multiple intakes were significantly different in terms of cost ($p<0.05$). Although multiple drug intakes are not fatal, clinicians may follow patients for more prolonged, thinking that it will have a challenging course, and therefore the cost may increase. Patient costs increase, especially in suicidal and multiple drug intakes. This situation can be attributed to the reasons such as changes in the follow-up and treatment periods of drugs with different half-lives in multiple intakes, the increase in the possibility of drug interaction, and creating the need for intensive care by producing multiple clinical results.

The cases that were admitted to the emergency service and were between 18-24 (48.2%), female (63.9%), suicidal (92.8%), and single drug intake (60.2%) were the ones most frequently encountered. As for the drug subgroups, it was revealed that the most commonly used ones are antidepressant drugs, which are very common among people. Following the literature, self-medication emerged as the most common cause of intoxication cases (13-15). This result may lead to an argument that as long as they do not harm the prognosis, single agents or agents that do not have synergistic effects in the case of intoxication should be preferred in young women with suicidal tendencies who use psychiatric drugs. Different clinical presentations should bring exposure to the differential diagnosis in intoxication cases into mind (16). The accompanying atypical trauma histories of the patients should not lead to abandoning the suspicion of intoxication (17). When treating such patients, their psychiatric

history can be questioned to prevent drug reactions (18). In this sense, a history of frequent use of psychiatric drugs may be suggestive in terms of exposure or self-harm in any clinical presentation in which the patient was admitted.

Study Limitations

Our study is a single-centre study and was conducted with a limited population of patients, which is a significant limitation. Prospective multicenter studies to be conducted with a broader patient population and in a more limited age group with no comorbid disease may contribute to the literature.

Conclusion

Most of the drug-induced intoxications occurred because of suicidal intake. An essential part of the drugs used for this purpose is psychiatric drugs. Therefore, psychiatric symptoms should be investigated in patients diagnosed with drug intoxication, and psychological support should be provided when necessary.

Ethics

Ethics Committee Approval: The study was approved by the Kahramanmaraş Sütçü İmam University Faculty of Medicine of Local Ethics Committee (decision no: 13, date: 21.03.2018).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices - Concept - Design - Data Collection or Processing - Analysis or Interpretation - Literature Search - Writing: M.K., H.H., A.İ.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2022.20633
Eurasian J Emerg Med. 2023;22(1): 18-23

Comparison of the Analgesic Effects of Intravenous Dexketoprofen, Ibuprofen and Fentanyl in Patients Suffering from Renal Colic Pain in the Emergency Department

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Abstract

Aim: Renal colic is a urological emergency usually caused by urolithiasis and manifested by severe pain. Emergency treatment's main purpose is to effectively relieve pain and urinary obstruction without impaired renal function. We measured the efficacy and safety of intravenous ibuprofen on renal colic pain.

Materials and Methods: Two-hundred thirty-five patients who were admitted to the emergency department between 01.01.2016-30.06.2017 and were suspected of renal colic that scored at least 2 points on the visual analog scale (VAS) or FLACC scale were included in the study after obtaining detailed consent. One hundred-fifty four patients whose diagnoses were confirmed radiologically, included in the study as Group A (dexketoprofen) (n=35), Group B (ibuprofen 400 mg) (n=37), Group C (ibuprofen 800 mg) (n=44), and Group D (fentanyl) (n=38). VAS and FLACC scales were re-evaluated on the 20th, 40th, and 60th minutes after drug administration.

Results: 64.9% of the patients were male and 35.1% were female, and the mean age was 42.31 (±15.46). It was observed that all 4 of the medications given to patients who applied to the emergency department with flank pain provided effective analgesia, but the drugs could not establish a statistically significant advantage over each other.

Conclusion: Intravenous administration of ibuprofen is considered as an effective and safe alternative in the treatment of renal colic pain in the emergency department.

Keywords: Analgesia, dexketoprofen, fentanyl, ibuprofen, renal colic

Introduction

Renal colic is a common urological emergency characterized by severe pain, usually associated with urolithiasis, diagnosed, and treated in emergency departments. Each year, more than 1 million patients in the United States present to emergency services due to renal colic (1,2). The cause of pain is usually the presence of an acutely obstructing stone in the urinary tract. Due to this obstruction, dilatation of the ureter and stretching and spasm of the ureteral smooth muscle cells are observed (3). The prevalence of kidney stones worldwide is estimated to be 5-15% in the general population (4).

Pain management is the first-line treatment of renal colic. In 80% of the patients, the stones pass spontaneously, and no additional treatment is needed (5,6). Non-steroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics are widely used all over the world for treating renal colic pain (2). However, opioid analgesics may have side effects such as nausea, vomiting, dizziness, respiratory depression as well as addictive effects (3,4). Therefore, physicians

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Received: 04.07.2022
Accepted: 30.12.2022

Cite this article as: Özdemir M, Çığşar G, Bağcıoğlu M, Çiftçi H, Güal E. Comparison of the Analgesic Effects of Intravenous Dexketoprofen, Ibuprofen and Fentanyl in Patients Suffering from Renal Colic Pain in the Emergency Department. Eurasian J Emerg Med. 2023;22(1): 18-23.

around the world are turning to equally effective and rapid, but safer alternatives for treating renal colic pain. An ideal pain reliever should have a high safety profile and the ability to stop pain quickly and effectively without significant interaction with other pharmacological agents (7). In the literature, there are many studies stating that NSAIDs are effective, fast, and safe for treating renal colic pain (8-11).

We investigate the superiorities and advantages of ibuprofen (400 mg and 800 mg doses), an NSAID used in oral form for many years, by intravenous (IV) administration and compare it with another NSAID, dexketoprofen, and an opioid analgesic, fentanyl, in terms of analgesic efficacy and rate.

Materials and Methods

The study was planned as a prospective, randomized single-blind study. The study was initiated with the approval of a Kafkas University Faculty of Medicine Hospital Ethics Committee (no: 01, date: 27.01.2016).

Study Population and Sample

Patients over the age of 18 who applied to the emergency department of a university hospital by themselves or via 112 Emergency Ambulance Service between 01.01.2016 and 30.06.2017 with flank pain and diagnosed with renal colic (urolithiasis) by physical examination and radiological imaging who scored 2 or higher on the visual analogue scale (VAS) or FLACC (Face, Legs, Activity, Cry, Consolability) pain scales were included in our study (Table 1, Figure 1) (12,13). Patients whose diagnosis could not be confirmed radiologically, and patients who were diagnosed other than renal colic during the evaluation process were excluded from the study. Patients who applied recurrently due to renal colic were accepted as new admissions, provided that at least 48 h had passed since the previous application.

Data Collection Form

Demographic data and medical history of the patients included in the study were recorded in the data collection form. FLACC and VAS scores were recorded at the 0th min after vital signs were obtained and they were examined. Patients scoring 2 points or more on at least one of both scales were randomized by simple random sampling by drawing one of the 4 previously determined cards (ace of spades for Group A, ace of hearts for Group B, ace of diamonds for Group C, and ace of clubs for Group D) from the deck of cards. According to the cards they drew, they were divided into 4 groups: IV 50 mg dexketoprofen (Group A), IV 400 mg ibuprofen (Group B), IV 800 mg ibuprofen (Group C), and IV 0.75 mcg/kg fentanyl (Group D). The medicines were administered IV as a 20-minute infusion in 100 cc 0.9% NaCl solution. Care was taken to ensure that the liquids given were colorless and odorless and that they were given in the same amount and at the same time. VAS and FLACC scores at 0, 20, 40, and 60 min were recorded for all patients.

Exclusion Criteria

Those who are allergic to fentanyl, NSAIDs, or opiates, have hemodynamic instability, fever ≥38 °C, peritoneal irritation findings on physical examination, pregnant or suspected pregnancy, breastfeeding, known or suspected aortic dissection or aneurysm, using pain medication in the last 24 h, and patients with cardiac, renal or hepatic insufficiency and a history of transplant were excluded from the study. Patients who developed drug-related side effects during infusion and whose treatment could not be completed were excluded from the study.

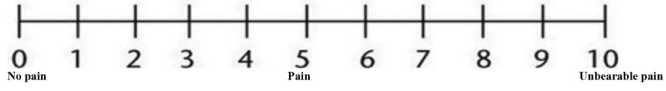

Figure 1. Visual analog scale

Use of the scale: The patient is asked to mark the most suitable place for her on the scale according to the severity of their pain, with 0 being the lowest and 10 being the highest

Table 1. FLACC pain scale

Categories	0	1	2
Face	No particular expression	Occasional grimaces or frown	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, and tense	Kicking or legs drawn up
Activity	Lying quietly, normal position moves easily	Squirming, shifting, back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimper, occasional complaint	Crying steadily, screams, or sobs, and frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or being talked to, distractible	Difficult to console or comfort

Use of the scale: The patient is evaluated using five parameters. A score between 0 and 2 is given for each parameter. The patient is given a total score of 0 to 10

Statistical Analysis

Data analysis was done with Statistical Package for the Social Sciences for Windows 22 package program. Whether the distribution of continuous variables was close to normal was investigated by the Kolmogorov-Smirnov Z test. Descriptive statistics were presented as mean±standard deviation or median (minimum-maximum) for continuous variables, and number of cases and (%) for categorical variables. The significance of the difference between the groups in terms of means was evaluated with Student's t-test and one-way ANOVA F, and the significance of the difference in terms of median values was examined using the Mann-Whitney U test. Categorical variables were evaluated using the chi-square test. The effect of independent factors was calculated by linear regression analysis. Results for $p<0.05$ were considered statistically significant.

Results

The data of 235 patients who presented to the emergency department of a university hospital with flank pain, either by themselves or through the 112 Emergency Ambulance Service, were analyzed for the study. Of these patients, 79 were excluded because the diagnosis of renal colic could not be confirmed radiologically, and 2 of them were excluded because of their missing data. A total of 154 patients, 100 (64.9%) male and 54 (35.1%) female, were included in the study. The ages of the patients ranged from 19 to 74, with a mean age of 40.96±13.68 for men and 44.80±18.19 for women.

62.3% of the patients had a history of renal colic. The most common complaint was flank pain (94.8%), and the most common physical examination findings were costovertebral angle tenderness (CVAT) (87.7%) and abdominal defense (48%). Hematuria was detected in urinalysis in 77.9% of the patients. Other complaints of admission to the emergency department and physical examination findings are given in Table 2.

Table 2. Complaint and anamnestic demographic data

Complaints and findings of physical examination	Number of patients n (%)
History of colic attack	96 (62.3)
Flank pain	146 (94.8)
Nausea	68 (44.2)
Burning sensation during urination	66 (42.9)
Presence of abdominal pain	56 (36.4)
Color changes in urine	41 (26.6)
Vomiting	36 (24.4)
CVAT	135 (87.7)
Hematuria	120 (77.9)

CVAT: Costovertebral angle tenderness

After the patients were diagnosed with renal colic, they were divided into four groups as Group A (dexketoprofen), Group B (ibuprofen 400), Group C (ibuprofen 800), and Group D (fentanyl) according to the given medication. The grouping of the patients according to the treatment given is given in Table 3. The reason for the difference in the number of patients in the four groups is that the groups were randomized before analgesic treatment, but the radiological examination could be performed after treatment.

Medication was started after VAS scoring was performed at the 0th minute. The analgesic efficacy of the given medications was compared by performing the VAS scoring at the 20th, 40th, and 60th minutes. However, there was no statistically significant difference (p=0.368, p=0.368 and p=0.368, respectively) (Figure 2).

Medication was started after FLACC scoring was performed at the 0th minute. The analgesic efficacy of the given medications was compared by performing the FLACC scoring at the 20th, 40th, and 60th minutes. However, there was no statistically significant difference (p=0.368, p=0.368 and p=1.000, respectively) (Figure 3).

No statistically significant difference was found between the medication groups in terms of analgesic efficacy. Notably, in the groups given ibuprofen 400 mg and ibuprofen 800 mg, no

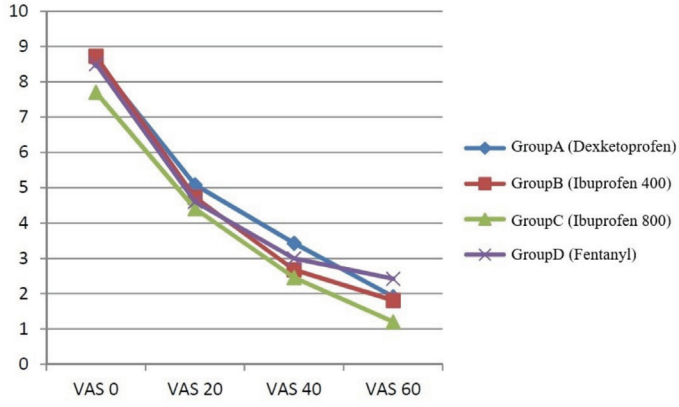

Figure 2. Pain relief efficacy between groups according to the VAS scale

VAS: Visual analog scale

Table 3. Distribution of patients by a given medication

	Medication	Number of patients n (%)
Group A	Dexketoprofen	35 (22.7)
Group B	Ibuprofen 400	37 (24.0)
Group C	Ibuprofen 800	44 (28.6)
Group D	Fentanyl	38 (24.7)
	Total	154 (100)

significant difference could be found in pain relief, although the drug dose was twice as high.

In terms of FLACC scoring, although it was not statistically significant, faster pain relief was found in Groups A and Group C in the first 20 min. In Group D, the pain relief activity at the 20th min was observed to be at the lowest. No similar situation was found for VAS scoring.

Additional treatment was needed in 9.1% of the patients who received treatment. Mild dizziness was observed after treatment in 1.3% of the patients included in the study, and no treatment was required. No statistically significant difference was found between the treatment given to the patients and the need for additional treatment (p=0.578).

Discussion

Renal colic is a disease frequently seen in emergency departments and is characterized by severe pain. There are many studies in the literature on pain management in patients with renal colic.

In our study, the most common complaint of the patients at the time of admission was flank pain (94.8%), which is consistent with the literature (14,15).

Defense, rebound, and rigidity can be detected in the abdominal examination. Nausea and vomiting occur in about half of the patients. Most patients have CVAT. Hematuria is present in 80% of patients, but it is obvious in only one-third. Upper ureteral stones may cause flank pain, and middle ureteral stones may cause pain that radiates to the lower abdominal quadrants (16). In middle ureter stones, the patient's clinic may be confused with appendicitis on the right and diverticulitis on the left. As the stones approach the bladder, signs of irritative micturition may be seen. Abdominal pain lasting less than 12 h, flank pain or costovertebral angle tenderness, and hematuria (>10 erythrocytes) are the most important findings of acute renal colic (17).

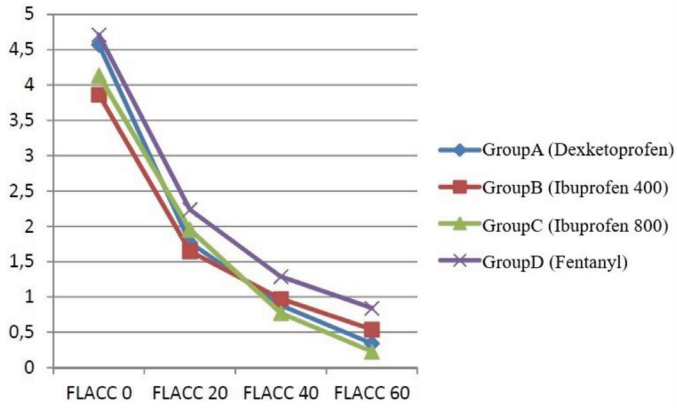

Figure 3. Pain relief efficacy between groups according to the FLACC scale

In the study published by Pathan et al. (18) in 2016, CVAT was found to be positive in 68.1% of the patients. In the study by Duran et al. (15) in 2014, 80.5% of the patients were found to be positive for CVAT. Similarly, our study detected unilateral or bilateral positive CVAT in 87.7% of the patients. In 79.9% of the patients, CVAT was positive unilaterally. The presence of unilateral CVAT positivity in patients who applied to the emergency department with the complaint of flank pain can be evaluated as an examination finding that strengthens the diagnosis of renal colic.

Considering the studies comparing drug efficacy in patients treated with renal colic, Serinken et al. (19) reported that there was no statistically significant difference in the pain relief effectiveness of both drugs in their 2012 study in which they compared the pain relief effects of morphine and acetaminophen on renal colic. In a similar study by Azizkhani et al. (20) in 2014, the analgesic effectiveness of morphine was found to be significantly higher than acetaminophen. Pathan et al. (18) in 2016 compared the pain efficacy of diclofenac, morphine, and acetaminophen on renal colic and concluded that the analgesic efficacy of NSAIDs was significantly higher than morphine. Masoumi et al. (21) reported in 2014 that acetaminophen was more effective in renal colic pain than morphine. Cevik et al. (10) in 2011 compared the effects of IV forms of tenoxicam, lornoxicam, and dexketoprofen on renal colic pain, and no significant difference was found in terms of pain effectiveness in all 3 drug groups. In a systematic review published in 2022 suggested that dexketoprofen has a similar pain relief effect compared to lidocaine and dexmedetomidine but is more potent than acetaminophen (22). Another systematic review and meta-analysis report that there is no significant difference between various NSAIDs, opioids, ketamine, and lidocaine in terms of pain relief (23). In 2018, Cenker et al. (7) compared the pain efficacy of 800 mg IV ibuprofen and 1000 mg IV acetaminophen in renal colic using VAS at the 15th and 30th min and reported that ibuprofen provided significantly more effective analgesia in both groups. A randomized double-blind study compared the analgesic effects of IV ibuprofen and IV tenoxicam in patients with acute musculoskeletal pain due to ankle injury. VAS scores were recorded at 15, 30, 60 and 120 minutes, and in conclusion, both drugs provided equal pain relief (24). In the study by Forouzanfar et al. (1) in 2019, 800 mg IV ibuprofen and 30 mg IV ketorolac were given to patients with renal colic pain, and it was determined that the pain relief effectiveness of ibuprofen was more effective than ketorolac at the 30th and 60th minutes. A randomized double-blind study compared the analgesic effects

of IV ibuprofen plus morphine, IV ketorolac plus morphine and morphine alone in patients with acute renal colic. VAS scores were recorded at 15, 30, 60 and 120 minutes, and in conclusion, both ibuprofen plus morphine and ketorolac plus morphine provided similar pain relief but better than morphine alone (4). In a study by Imamoglu et al. (2) in 2017 on 125 patients, the effects of IV fentanyl and nebulized fentanyl on VAS and verbal pain scale (VPS) at 15th and 30th min were compared, and no significant difference was found. In the study by Zamanian et al. (8), published in 2016, on 158 patients, suppository forms of morphine, an opiate analgesic, and indomethacin, an NSAID, were compared in terms of pain relief in renal colic, using VPS at the 20th, 40th, 60th, and 90th minutes. The pain relief effectiveness of morphine at the 20th min was statistically significant, but no significant difference was found at the 40th, 60th, and 90th minutes. In our study, no statistically significant difference was found in terms of VAS scores at the 20th, 40th and 60th minutes in the pain relief activities of the four groups, which is consistent with the literature. Additionally, no statistically significant difference was found between the pain relief activities of the four groups at the 20th, 40th and 60th minutes in terms of FLACC scoring. In our literature search, no study was found in which the FLACC pain scale was used in renal colic.

In our study, no statistically significant results were obtained in terms of the need for additional medication, medication given, gender, CVAT localization, or history of renal colic, which was consistent with the literature. Similar results are also observed in studies in the literature. This shows that the demographic characteristics of the patients do not affect the requirement for additional medication. The fact that there is no statistically significant difference between the pain relievers given in terms of analgesic effectiveness may result in the absence of a significant difference in terms of the need for additional medication.

Study Limitations

Our study had some limitations. Only the patients who presented to the emergency department with flank pain and whose radiological diagnosis of urolithiasis was confirmed were included in the study. Patients whose diagnosis was not confirmed radiologically could also be evaluated in another group, and the analgesic efficacy of medications could be compared. In our study, the patients were followed for 60 min after analgesia was given, and after the 60th minute, the patients were not followed up in terms of pain relief effectiveness. In our study, to minimize the placebo effect, the colour, odor, and volume of the medications were the same. All medications were given as IV infusions over the same period. Administration of different analgesics at different times or in different ways (intramuscular, inhaler, etc.) was not preferred since it would affect the absorption volume and absorption time of the medication. Studies with larger patient samples comparing different opioids and NSAIDs are needed for safe analgesia choices for treating renal colic.

Conclusion

NSAIDs cause fewer side effects than opioid analgesics and do not have addictive effects. It is seen that the pain relief efficacy and speed are the same as opioid analgesics. There are different treatment methods in the literature for treating renal colic pain. It is possible to find studies on the administration of different analgesics at different doses or in different ways. As seen in our study, different analgesics or different doses of the same analgesic do not make a significant difference for treating renal colic pain. Almost all drugs used for treating renal colic provide effective and rapid analgesia. Considering the patient's medical history, the analgesic to be chosen for treating renal colic pain should be the most comfortable treatment with the least side effects.

Ethics

Ethics Committee Approval: The study was approved by the Kafkas University Faculty of Medicine of Local Ethics Committee (no: 01, date: 27.01.2016).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.Ö., G.Ç., H.Ç., E.G., Concept: G.Ç., M.B., Design: G.Ç., M.B., Data Collection or Processing: M.Ö., G.Ç., H.Ç., E.G., Analysis or Interpretation: M.Ö., G.Ç., M.B., Literature Search: M.Ö., H.Ç., Writing: M.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2022.21549
Eurasian J Emerg Med. 2023;22(1): 24-7

The Incidence of Thrombocytopenia and Its Association with Mortality in Patients with Sepsis Followed in Intensive Care Unit

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Abstract

Aim: Thrombocytopenia is common in intensive care units (ICU) and is associated with high mortality. The aim of this study aimed to determine the incidence of thrombocytopenia in patients diagnosed with sepsis and its relationship with mortality and morbidity.

Materials and Methods: This study was conducted in the reanimation ICU of a university hospital. Patients followed and diagnosed with sepsis between January 2014 and January 2018 were collected and the recorded data analyzed retrospectively. Demographic data, comorbidities, disease severity scores, hematological laboratory values, and outcome were recorded. Thrombocytopenia was defined as the platelet count to be less than $100x10^3/\mu L$. Patients were divided into two groups as with or without thrombocytopenia, and statistical analysis was performed.

Results: The number of patients followed with the diagnosis of sepsis was 299. The median age of the patients was 68 years, and 62.9% (n=188) was male. The rate of invasive mechanical ventilation was 97.7%. Thrombocytopenia was detected in 36.8% of the patients. The Sequential Organ Failure Assessment score was higher in the thrombocytopenia group ($p<0.0001$). Additionally, the rate of acute renal failure was 24.1%, which was higher in the thrombocytopenia group ($p=0.011$). In the thrombocytopenia group, the blood product transfusion rates were higher ($p=0.004$). Median ICU hospitalization time was 15 (6-28) days. While the total mortality of sepsis patients was 43.1%, this rate was higher in the thrombocytopenia group ($p=0.011$).

Conclusion: Thrombocytopenia, which is commonly seen in ICU's and especially in the septic patients, is thought to be associated with mortality and morbidity.

Keywords: Thrombocytopenia, sepsis, intensive care unit, mortality, morbidity

Introduction

Thrombocytopenia was defined as the platelet count to be less than $100x10^3/\mu L$ (1) and is common in intensive care units (ICUs) and closely associated with high mortality. Sometimes, thrombocytopenia may occur due to sepsis. Sepsis is a life-threatening organ dysfunction induced by a dysregulated host response. In septic shock, there is circulatory and cellular metabolic dysfunction (2). The relationship between sepsis-septic shock and thrombocytopenia is known, but the mechanism of thrombocytopenia in sepsis is still unclear (3). This study aimed to determine the incidence of thrombocytopenia in patients with sepsis in the ICU and its relationship with mortality and morbidity.

Materials and Methods

This study was conducted in the Anesthesiology and Reanimation ICU of a university hospital. Between January 2014 and January 2018, the data collected from sepsis patients in the ICU were analyzed retrospectively. Demographic data, comorbidities, disease severity scores, some laboratory values, including platelet values, and intensive care results were recorded.

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Cite this article as: Bayraktar YŞ, Açıkgöz A, Eyiol H, Bayram HH, Kara İ, Duman A, Çelik J. The Incidence of Thrombocytopenia and Its Association with Mortality in Patients with Sepsis Followed in Intensive Care Unit. Eurasian J Emerg Med. 2023;22(1): 24-7.

Received: 06.07.2022
Accepted: 13.10.2022

Thrombocytopenia was defined as the platelet count to be less than 100x10^3/μL. Then, patients were then divided into two groups with or without thrombocytopenia and statistical analysis was performed.

Statistical Analysis

Data were statistically evaluated using the Statistical Package for the Social Sciences (SPSS) version 22 (SPSS Inc., Chicago, IL, USA) program. Descriptive statistics were performed on the patient group; numerical data were indicated as median (interquartile range), and categorical data as percentages. Later, the patients were divided into two groups as those with and without thrombocytopenia; the characteristics of the patients were compared using the chi-square test for categorical data and the Mann-Whitney U test for numerical data. Logistic regression was applied to find independent risk factors that determine mortality. A p value <0.05 was considered statistically significant.

Results

In this period, the number of patients followed with the diagnosis of sepsis in the ICU was 299. The median age of the patients was 68 (52-77) years, and 62.9% (n=188) was male. The rate of invasive mechanical ventilation was 97.7%. Thrombocytopenia was detected in 36.8% of sepsis patients. The Sequential Organ Failure Assessment (SOFA) score was higher in the thrombocytopenia group (p<0.0001). The rate of acute renal failure was 24.1%, and this rate was higher in the thrombocytopenia group (p=0.011). The blood product transfusion rates were higher in the thrombocytopenia group (76.4% vs. 59.3% and p=0.004). White blood cell (p=0.028), procalcitonin (p=0.001), and lactate (p=0.002) levels were significantly higher in the thrombocytopenia group. Median ICU hospitalization time was 15 (6-28) days. While the total mortality of sepsis patients was 43.1%, this rate was higher in the thrombocytopenia group (p=0.011) (Table 1).

Data that were significant in univariate analysis (acute renal failure, blood transfusion, platelets, white blood cell, procalcitonin and lactate) were evaluated in multivariate analysis. The high SOFA score and the development of acute renal failure were independent risk factors for mortality [p=0.001, Odds ratio (OR): 1.139, 95% confidence interval (CI): 1.058-1.226 and p=0.001, OR: 2.704, 95% CI: 1.541-4.743, respectively] (Table 2).

Discussion

In this retrospective study, 299 patients with sepsis were admitted to the ICU between 2014 and 2018 were evaluated. Local Ethics Committee approval was taken from the Selçuk University Ethics Committee (no: 2019/02, date: 20.03.2019). The development of thrombocytopenia in sepsis is well known. At the same time, the presence of changes in platelet counts is a common clinical condition in ICU. In a previous review, the incidence of thrombocytopenia was found to be 8.3-67.6% in ICUs (4). 20-50% of patients with sepsis in the ICUs suffer from thrombocytopenia (5-8). The differences in the incidence of thrombocytopenia may be due to differences in the definition of thrombocytopenia

Table 1. Patient features and laboratory parameters

	Total patients n=299 (100%)	**Thrombocytopenia group n=110 (36.8%)**	**Non-thrombocytopenia group n=189 (63.2%)**	**p value**
Age (year)	68 (52-77)	68 (54.7-78)	67 (48-77)	0.382
Gender (male)	188 (62.9%)	67 (60.9%)	121 (64%)	0.234
APACHE 2 score	23 (17-28)	24 (19-29)	22 (16-26)	0.156
SOFA score	10 (8-13)	13 (11-14)	10 (7-11)	**<0.0001**
Mechanical ventilation	292 (97.7%)	108 (98.2%)	184 (97.4%)	1.000
Acute renal failure	72 (24.1%)	36 (32.7%)	36 (19%)	**0.011**
Blood transfusion	196 (65.6%)	84 (76.4%)	112 (59.3%)	**0.004**
Laboratory parameters				
Platelets (x10^3/μL)	130 (73-193)	49.5 (31.5-80)	170 (135-230)	**<0.0001**
Hemoglobin (g/dL)	8.7 (7.2-10.5)	8.4 (7-10)	8.7 (7.5-11)	0.059
White blood cell (x10^3/L)	18 (13-27)	20.3 (14-30)	16.7 (12.6-25)	**0.028**
Procalcitonin (ng/mL)	4.5 (1.1-19.09)	9.8 (2.07-31.9)	3.3 (1-15.2)	**0.001**
Lactate (mEq/L)	4.4 (3-8.6)	4.8 (3.4-9.8)	3.8 (3-6.8)	**0.002**
Length of ICU stay (days)	15 (6-28)	16 (7-28)	15 (6-29)	0.774
Mortality	129 (43.1%)	58 (52.7%)	71 (37.6%)	**0.011**

APACHE 2: Acute Physiologic Assessment and Chronic Health Evaluation 2, SOFA: Sequential Organ Failure Assessment, ICU: Intensive care units

(9). Some studies defined thrombocytopenia as a platelet count of <100x10^3/µL and reported that the incidence was 33-36% (10,11). However, a previous study defined thrombocytopenia as a platelet count of <150x10^3/µL and found that the incidence was 47.6% (9). In our study, thrombocytopenia was defined as the platelet count to be less than 100x10^3/µL and found that the incidence of thrombocytopenia was 36.8%.

Several factors are responsible for tubular lesions in sepsis -related acute kidney injury (AKI), such as metabolic changes, mitochondrial dysfunction, autophagy, and cell cycle arrest (12-15). Additionally, the role of immune response pathways and particularly inflammation in AKI progression is increasingly stressed (16,17). Platelets can also be activated by ischemic blood flow disturbances in the septic kidney, and the rate of acute renal failure was found to be higher in patients with thrombocytopenia (3). In our study, the rate of acute renal failure was 32.7%. Patients with sepsis are prone to the propagation of homeostasis, thrombosis, and bleeding disorders due to injured endothelium (18,19). It is important to know that critically ill patients with thrombocytopenia are prone to bleeding. Various studies have found that patients with thrombocytopenia were more likely to develop major bleeding and received more blood product transfusions (9). In our study, we found that the blood product transfusion rate was higher in the thrombocytopenic group. Because thrombocytopenia causes many undesirable events, patients with thrombocytopenia can be expected to have a longer hospital stay. In our study, the median ICU hospitalization time was 15 (6-28) days, but there was no significance between the two groups (p=0.774).

It is shown that thrombocytopenia is associated with poor outcome (4,9,20-23). Platelets are central to coagulation metabolism. Therefore, thrombocytopenia may cause bleeding and/or the need for more blood transfusions. Additionally, platelets contribute to vascular and tissue injury in acute or chronic inflammation (24-26). Many previous studies have show that thrombocytopenia is an independent risk factor for mortality in ICU patients and sepsis was found to be the most common risk factor for thrombocytopenia (27-30). There are several studies on the mortality of patients with thrombocytopenia in ICUs. Strauss et al. (31) found that thrombocytopenia alone was not a predictor of mortality. In another study found that ICU mortality increased significantly when the initial platelet count was less than 50x10^3/µL (32). Venkata et al. (9) found that thrombocytopenia was associated with a high mortality rate. In a previous study, the overall mortality was found to be 42.5% (33). In our study, we found that overall mortality was 43.1%, which was higher than the non-thrombocytopenic group (p=0.011).

Table 2. Logistic regression

Parameters	p value	OR (95% CI)
SOFA score	0.001	1.139 (1.058-1.226)
Acute renal failure	0.001	2.704 (1.541-4.743)

SOFA: Sequential Organ Failure Assessment, OR: Odds ratio, CI: Confidence interval

Study Limitations

There were several limitations to our study. First, this study was a retrospective, single-center study. Second, we did not differentiate sepsis and septic shock. Finally, we evaluated overall mortality not as early and/or long-term mortality.

Conclusion

Thrombocytopenia, which is commonly seen in ICUs and particularly in the sepsis patient group, is thought to be associated with mortality and morbidity.

Ethics

Ethics Committee Approval: The study was approved by the Selçuk University of Local Ethics Committee (no: 2019/02, date: 20.03.2019).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Y.Ş.B., İ.K., J.Ç., Concept: A.D., J.Ç., Design: İ.K., A.D., Data Collection or Processing: Y.Ş.B., A.A., H.E., H.H.B., Analysis or Interpretation: İ.K., A.D., Literature Search: Y.Ş.B., A.A., İ.K., Writing: Y.Ş.B., A.A., İ.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2022.02703
Eurasian J Emerg Med. 2023;22(1): 28-33

Effectiveness of OxyMask™ vs. Simple Oxygen Mask Against Chronic Obstructive Pulmonary Disease Exacerbation

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Abstract

Aim: In our study, it was aimed to compare the effectiveness of a diffuser mask (OxyMask™) and a simple nebulizer set oxygen mask on the blood gas values of patients with the diagnosis of chronic obstructive pulmonary disease (COPD) exacerbation who presented to the emergency department.

Materials and Methods: Our research is a prospective, single-blind, randomized controlled study conducted in the Emergency Department of Atatürk University Medical Faculty Hospital. Our study was completed with 213 patients after the exclusion criteria were applied. Of these patients, 93 were administered breathing treatment with a diffuser mask, and 120 were given treatment with a simple nebulizer set oxygen mask.

Results: After the treatment with COPD exacerbation, the SO_2 and PO_2 values of the diffuser mask group were found to be significantly higher than those in the simple oxygen mask group ($p<0.05$). After the treatment, the PCO_2 values of the diffuser mask group were significantly lower than those in the simple oxygen mask group ($p<0.05$). The diffuser mask also reduced the hospitalization rate of the patients.

Conclusion: We suggest that a diffuser mask, which provides better oxygenation in the blood and lowers the carbon dioxide concentration in the blood to a higher extent, can be used in administering breathing treatment to COPD patients with exacerbation who presented to the emergency department with dyspnea.

Keywords: Breathing treatment, chronic obstructive pulmonary disease, diffuser, OxyMask™, simple oxygen mask

Introduction

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease characterized by chronic respiratory symptoms and airflow restrictions in the airways and lung parenchyma, mostly caused by the significant exposure of the airways to hazardous particles and gasses and/or alveolar abnormalities (1). There are 2 groups of risk factors for COPD, genetic risk factors (alpha-1 antitrypsin deficiency) and environmental risk factors (smoking, occupational exposure, air pollution, and infections). The most significant risk factor is active smoking (2).

COPD should be considered a diagnosis in individuals with chronic cough, sputum production, dyspnea complaints, and/or a history of exposure to risk factors, and spirometry is required for diagnosis in these patients. FEV_1/FVC values smaller than 0.70 after bronchodilator therapy in patients with clinically relevant symptoms and exposure to harmful excitants indicated a permanent airflow restriction, and therefore, the presence of COPD (1,3).

COPD exacerbation is defined as an acute increase and worsening in the symptoms of COPD that may require additional treatment (4). COPD exacerbations are usually associated with increased

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Received: 25.08.2022
Accepted: 30.12.2022

Cite this article as: Sanalp Menekşe T, Çakır Z, Menekşe B, Betos Koçak M, Koçak AO. Effectiveness of OxyMask™ vs. Simple Oxygen Mask Against Chronic Obstructive Pulmonary Disease Exacerbation. Eurasian J Emerg Med. 2023;22(1): 28-33.

airway inflammation and increased mucus production (5). Exacerbations are mainly triggered by viral respiratory infections, but factors such as bacterial infections, environmental pollution, and ambient temperature can also trigger or worsen this condition (6).

Beta agonists and anticholinergic drugs are the first choice for treating COPD-exacerbated patients admitted to the emergency department. Oxygen therapy and the types of masks used while administering these drugs are critical for the effectiveness of the treatment. The diffuser mask is a face mask that delivers oxygen to the mouth and nose through a small diffuser. With the low current passing through the jet inside, a high concentration of oxygen is provided. Owing to the small holes on it, carbon dioxide trapping is reduced to a minimum (7). In this study, the effectiveness of a diffuser mask and a simple oxygen mask with a chamber in patients with COPD who applied to the emergency department with shortness of breath will be evaluated objectively by blood gas values. In this way, it will be evaluated which treatment method is effective for the patients.

Materials and Methods

Our study was approved by the Atatürk University Faculty of Medicine Clinical Research Ethics Committee (decision number: 08-11, date: 26.12.2019). The patients participating in this study signed an informed consent form. This is a single-blind, randomized-controlled study conducted in the Emergency Department of Atatürk University Faculty of Medicine Hospital between 01.01.2020 and 31.05.2020. Patients with a diagnosis of COPD who presented to the Emergency Department of Atatürk University Faculty of Medicine Hospital with complaints of dyspnea and displayed signs of COPD exacerbation according to the 2020 Global Initiative for Obstructive Lung Disease (GOLD) COPD guidelines were included in this study.

Patients who were older than 18 years, diagnosed with COPD, had an exacerbation of COPD (according to the GOLD 2020 COPD guidelines), and volunteered to participate in the study were included in the study. Patients who did not volunteer to participate in the study, patients younger than 18 years, pregnant patients, patients with mental deficiencies, uncooperative patients, patients with anatomical barriers to wearing masks, patients with shortness of breath after trauma, and patients with unexpected comorbidities or exitus during the study were excluded.

Two hundred and sixty patients with COPD who presented to the Emergency Department of Atatürk University Faculty of Medicine Hospital with complaints of dyspnea and were diagnosed with COPD exacerbation were screened as potential participants. They were divided into two groups: 130 patients treated with a simple nebulizer set oxygen mask (group 1) and 130 patients treated with a diffuser mask (group 2). For various reasons, 10 patients in group 1 and 37 patients in group 2 could incomplete the study. The study was completed with 120 patients in group 1 and 93 patients in group 2, constituting 213 patients.

Two hundred and thirteen patients were divided into two groups: 93 patients treated with a diffuser mask (OxyMask™, Southmedic Inc, Canada) (Figures 1, 2, 3) and 120 patients treated with a simple nebulizer set oxygen mask (nebulizer set mask®, CGR Medical) with the same pharmacological agents. Beta agonist and anticholinergic treatment as inhaler treatment (Iprasal® 0.5+2.5 mg/2.5 mL) was administered. During the treatment of COPD exacerbation, a diffuser mask was used in one group, and a simple nebulizer set oxygen mask was used in the other group. Arterial blood samples taken from the patients before and after their COPD exacerbation treatments were compared in terms of their blood gas values. Among the blood gas parameters, the values of pH, SO_2, carboxyhemoglobin (COHb), MetHb, lactate, HCO_3, SBE, PCO_2, and PO_2 were evaluated. Additionally, the demographic characteristics of the patients and their values, including vital signs, chronic diseases, hospitalization status (determined according to the GOLD 2020 COPD guidelines), a type of mask used during COPD exacerbation treatment, symptom onset time, history of smoking, biomass exposure history, and whether they used an oxygen concentrator at home were recorded (Table 1).

Statistical Analysis

The IBM Statistical Package for the Social Sciences 20.0 statistical analysis program was used to analyze the data. The data are

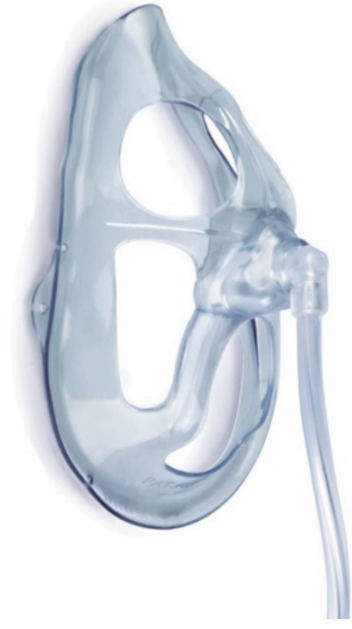

Figure 1. Diffuser mask (OxyMask™, Southmedic Inc, Canada)

presented with mean, standard deviation, median, minimum, maximum, percentage, and frequency values. According to the Kolmogorov-Smirnov test results, the data were normally distributed. Then, the numeric variables were analyzed by paired-samples t-test, and the categorical variables were analyzed with Pearson's chi-squared test. A p value of <0.05 was considered significant for all the statistical analysis results.

Results

Two hundred-thirteen patients who met the criteria were included in the study. Of the patients participating in our study, 65.7% (n=140) were male and 34.3% (n=73) were female. Patients were divided into two groups as patients who used simple chamber oxygen masks for treating attacks (group 1, n=120) and patients who used diffuser masks (group 2, n=93). The mean age of all patients participating in the study was 64.39±8.9 years. The mean age of the patients in group 1 was 63.95±8.46 years, of which 61.7% (n=74) were male and 38.3% (n=46) were female. The mean age of the patients in group 2 was 64.96±9.37 years, of which 71% (n=66) were male and 29% (n=27) were female. The statistical results of the groups using a diffuser mask and a simple chambered oxygen mask, except for blood gas, are shown in Table 1.

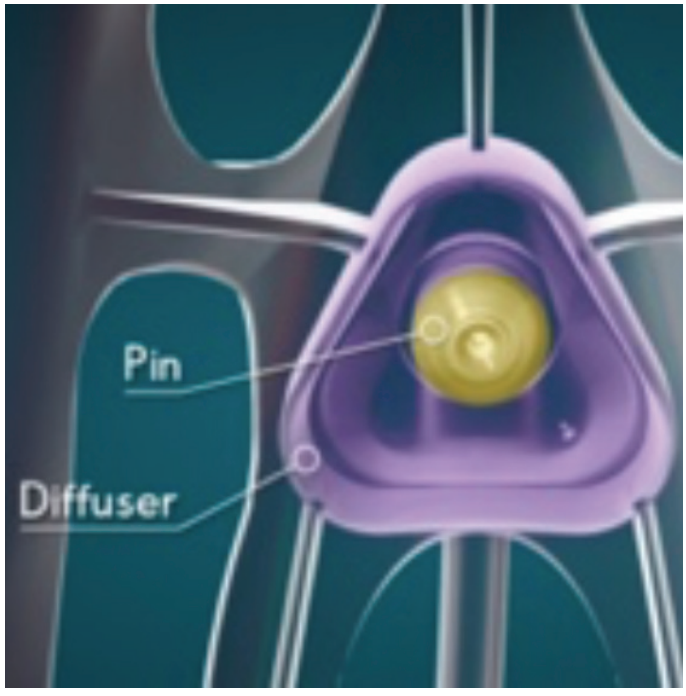

Figure 2. Diffuser mask pin and diffuser technology

While 75.1% of all patients participating in the study had a history of home oxygen concentrator use, 24.9% of them did not use oxygen concentrators at home. When the hospitalization status of all patients after COPD attack treatment was examined, it was found that 32.9% (n=70) were hospitalized and 67.1% (n=143) were discharged from the emergency department. The mean age of the patients who were admitted to the clinic was found to be 4.02 years higher than the mean age of the patients who were discharged from the emergency department with COPD attack treatment. When the patients who used a diffuser mask were admitted to the clinic after COPD attack treatment, it was seen that 22.5% (n=21) were hospitalized and 77.5% (n=72) did not need to be admitted to the clinic. When the hospitalization status of the patients who used a simple oxygen mask with a chamber was examined after COPD attack treatment, it was seen that 40.8% (n=49) were hospitalized and 59.2% (n=71) did not need to be hospitalized. The most common comorbidity was hypertension (38%). Subsequently, she had a history of diabetes mellitus (30.5%), congestive heart failure (17.8%),

Table 1. Statistical results of the parameters, except for blood gas, of the groups using diffuser mask and simple oxygen mask with chamber

	Group 1	Group 2	p
Gender (male/female)	74/46	66/27	0.190
Age	63.95 (8.46)	64.96 (9.37)	0.412
Complaint start time (hours)	44.74	44.98	0.969
Duration of smoking (pack-years)	41.29 (33.36)	38.14 (37.38)	0.420
Chronic biomass exposure (%)	37.5	33.3	0.566
Oxygen concentrator usage at home (%)	73.3	76.3	0.638
Systolic blood pressure (mmHg)	134.33 (18.96)	131.65 (20.37)	0.322
Diastolic blood pressure (mmHg)	89.88 (19.20)	91.27 (19.15)	0.599
Fingertip oxygen saturation (%)	76.65	75.53	0.506
Respiratory rate (/min)	21.88	22.35	0.198
Pulse rate (/min)	102.11	100.74	0.536
Body temperature (°C)	37.02	36.93	0.3

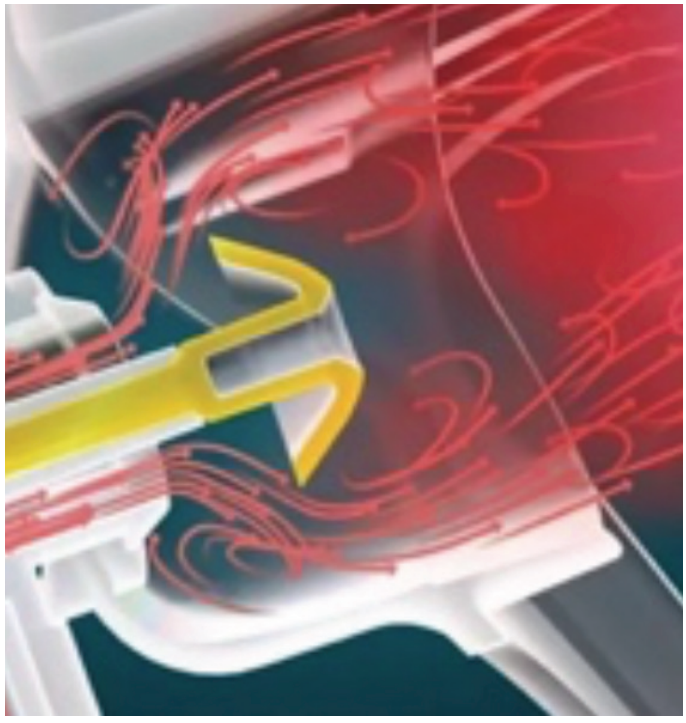

Figure 3. Cork-shaped pin directing the oxygen flow (accessed date: 17.02.2022. Available from: http://thebetteroxygenmask.com/oxymask-technology/)

coronary artery disease (16.9%), chronic kidney disease (8.9%), cancer (8.9%), and cerebrovascular accident (8%).

After COPD exacerbation treatment, 22.5% of the patients in group 2 were admitted to the clinic, whereas 40.8% of the patients in group 1 were admitted to the clinic. The frequency of hospitalization in group 2 was significantly lower than that in group 1 ($p<0.05$).

Having compared the parameters in the arterial blood gas analyses of the patients in groups 1 and 2, after the COPD exacerbation treatments, the SO_2 values in group 2 were found significantly higher compared with those in group 1 ($p<0.05$), the PO_2 values in group 2 were significantly higher than those in group 1 ($p<0.05$), and the PCO_2 values in group 2 were significantly lower compared with those in group 1 ($p<0.05$) (Table 2).

Discussion

COPD is a disease that progress with exacerbations and whose emergency applications are frequently seen. While effective treatment improves the prognosis of the disease, it will decrease the hospitalization rates and the frequency of admission (8). A retrospective study was conducted by Russell et al. (9) on 537 patients who presented to the emergency department with a

Table 2. Statistical results of the blood gas parameters of the groups using diffuser mask and simple oxygen mask with chamber

	Group 1 average	Group 2 average	p
	Before COPD attack treatment		
pH	7.401	7.398	0.706
SO_2 (%)	76.973	77.313	0.855
COHb (%)	2.601	2.831	0.259
MetHb (%)	1.553	1.494	0.292
Lactate (mmol/L)	2.293	2.367	0.755
HCO_3 (mmol/L)	25.394	24.453	0.191
SBE (mmol/L)	1.678	0.544	0.327
PCO_2 (mmHg)	42.169	41.355	0.567
PO_2 (mmHg)	50.338	50.727	0.844
	After COPD attack treatment		
pH	7.392	7.398	0.502
SO_2 (%)	83.278	87.30	0.010*
COHb (%)	2.523	2.840	0.092
MetHb (%)	1.498	1.613	0.462
Lactate (mmol/L)	2.040	1.869	0.291
HCO_3 (mmol/L)	25.317	24.539	0.236
SBE (mmol/L)	0.878	0.322	0.381
PCO_2 (mmHg)	43.496	40.346	0.024*
PO_2 (mmHg)	57.406	61.856	0.020*

*Data that were found statistically significant at the $p<0.05$ level.
COPD: Chronic obstructive pulmonary disease, SBE: Standard base excess, COHb: Carboxyhemoglobin

COPD exacerbation. Of these patients, 57% were hospitalized for COPD exacerbation, and 43% were treated in the emergency department and discharged. Additionally, it was observed that the average age of the patients who were hospitalized was 2.4 years higher than the average age of the patients treated in the emergency department. In our study, 32.9% of the patients were hospitalized due to COPD exacerbation, and 67.1% were treated in the emergency department and discharged. Similarly, it was observed that the average age of the patients who were hospitalized was 4.02 years higher than the average age of the patients treated in the emergency department. This difference was statistically significant ($p<0.05$).

COPD can be associated with many systemic diseases. The most common comorbid diseases in COPD are hypertension, coronary artery disease, and diabetes mellitus. The risk factors in COPD are well known, and if they are controlled in the early period, the natural course of the disease is positively affected (10). In a study by Garcia-Gutierrez et al. (11), 34.6% of 2841 patients had previously used oxygen concentrators at home. In addition to the diagnosis of COPD exacerbation, 21.66% of these patients have diabetes mellitus and 21.6% have cardiac disease. In our study, it was learned from the anamnesis of the patients that 75.1% of the patients had previously used oxygen concentrators at home. It was thought that this situation was due to the better oxygen concentrator supply conditions applied in our country. Additionally, the most common accompanying chronic diseases were hypertension (38%), followed by diabetes mellitus (30.5%) and congestive heart failure (17.8%).

The diffuser mask is an open oxygen mask developed in 2005, which can provide various oxygen concentrations from 24% to 90% between the flowrate values of 1 and 15+ liters per minute. It provides a very high FiO_2, especially in patients with COPD with chronic hypoxemia, and it can be used safely without causing carbon dioxide retention thanks to its diffuser feature. The diffuser mask features innovative technology designed to concentrate and direct the flow of oxygen. The mushroom-shaped pin creates an organized pattern of vortices and a cloud of concentrated oxygen molecules. The triangular diffuser corrects the shape of the oxygen vortices and directs the flow to the patient's nose and mouth (12-14).

In the literature, there are few studies on diffuser masks. In a study by Lamb and Piper (15) in which a non-rebreather mask and a diffuser mask were compared in a laboratory environment, a low flowrate (2 L/min) was provided in one group, and a high flowrate (15 L/min) was provided to the other group. At respiratory rates of 15/min, 20/min, and 24/min in each flow group, the percentages of decrease in the values of $etCO_2$, FiO_2, inspired CO_2 fraction, and CO_2 were compared. As a result, the diffuser mask performed significantly better in each category than the non-rebreather mask. Especially at very low flowrate with the diffuser mask, higher inspiratory oxygen levels, lower inspiratory CO_2 levels, and more efficient CO_2 clearance were achieved. In a single-blind, randomized, crossover study by Beecroft and Hanly (13), 13 of 26 chronic oxygen-dependent patients were treated with oxygen with a venturi mask, and the remaining 13 were treated with a diffuser mask for 60 min. Oxygen flowrate were lower when the diffuser mask was being used, whereas inspired PO_2 values were higher, and expired PO_2 values were lower. Thus, the diffuser mask provided a higher PO_2 concentration compared to the venturi mask at a lower flowrate without causing carbon dioxide retention.

Hocagil et al. (16) investigated the COHb lowering capabilities of a diffuser mask and a simple mask used to deliver oxygen therapy in a patient group without an indication for hyperbaric oxygen therapy in carbon monoxide poisoning cases. After their treatments, patients who received oxygen therapy with the diffuser mask had significantly lower COHb (mg/dL) levels [9.6 (5.0) vs. 12.8 (6.2), $p=0.0203$] and higher PaO_2 (mmHg) levels [224.4 (56.5) vs. 183.4 (63.7)] ($p=0.0046$) compared with those in the simple mask group. Iscanli et al. (17) compared the effectiveness of diffuser masks and simple oxygen masks in reducing carbon dioxide levels and increasing peak expiratory flow (PEF) values in patients who presented to the emergency department with asthma and COPD attacks. It was shown to provide a good PEF value for COPD and asthma attacks.

In our study, after the COPD exacerbation treatments of the patients with used diffuser masks and simple nebulizer set oxygen masks, the blood gas analyses results of the patients revealed that the SO_2 values in the diffuser mask group were significantly higher than those in the simple oxygen mask group ($p<0.05$), the PCO_2 values in the diffuser mask group were significantly lower than those in the simple oxygen mask group ($p<0.05$), and the PO_2 values in the diffuser mask group were significantly higher than those in the simple oxygen mask group ($p<0.05$).

In the literature review conducted for this study, it was seen that the number of studies on the use of diffuser masks in patients with COPD was limited, and the patient populations of the available studies were also small. Likewise, most studies conducted with diffuser masks were those performed under simulation in a laboratory environment. The fact that our study was conducted with a large population and real patients differs from other studies.

Study Limitations

There may be some possible limitations in this study. The main limitation of our study is that it is single-centered. Additionally,

our study does not show a homogeneous distribution in terms of gender, socioeconomic level, and education levels.

Conclusion

In our study, the diffuser mask significantly increased SO_2 and PO_2 values and significantly reduced PCO_2 values compared to the simple nebulizer set oxygen mask. It was determined that the patients who received COPD exacerbation treatment with a diffuser mask were discharged more frequently and hospitalized less frequently. Consequently, we suggest that the diffuser mask can be used as a successful adjunctive therapy method for treating patients with acute exacerbation of COPD who presented to the emergency department with dyspnea, considering its advantages such as high patient compliance.

Ethics

Ethics Committee Approval: The study was approved by the Atatürk University Faculty of Medicine of Clinical Research Ethics Committee (decision number: 08-11, date: 26.12.2019).

Informed Consent: The patients participating in this study signed an informed consent form.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.S.M., A.O.K., Concept: T.S.M., Z.Ç., M.B.K., Design: T.S.M., Z.Ç., Data Collection or Processing: T.S.M., Z.Ç., Analysis or Interpretation: T.S.M., B.M., Literature Search: T.S.M., B.M., Writing: T.S.M., M.B.K., A.O.K.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2023.68542
Eurasian J Emerg Med. 2023;22(1): 34-40

The Impact of the COVID-19 Pandemic on Emergency Surgical Operations in State Hospitals in Turkey: A Retrospective and Descriptive Study

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Abstract

Aim: Emergency surgery can be defined as surgical interventions and operations necessary to deal with an acute threat to life, organ, limb, or tissue. Our study examined the impact of the Coronavirus disease-2019 (COVID-19) pandemic on emergency surgical operations (ESOs) performed in state hospitals in Turkey.

Materials and Methods: In this national, retrospective, and descriptive study, ESOs performed in 2nd and 3rd-level state hospitals in Turkey in 2021 were recorded for the study. ESOs performed in 2019 were taken as the control group, and the changes between the two groups were examined.

Results: A total of 1,822,075 ESOs were included in the analysis. There was a 7.6% decrease in ESOs in 2021 compared to 2019. In both 2019 and 2021, cesarean section, surgical treatment of upper/lower extremity fractures and dislocations, and cholecystectomy were the most frequently performed ESOs. An increase in the number of ESOs in 2021 compared to 2019 was observed only in the urology department (7.1%) and orthopedics and traumatology department (2.7%). The surgical departments with the greatest decreases were neurosurgery (-28.1%), Otolaryngology-Head and Neck Surgery (-27.7%), and thoracic surgery (-20.9%)

Conclusion: During the COVID-19 pandemic, the number of ESOs performed in the 2nd and 3rd-level state hospitals in Turkey decreased compared with the previous year.

Keywords: Emergency surgery, emergency department, cesarean section, cholecystectomy, COVID-19

Introduction

Emergency surgical operation (ESO) can be defined as surgery needed to deal with an acute threat to life, tissue, limb, or organ caused by an acute disease process, trauma, complication of an interventional or surgical procedure, or acute exacerbation of a chronic disease process (1). Patients undergoing ESOs risk higher mortality and morbidity than elective operations due to the limited preoperative anesthesia preparation time (2-4). In developing countries, perioperative cardiac arrest rates range from 2.99 to 40.4 per 10,000 (5,6). The rate of perioperative cardiac arrest is higher in ESO patients, ranging from 6.48 to 62.1 per 10,000 (7,8). Two studies reported that 50-60% of all cardiac arrest episodes in surgical patients occurred in patients undergoing emergency surgery (9,10).

Declared a pandemic by the World Health Organization (WHO) in March 2020, the COVID-19 and its indirect effects had negative consequences on health systems and the habits of patients (11-13). The number of examinations in Turkey's 2nd and 3rd-level state hospitals, which exceeded 321 million in 2019, decreased to approximately 205 million in 2020 (14). Decreased emergency department (ED) visits, including critically ill patients, have been reported during the pandemic period (11). There have also been delays in accepting and treating surgical emergencies (12,13). During the pandemic period, a significant decrease was observed

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Cite this article as: Beştemir A, Aydın H, Tuncar A. The Impact of the COVID-19 Pandemic on Emergency Surgical Operations in State Hospitals in Turkey: A Retrospective and Descriptive Study. Eurasian J Emerg Med. 2023;22(1): 34-40.

Received: 01.09.2022
Accepted: 18.01.2023

in blood transfusions along with a decrease in the hospital admissions and a decrease in the number of surgical operations (15). This study examines the effects of the COVID-19 pandemic on the number of ESOs performed in state hospitals and their distribution by clinics throughout Turkey. It also provides a perspective for similar outbreaks we may encounter in the coming years.

Materials and Methods

In this retrospective, descriptive, observational study, ESOs performed in 2nd and 3rd-level state hospitals in Turkey in 2019 and 2021 were discussed. The number of ESOs performed by general surgery, orthopedics and traumatology, thoracic surgery, neurosurgery, cardiovascular surgery, plastic surgery, urology, ophthalmology, gynecology and obstetrics, and otolaryngology departments in Turkey in 2021 and the distribution according to surgical departments was recorded in the study form. ESOs performed in 2019 were taken as the control group. The same ESOs were recorded for the control group. The changes between the two groups were calculated. The primary outcome of this study was ESOs performed throughout Turkey in 2021 (pandemic period). The secondary outcome was to compare the 2021 data with the 2019 (pre-pandemic period) data.

Statistical Analysis

In this descriptive study, data were presented as number and percentages. The number and rates of surgical treatments included in the study and the changes over the years are summarized in Table 1. The distribution of ESOs according to departments is presented in Table 2. The changes in the number of ESOs performed in the departments in 2021 compared to 2019 are presented in Figure 1.

Table 1. Distribution of emergency surgical operations performed in public hospitals in Turkey in 2019 and 2021

Emergency surgical operations	Year 2019 n (%)	Year 2021 n (%)	Diff. * n (%)
Otolaryngology-Head and Neck Surgery			
Repair of facial bone fractures	3055 (0.32)	2320 (0.27)	-24.06
Repair of nasal/septal fracture or perforation	19883 (2.10)	12402 (1.42)	-37.63
External auditory canal or nose foreign body removal, surgical	21614 (2.28)	17501 (2.00)	-19.03
Surgical drainage of parotid abscess	1052 (0.11)	743 (0.08)	-29.37
Ophthalmology			
Repair of eye or eyelid injuries	12567 (1.33)	11086 (1.27)	-11.78
Intraocular foreign bodies removal	334 (0.04)	277 (0.03)	-17.07
Retinal detachment surgery	311 (0.03)	332 (0.04)	6.75
Thoracic Surgery			
Rib fracture/sternum fracture, surgical stabilization	991 (0.10)	577 (0.07)	-41.78
Thoracotomy, foreign body removal, or bleeding control	1085 (0.11)	1066 (0.12)	-1.75
Cardiovascular Surgery			
Pericardiocentesis, pericardiotomy, or pericardial window opening	1807 (0.19)	1777 (0.20)	-1.66
Heart repair after injury	426 (0.04)	362 (0.04)	-15.02
Ruptured aortic or/and its branches aneurysm	539 (0.06)	631 (0.07)	17.07
Vascular repair	13410 (1.42)	12256 (1.40)	-8.61
General Surgery			
Intervention for rectus sheath hematoma	77 (0.01)	49 (0.01)	-36.36
Repair of incarcerated/strangulated inguinal hernia	14466 (1.53)	11235 (1.28)	-22.34
Repair of esophageal perforation	70 (0.01)	49 (0.01)	-37.14
Endoscopic removal of foreign bodies	11642 (1.23)	11065 (1.26)	-4.96
Laparotomy for removal of the foreign body	300 (0.03)	300 (0.03)	0
Repair of the perforated stomach or duodenum	4532 (0.48)	4650 (0.53)	2.60
Small bowel perforation, primary suture	4881 (0.52)	4247 (0.49)	-12.99
Ileus and obstruction, surgical treatments	22326 (2.36)	20704 (2.37)	-7.27
Appendectomy	95913 (10.13)	86076 (9.84)	-10.26

Table 1. Continued

Emergency surgical operations	Year 2019 n (%)	Year 2021 n (%)	Diff. * n (%)
Colon perforation, primary suture	2834 (0.30)	2480 (0.28)	-12.49
Sigmoid volvulus reduction	105 (0.01)	113 (0.01)	7.62
Drainage of abscess in the biliary system or liver	235 (0.02)	179 (0.02)	-23.83
Liver/gallbladder injuries, primary suture	1269 (0.13)	1121 (0.13)	-11.66
Cholecystectomy	129719 (13.70)	97268 (11.12)	-25.02
Acute pancreatitis. debridement, drainage	100 (0.01)	77 (0.01)	-23.00
Interventions for pancreatic injuries	85 (0.01)	72 (0.01)	-15.29
Splenectomy	2241 (0.24)	2007 (0.23)	-10.44
Urology			
Fournier's gangrene: surgical debridement	3887 (0.41)	4185 (0.48)	7.67
Repair of traumatic kidney rupture	48 (0.01)	45 (0.01)	-6.25
Repair of bladder perforation	1143 (0.12)	1131 (0.13)	-1.05
Repair of penile fracture	340 (0.04)	332 (0.04)	-2.35
Repair of urethral injury	73 (0.01)	100 (0.01)	36.99
Testicular detorsion	1679 (0.18)	1889 (0.22)	12.51
Obstetrics and Gynecology			
Cesarean section	271921 (28.71)	265933 (30.39)	-2.20
Ectopic pregnancy operation	1898 (0.20)	2157 (0.25)	13.65
Ovarian detorsion-cyst excision	18680 (1.97)	16449 (1.88)	-11.94
Repair of uterine perforation	442 (0.05)	699 (0.08)	58.14
Neurosurgery			
Epidural/subdural hematoma drainage	7453 (0.79)	6815 (0.78)	-8.56
Surgical management of depressed cranial fractures	921 (0.10)	731 (0.08)	-20.6
Surgical treatment of spinal fracture-dislocations	6730 (0.71)	3312 (0.38)	-50.8
Orthopedics and Traumatology			
Surgical treatment of upper/lower extremity fractures and dislocations	164315 (17.35)	169073 (19.32)	2.9
Foreign body removal from deep tissue, fasciotomy	52270 (5.52)	53367 (6.10)	2.1
Plastic and Reconstructive Surgery			
Tendon repair	37445 (3.95)	34403 (3.93)	-8.1
Amputation of fingers or stump repair	10030 (1.06)	11293 (1.29)	12.6

*Difference between 2019 and 2021.
Values below 0.01% were expressed as 0.01%.

Results

A total of 1,822,075 [947,144 cases (52.0%) in 2019 vs. 874,931 cases (48.0%) in 2021] were included in the analysis. There was a 7.6% decrease in the total number of ESO in 2021 compared to 2019.

The most common ESO performed in 2019 and 2021 was a cesarean section, followed by surgical treatment of upper/lower extremity fractures and dislocations, and cholecystectomy, respectively. The highest increase in 2021 compared to 2019 was the repair of uterine perforation (442 cases in 2019 vs. 699 cases in 2021, a difference of 58.14%), repair of urethral injury (73 cases in 2019 vs. 100 cases in 2021, a difference of 36.99%), and repair of the ruptured aorta and/or aneurysm of its branches (539 cases in 2019 vs. 631 cases in 2021, a difference was 17.07%). The greatest decrease in 2021 compared to 2019 was the surgical treatment of spinal fracture-dislocations (6730 cases in 2019 vs. 3312 cases in 2021, a difference of -50.8%), surgical stabilization of rib fracture/sternum fracture, (991 cases in 2019 vs. 577 cases in 2021 cases, a difference of 41.78%), and repair of esophageal

perforation (70 cases in 2019 vs. 40 cases in 2021, a difference of 37.14%). ESO numbers and change rates in 2021 and 2019 are summarized in Table 1.

In 2019, the most ESO was performed in the obstetrics and gynecology department with 292,941 cases (30.93%) followed by the general surgery departments with 290,795 cases (30.70%) and orthopedics and traumatology departments with 216,585 cases (22.87%). In 2021, the most ESO was performed in the obstetrics and gynecology departments with 285,238 cases (32.60%), followed by general surgery departments with 241,683 cases (27.62%) and orthopedics and traumatology departments with 227,079 cases (25.42%). The distribution of the ESOs according to the departments is summarized in Table 2.

An increase in the number of ESOs in 2021 compared to 2019 was observed only in the urology department (7.1%) and orthopedics and traumatology department (2.7%). Surgical departments with the greatest decreases were neurosurgery (-28.1%), Otolaryngology-Head and Neck Surgery (-27.7%), and thoracic surgery (-20.9%) (Figure 1).

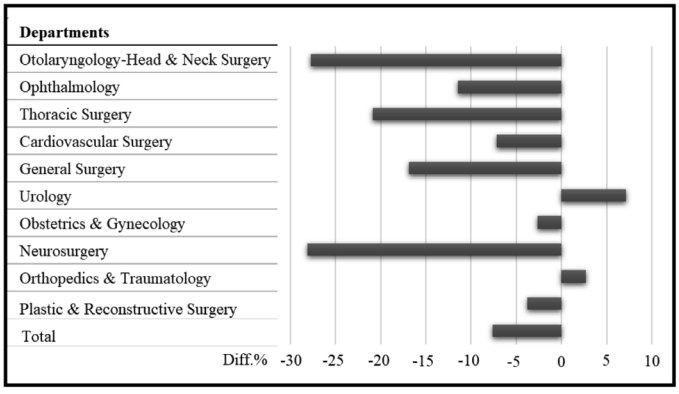

Figure 1. Change in the number of emergency surgical interventions performed in departments in 2021 compared to 2019

Discussion

In this national retrospective study, ESOs performed in state hospitals in 2021 (pandemic period) were analyzed and the results were compared with 2019 (pre-pandemic) data. This study found a 7.6% decrease in the number of ESOs performed in state hospitals in 2021 compared to 2019. The most frequently performed ESOs in both periods were cesarean section and surgical treatment of upper/lower extremity fractures and dislocations. The ESOs with the highest increase in 2021 compared to 2019 were perforated uterus repair and repair of urethral injury. The most decreased ESOs were surgical treatment of spine fracture-dislocations and surgical stabilization of rib fracture/sternum fracture.

WHO reported that as of October 19, 2022, there had been more than 623 million confirmed cases of COVID-19, including 6,550,033 deaths, since the pandemic's start (16). COVID-19 has deeply affected the entire healthcare system (11,17,18). The question that inevitably arises is how the COVID-19 pandemic has affected our ability to maintain the highest quality of care for all of our patients, not just COVID-19 patients. In this process, elective surgical operations have come to a standstill in many hospitals, and a change is needed in the treatment protocols of ESOs (18,19). Additionally, a general decrease in surgical emergency procedures has been observed during the COVID-19 pandemic (12,20). Cano-Valderrama et al. (12) reported that there was a 65.4% decrease in emergency surgical activity during the pandemic period, and the number of patients who underwent emergency surgery in each hospital decreased from 2.6 during the control period to 0.9 during the pandemic period. Alimoglu et al. (21) reported that emergency surgical case consultations, hospitalizations, and ESOs decreased significantly during the

Table 2. Distribution of emergency surgical operations by surgical departments

Departments	Year 2019 n (%)	Year 2021 n (%)
Otolaryngology-Head and Neck Surgery	45604 (4.81)	32966 (3.77)
Ophthalmology	13212 (1.39)	11695 (1.34)
Thoracic Surgery	2076 (0.22)	1643 (0.19)
Cardiovascular Surgery	16182 (1.71)	15026 (1.72)
General Surgery	290795 (30.70)	241687 (27.62)
Urology	7170 (0.76)	7682 (0.88)
Obstetrics and Gynecology	292941 (30.93)	285238 (32.60)
Neurosurgery	15104 (1.59)	10858 (1.24)
Orthopedics and Traumatology	216585 (22.87)	227440 (25.42)
Plastic and Reconstructive Surgery	47475 (5.01)	45696 (5.22)
Total	947144 (100)	874931 (100)

pandemic period compared with 2018 and 2019. Rausei et al. (22) reported a 45% decrease in emergency surgery admissions and a 41% decrease in ESOs in March 2020 compared with March 2019. Kamine et al. (23) reported a decrease in the number of hospitalizations in trauma patients during the pandemic period, but no change in the number of emergency surgeries. The inclusion of all types of emergency surgery patients in our study may have caused this difference. İlhan et al. (24,25), in their study in a tertiary hospital with a trauma center, reported that there was a decrease in the number of patients visited with trauma during the pandemic period, but there was no change in the emergency surgical needs of the patients. The lack of a decrease in the number of ESOs may be because the hospital where the study was conducted was an important trauma center in the region and the selected patient group. All secondary and tertiary state hospitals were included in our study. One of the leading reasons for the decrease in the number of ESOs in this study may be the hospitals where the data were obtained. Our study excluded data from private and university hospitals. Along with the pandemic, many state hospitals have been declared as pandemic hospitals. Therefore, patients requiring ESO may have preferred universities or private hospitals more than in previous years. Additionally, during the pandemic period, the ministry of health encouraged emergency health services to move more patients to private health institutions. The abovementioned situations may have contributed to the decrease in the number of ESOs performed in state hospitals compared to the pre-pandemic period. Moreover, the COVID-19 pandemic has affected the habits of patients and the healthcare system (26-28). A significant decrease in ED visits for acute life-threatening conditions has been reported during the COVID-19 pandemic (17,29). There has also been an increase in the rates of refusal of treatment despite medical advice in patients visiting the ED during the pandemic (26). Patients may have delayed or avoided medical care because of the risk of catching COVID-19, stay-at-home advice, or other reasons.

In our study, most of the ESO was performed in obstetrics and general surgery departments in both years. In both periods, the most frequently performed ESO was a cesarean section. Cesarean section was the most frequently performed major operating room procedure in the United States of America (USA) (30). In the USA, cholecystectomy with a rate of 129.4 per 100,000 people, and appendectomy with a rate of 93.3 are the most commonly performed operating room procedures, except for non-mother and newborn hospitalizations (31). Although their numbers decreased during the pandemic period in this study, cholecystectomy and appendectomy were among the most frequently performed ESOs in both periods.

A significant proportion of the patients in this study were trauma patients. The number of trauma surgeries decreased during the pandemic period compared with the previous period. However, the surgical treatment of upper/lower extremity fractures and dislocations increased by 2.9% in 2021 compared to 2019. İlhan et al. (24) reported that the frequency of multiple trauma decreased during the pandemic period compared to the previous period, but the frequency of upper and lower extremity injuries increased. Similarly, in the study by Esteban et al. (32), the incidence of upper and lower extremity injuries increased during the pandemic period. With the pandemic restrictions, people had to spend more time at home. This situation may be demonstrated as the reason for the decrease in high-energy trauma such as traffic accidents and the increased incidence of lower-energy extremity injuries such as home accidents.

Considering these findings, healthcare systems should guide to help patients choose the most appropriate hospital to receive care and ensure that patients with severe illnesses and injuries continue to visit EDs without fear of contamination or inefficiency. A careful balance must be struck between patient needs and resource availability during the pandemic. To respond effectively to the COVID-19 pandemic, hospitals should prepare detailed pandemic preparedness plans for emergency surgical services. Otherwise, secondary damage from health problems unrelated to outbreaks can have enormous social and economic consequences for the entire health system.

Study Limitations

This was a retrospective study that could lead to selection bias. The data only belong to state hospitals; data from private hospitals are excluded. However, in our study, emergency elective differentiation could not be made in some surgical procedures such as cholecystectomy and splenectomy. Finally, we could not distinguish in which department some surgical interventions were performed. Spinal trauma surgery was included in the neurosurgery department, and Fournier's gangrene was included in the urology department. Finally, we could not differentiate between pediatric surgery because we did not know the ages of the patients.

Conclusion

It is important to underline the points learned from the past in the 3rd year of the COVID-19 pandemic. This article provides an overview of Turkey's statistics on ESOs during the pandemic. The number of ESOs performed in 2nd and 3rd-level state hospitals in Turkey decreased compared to the previous year during the COVID-19 pandemic. This decrease in ESO numbers is likely

attributable to the strict stay-at-home policy, many patients staying away from healthcare facilities for fear of contracting Severe acute respiratory syndrome-Coronavirus-2 in the hospital, or opting for private healthcare facilities they consider more reliable.

Ethics

Ethics Committee Approval: The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. The study was approved by the Ethical Committee of Ankara City Hospital (date: 27/05/2022, no: E2-22-1883).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.B., A.T., Design: A.B., H.A., Data Collection or Processing: A.B., A.T., Analysis or Interpretation: A.B., A.T., Literature Search: A.B., H.A., Writing: A.B., H.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2022.37640
Eurasian J Emerg Med. 2023;22(1): 41-8

One-man Below-knee Analgesia in the Emergency Department with Minimal Equipment Using the Single-operAtor Nerve block under Direct ultrasound visualization in emergencY ('SANDY') Technique: A Retrospective Analysis

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Abstract

Aim: To demonstrate the efficacy of single-person bedside ultrasound guided (USG) Popliteal-Sciatic Nerve Block (PSNB) using minimal equipment in the emergency department (ED) for managing below-knee trauma.

Materials and Methods: This single-centre retrospective analysis was done at the ED of a tertiary care centre in Southern India from 01/12/2021 to 31/06/2022. The charts of all adult patients who received the block were reviewed and the reduction in pain score after the block, block success rate, and incidence of side effects were analyzed.

Results: One hundred and three patient records were reviewed during the study period. Ninety-eight males (95.1%) and 5 females (4.9%) had received the block. 87.4% of the patients were road accident victims. The block was given by a single operator under ultrasound guidance with the stylet of an 18 gauge intravenous cannula mounted on a syringe filled with 1% lidocaine. The mean pain score before and 10 minutes after administering the block was 8.85 [standard deviation (SD) ±0.78] and 2.06 (SD ±1.75) respectively. The block success rate was found to be 93.2%. Except for 7 failed blocks, there were no adverse events following the procedure.

Conclusion: USG PSNB is a safe, consistent, and relatively long-lasting anesthetic technique in the management of below-knee trauma in the ED.

Keywords: Analgesia, emergency department, nerve block, Popliteal-Sciatic, ultrasound

Introduction

Open lower limb trauma is a common presenting complaint in any emergency department (ED) and is most often due to high-velocity road traffic accidents, or workplace-related injuries (1,2). Assessing the degree of pain can be challenging and often requires a multimodal approach that can be difficult in the emergency setting. Thus, for acutely traumatized patients in pain, the Numerical Rating Scale (NRS) is a quick and useful tool to quantify and triage patients accordingly. Primary wound care is the responsibility of the emergency physician (EP), and the widespread availability of intravenous (IV) anesthetic agents in the ED facilitates early wound washing, debridement, and splintage often in conjunction with the orthopaedic and trauma surgery team. However, procedural sedation and analgesia (PSA) in the ED are not without challenges, like the chance of excessive sedation in at-risk patients such as the elderly or the obese, or post-anesthetic complications such as vomiting, delirium, and hypoxia. The response among different patients to anesthetic doses also varies, with some having blunted or exaggerated responses to "standard" doses of anesthetic drugs. Therefore, PSA is ideally a monitored service, and a healthcare provider should be designated to monitor the patient and administer titrated doses of anesthetic or dissociative drugs throughout the period of wound care. This can put a logistic strain on personnel, especially in a high-volume ED with staff numbers already stretched thin.

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Cite this article as: David SN, Katumalla PD, Ganesan P, Abhilash Kundavaram PP. One-man Below-knee Analgesia in the Emergency Department with Minimal Equipment Using the Single-operAtor Nerve block under Direct ultrasound visualization in emergencY ('SANDY') Technique: A Retrospective Analysis. Eurasian J Emerg Med. 2023;22(1): 41-8.

Received: 05.09.2022
Accepted: 23.12.2022

Bedside ultrasound guided (USG) nerve blocks of the lower limb are an attractive alternative that obviates the need for IV agents, and all the side effects that come with them, as well as freeing up ED personnel for other more pressing tasks. In our study, we used the USG Popliteal-Sciatic Nerve Block (PSNB) as the sole anesthetic technique for lower limb wound management, as it is relatively safe with a wide sensori-motor coverage below the knee, save for the medial aspect of the leg. It is commonly performed by anesthesiologists for below-knee surgeries and post-operative analgesia. This study was undertaken to demonstrate the easy and effective pain management for lower limb injuries in the ED while conserving labor and resources, without the need for specialized equipment. Furthermore as there is a dearth of published large -scale regional-anaesthesia-based studies from an ED standpoint and with the portable ultrasound machine now being ubiquitous and invaluable in any ED, this could show the potential of bedside USG nerve blocks and can be potentially expanded to provide effective analgesia to other common injuries as well such as upper limb trauma and rib fractures as a standard analgesic practice. We hypothesized that USG PSNB can be used as an effective technique for safe and consistent lower limb analgesia for wound management. Our study aimed to demonstrate the efficacy of single-person bedside USG PSNB using minimal equipment in the ED for managing below-knee trauma. Our objectives were to analyse the reduction in pain score following the nerve block, to determine the success rate of the nerve block being done in the ED, to determine the incidence of supplemental analgesia during wound care following the nerve block, and to determine the incidence of side effects following the nerve block.

Materials and Methods

Study Design and Setting: This retrospective observational cohort-based single-centre study was undertaken at a 60 bedded ED in a major tertiary care hospital and referral center in Southern India. The chart review process was initiated after approval by the Christian Medical College Institutional Review Board Ethics Committee (IRB number: 14288, date: 29/9/2021). The authors attest that the STROBE guidelines were adhered to during the preparation of this manuscript.

The Selection of Participants: The charts of all patients with below-knee trauma who presented between the months of December 2021 and May 2022 and received bedside PSNB before primary wound care were reviewed. Informed consent for publication was not obtained from the patients due to retrospective design; however, procedural consent was sought from all patients. Patients included consisted of all those 16 years and above presenting with below-knee trauma along the distribution of the tibial and common peroneal nerves who received the block. The excluded charts comprised of those patients for whom the trauma lay outside the distribution of the sciatic nerve, those who did not consent for the procedure, those who were taking oral anticoagulant drugs, and those with pre-existing neuropathies or clinically evident nerve damage following the trauma as per their medical records. Furthermore, since only a few EPs were trained to administer the block, a significant number of patients were excluded due to the unavailability of the concerned doctors.

Measurements: The nerve block was given at the bedside by a single operator before wound management, such as wound wash, splintage, or debridement by the orthopaedic team. The local anesthetic (LA) used was 10 to 15 mL of 1% lidocaine (Jackson Laboratories Pvt Ltd., 22-24 Majitha Road, By-Pass, Amritsar, India. 143001), and was injected using the stylet of an 18 gauge IV cannula (Vasofix® Luer Lock, B. Braun Medical Industries Bayan Lepas-free Industrial Zone 11900, Penang, Malaysia) with direct visualization of the nerve using a high frequency ultrasound probe (6-13-Hz HFL38, SN 04QGNX, FUJIFILM SonoSite Inc. 21919 30th Drive SE Bothell, WA 98021. USA). The block was performed with the patient in the supine position with the ipsilateral knee in the semi-flexed position. A check-scan was performed to pre-emptively locate the sciatic bifurcation above the popliteal fossa and to look for the presence of any aberrant vessels or other anatomical variations. Once the injection site was confirmed, an antiseptic solution was applied to the lateral side of the distal thigh. The probe was reapplied to the area held by the non-dominant hand of the EP, keeping the sciatic bifurcation in view. Using a lateral-to-medial approach, the stylet attached to a syringe pre-loaded with LA was inserted into the lateral thigh with the dominant hand of the EP, and using in-plane needling under direct vision, the needle was gently guided to the bifurcation of the sciatic nerve into the tibial and common peroneal nerves (Figure 1). 1% lidocaine was slowly injected sub-paraneurally after negative aspiration, followed by caudal screening to look for the spread of the drug around both nerves (Figure 2). The spread around both nerves was visually confirmed by the gradual appearance of an owl-eyes sign around both nerves. After every needle reposition, gentle aspiration was done to ensure no ingress of any vessels, and during injection constant slow pressure was given to the syringe while looking for severe shooting pain, which would indicate intrafascicular injection. The pain score 10 minutes after the block was noted, and the patient underwent the procedure. The block was deemed successful if the NRS 10 minutes post block was at least 50% of the initial score, and if the patient could undergo wound management without any PSA. The success rate of the block and how often rescue analgesia had to be administered during the

procedure was determined, and the patient was monitored till the return of sensation for any side effects such as LA toxicity or prolonged paraesthesia.

Statistical Analysis

The data was collected from the patients' records using the hospital's electronic medical system and compiled on Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA). Demographic details such as the patient's age and sex were noted, along with the mechanism of injury. The degree of pain was recorded using the NRS before and after the block. The success rate of the block was calculated and the incidence of side effects such as neuropraxia was looked for (Table 1). The mean [standard deviation (SD)] was calculated for the continuous variables, and categorical variables were expressed in percentages.

Figure 1. Bedside ultrasound guided Popliteal-Sciatic Nerve Block

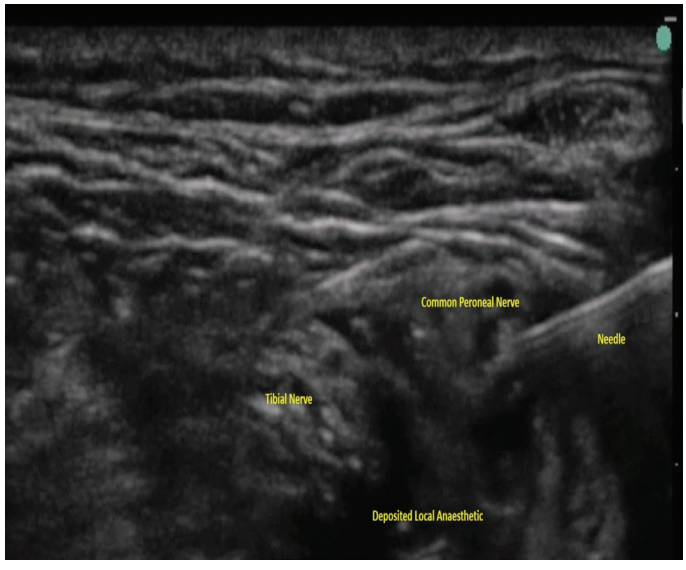

Figure 2. Ultrasound image of the nerve block

Results

The charts of 3689 trauma patients who presented to our ED were screened, and 405 patients were identified as having presented with below-knee trauma. Of that cohort, 302 patients were excluded as they did not meet the inclusion criteria, or because they presented at a time when the doctors trained in USG-PSNB administration were not on shift. A total of 103 eligible patients were subsequently included in the review process (Figure 3). The mean age was found to be 51.17 (±14.17) years, the majority of patients were male (n=98; 95.1%). Ninety patients were road traffic accident victims (87.4%) and 13 patients were victims of trauma by occupational injuries (12.6%). Out of the patients screened, 96 out of 103 (93.2%) patients had successful blocks and underwent wound care without additional or rescue analgesics, with the rest having pain either before or during the procedure and needing rescue analgesia (Figure 4). The mean pain score at presentation was 8.85 (±0.78), and the mean pain score 10 minutes after the block was found to be 2.06 (±1.75). The success rate of the block when performed in the ED was found to be 93.2%, and all patients with successful blocks underwent the wound care procedures such as wound decontamination, splintage, suturing, or even K-wire fixation without any additional sedo-analgesia. Seven patients (6.8%) had a failed block and required supplemental sedo-analgesia for primary wound management by the orthopaedic or trauma surgery team. Besides block failure, there was no incidence of significant side effects such as LA toxicity, adverse drug reaction or neuropraxia after administration of the USG-PSNB, and the duration of action of the blocks using 1% lidocaine lasted between 3-4 hours.

Discussion

The USG-PSNB is an extremely useful tool in the armament of anesthesiologists, often performed as the sole method of anesthesia in below-knee surgery with an additional saphenous nerve block given for medial leg coverage if required (3,4). Although sedation and analgesia in the ED has come a long way with regards to access to drugs and better understanding of drug pharmacokinetics and pharmacodynamics, it is not without risks including vomiting, over-sedation, and airway compromise (5-7). Drugs such as propofol, midazolam, fentanyl, ketamine, and dexmedetomidine, though short acting, would require continuous monitoring and experience in their usage. Patients such as the elderly or those on cardio-respiratory medications are also at higher risk for immediate and delayed adverse

Table 1. Demographic details, injury profile and pain scores of the patients analysed in the study period

S. no	Sex	Age	Mechanism of Injury	Initial NRS	Post-block NRS	Successful block
1	M	43	Road traffic accident	10	3	Yes
2	M	54	Road traffic accident	8	1	Yes
3	M	36	Road traffic accident	9	1	Yes
4	M	72	Road traffic accident	10	3	Yes
5	M	65	Occupational injury	10	1	Yes
6	M	47	Road traffic accident	9	2	Yes
7	M	64	Road traffic accident	8	2	Yes
8	M	53	Road traffic accident	8	1	Yes
9	F	26	Road traffic accident	9	3	Yes
10	M	32	Road traffic accident	8	1	Yes
11	M	41	Road traffic accident	9	2	Yes
12	M	52	Road traffic accident	10	2	Yes
13	M	67	Road traffic accident	10	3	Yes
14	M	58	Occupational injury	9	3	Yes
15	M	82	Road traffic accident	8	2	Yes
16	M	65	Road traffic accident	9	1	Yes
17	F	25	Road traffic accident	8	1	Yes
18	M	20	Road traffic accident	10	2	Yes
19	M	47	Road traffic accident	10	1	Yes
20	M	42	Occupational injury	9	9	No
21	M	34	Road traffic accident	10	1	Yes
22	M	37	Road traffic accident	9	1	Yes
23	M	64	Road traffic accident	8	1	Yes
24	M	38	Road traffic accident	8	1	Yes
25	M	74	Road traffic accident	9	2	Yes
26	M	25	Road traffic accident	10	4	Yes
27	M	58	Road traffic accident	10	1	Yes
28	M	63	Road traffic accident	9	1	Yes
29	M	72	Road traffic accident	8	1	Yes
30	M	62	Road traffic accident	9	2	Yes
31	M	93	Occupational injury	9	1	Yes
32	M	46	Road traffic accident	8	2	Yes
33	M	34	Road traffic accident	9	1	Yes
34	M	52	Road traffic accident	10	1	Yes
35	M	62	Road traffic accident	9	2	Yes
36	M	57	Occupational injury	10	1	Yes
37	M	66	Road traffic accident	9	9	No
38	M	72	Road traffic accident	10	1	Yes
39	M	84	Road traffic accident	8	1	Yes
40	M	35	Road traffic accident	9	1	Yes
41	M	47	Road traffic accident	10	2	Yes
42	M	41	Road traffic accident	9	1	Yes
43	M	57	Occupational injury	10	3	Yes
44	M	43	Road traffic accident	9	1	Yes

Table 1. Continued

S. no	Sex	Age	Mechanism of Injury	Initial NRS	Post-block NRS	Successful block
45	M	77	Road traffic accident	9	8	No
46	M	39	Road traffic accident	10	1	Yes
47	M	37	Occupational injury	8	1	Yes
48	M	48	Road traffic accident	10	2	Yes
49	M	71	Road traffic accident	9	1	Yes
50	M	47	Road traffic accident	10	2	Yes
51	M	53	Occupational injury	9	1	Yes
52	M	57	Road traffic accident	8	2	Yes
53	M	62	Road traffic accident	9	3	Yes
54	M	36	Road traffic accident	8	1	Yes
55	M	42	Road traffic accident	8	1	Yes
56	M	47	Road traffic accident	8	1	Yes
57	M	39	Road traffic accident	9	8	No
58	M	42	Road traffic accident	8	1	Yes
59	M	74	Road traffic accident	9	2	Yes
60	M	65	Road traffic accident	10	3	Yes
61	M	69	Road traffic accident	8	8	No
62	M	47	Road traffic accident	9	2	Yes
63	M	52	Occupational injury	8	1	Yes
64	M	37	Road traffic accident	9	1	Yes
65	F	58	Road traffic accident	9	1	Yes
66	M	63	Road traffic accident	9	1	Yes
67	M	49	Occupational injury	8	2	Yes
68	M	57	Road traffic accident	8	5	No
69	M	52	Road traffic accident	9	2	Yes
70	M	61	Road traffic accident	9	1	Yes
71	M	44	Road traffic accident	8	2	Yes
72	M	76	Road traffic accident	8	2	Yes
73	M	54	Road traffic accident	9	1	Yes
74	M	57	Road traffic accident	9	2	Yes
75	M	68	Road traffic accident	9	1	Yes
76	M	43	Road traffic accident	10	8	No
77	M	46	Road traffic accident	8	1	Yes
78	M	47	Occupational injury	9	1	Yes
79	M	52	Road traffic accident	8	2	Yes
80	M	68	Road traffic accident	9	3	Yes
81	M	62	Road traffic accident	9	2	Yes
82	M	37	Road traffic accident	8	1	Yes
83	M	39	Road traffic accident	7	2	Yes
84	M	31	Road traffic accident	7	2	Yes
85	M	46	Road traffic accident	8	2	Yes
86	M	48	Road traffic accident	10	1	Yes
87	M	54	Road traffic accident	10	2	Yes
88	M	42	Occupational injury	9	1	Yes

Table 1. Continued

S. No	Sex	Age	Mechanism of Injury	Initial NRS	Post-block NRS	Successful block
89	M	48	Road traffic accident	10	2	Yes
90	M	58	Road traffic accident	9	1	Yes
91	M	54	Road traffic accident	8	2	Yes
92	F	57	Road traffic accident	9	2	Yes
93	M	35	Road traffic accident	8	2	Yes
94	M	33	Road traffic accident	8	1	Yes
95	M	31	Road traffic accident	8	2	Yes
96	M	37	Road traffic accident	9	2	Yes
97	M	39	Road traffic accident	8	1	Yes
98	F	49	Occupational injury	9	2	Yes
99	M	49	Road traffic accident	9	2	Yes
100	M	48	Road traffic accident	9	2	Yes
101	M	47	Road traffic accident	8	3	Yes
102	M	36	Road traffic accident	9	2	Yes
103	M	47	Road traffic accident	8	2	Yes

*The failed blocks are highlighted.
F: Female, M: Male, NRS: Numerical Rating Scale

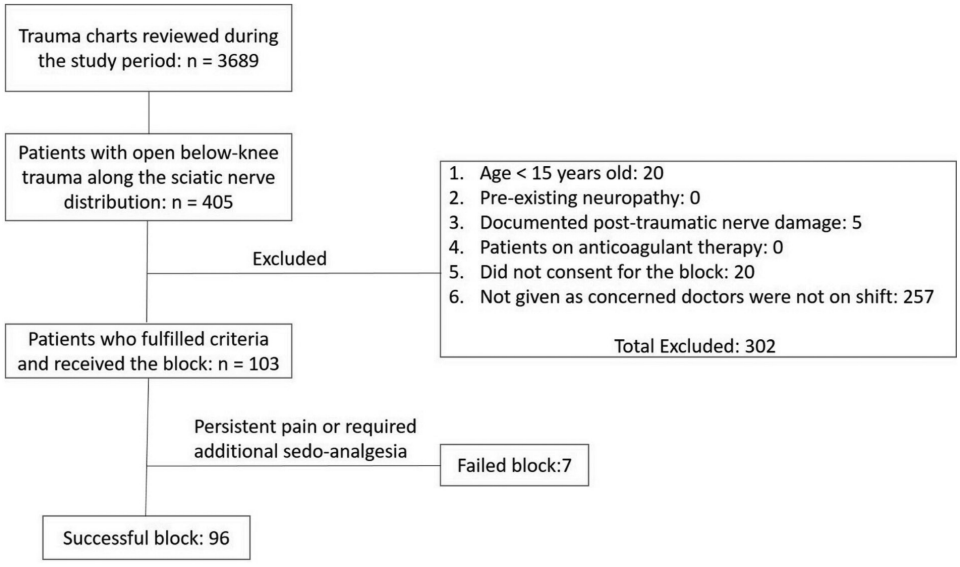

Figure 3. STROBE diagram of patient analysis and results

effects of PSA. Additionally, PSA requires a designated healthcare professional to monitor the patient throughout the procedure, taking someone away from an already busy ED floor when their presence may be needed elsewhere for more pressing matters.

Although USG nerve blocks are being performed in EDs with increasing frequency, published data is largely restricted to case reports and instructional articles (8-10). Furthermore, regional anesthesia is typically administered by anesthesiologists in a separate block room by 2 or more individuals using specialized equipment such as block needles and peripheral nerve stimulators (11-13). Given the dearth of large -scale published data and considering the need for logistic and ergonomic conservation in a busy ED, we modified the existing anesthesiology technique of the PSNB to a bedside single-person-delivered nerve block using the stylet of an 18 gauge IV cannula, termed the 'SANDY' approach as many open injuries or mangled

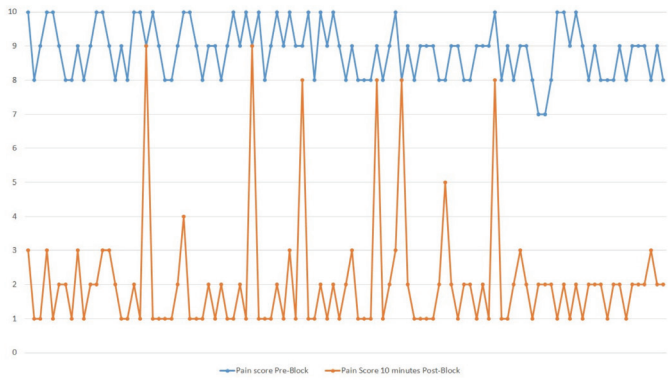

Figure 4. Graphical representation of pre and post-block pain scores

limbs are contaminated with mud or sand. Under USG and with repeated negative aspirations, the drug was slowly injected sub-paraneurally, which has been described by Perlas et al. (14) and Cappelleri et al. (15) to be safe for administering nerve blockade without causing nerve damage. The intrafascicular injection was prevented by constantly monitoring for sudden shooting limb pain or paraesthesia, along with careful slow injection of the drug. All our patients were given 10-15 mL of 1% lidocaine sub-paraneurally regardless of age, sex, or weight. Following the block, the mean pain score dropped significantly from 8.85 to 2.06 within 10 minutes. We had an ED block success rate of 93.2%, with 7 block failures that required additional sedo-analgesia during the wound management procedure. This is encouraging from an ED standpoint and comparative to several anesthesiology-based perioperative nerve block studies with similar success rates; David et al. (4) performed USG-PSNB on 50 pre-operative patients using 0.2% Ropivacaine with a success rate of 94%; meaning that patients underwent the surgical procedure purely under regional anesthesia without any IV agents. Arjun et al. (16) showed a 100% success rate when this block was combined with a saphenous nerve block for lower limb surgeries and Jeon et al. (17) reported a patient satisfaction rate of 95% in a study comparing post-operative pain relief following PSNB with nerve catheter insertion compared with spinal anesthesia. A recent Cochrane Database analysis and several published review articles further demonstrate the utility and efficacy of USG nerve blocks, and could give hope that ED-based nerve blocks using the SANDY approach can have similar rates of success as those done in the operating room while conserving resources and labor (18-21). To the authors' knowledge, this is the largest ED-based study under these parameters with results comparable to regional anesthesia techniques done with ideal anesthetic conditions and equipment. As most EDs have in-house portable ultrasound machines, this technique could be adopted and be an effective tool in wound management.

Regional anesthesia techniques in the ED have a promising future and could be beneficial from the viewpoint of efficient and competent patient care, as well as being safe and long lasting for patients at risk of systemic anesthesia (22-24). Nerve blocks when done in the ED have the advantage of sparing labor while obviating the need for potentially dangerous or dependence forming drugs such as opioids or ketamine. Looking ahead, more robust studies could be done in the future such as prospective observational studies and randomized controlled trials comparing nerve blocks using the SANDY approach to the usual departmental methods of analgesic care, and expanding the one-man technique for other described nerve blocks such as axillary, supraclavicular, or fascia iliaca blocks in the ED. The procedure performed with the short -acting agent lidocaine did not manifest any unwanted effects such as nerve damage or LAST. Hence, longer acting LA agents such as Bupivacaine and Ropivacaine could be potentially be used for the procedure, which could result in even longer periods of safe and consistent analgesia.

Study Limitations

As the study is a retrospective analysis, no comparison arm with standard analgesic protocols could be analyzed. Furthermore, case numbers were relatively limited because the doctors administering the block were not always on shift.

Conclusion

Popliteal-Sciatic block using the 'SANDY' technique is an effective, long -lasting, consistent, and safe method for wound management for below-knee trauma in the ED. It is promising as an anesthetic - sparing method for analgesia and can save valuable labor and patient cost as well.

Ethics

Ethics Committee Approval: The study was approved by the Christian Medical College Institutional Review Board Ethics Committee (IRB number: 14288, date: 29/9/2021).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: S.N.D., P.D.K., Design: S.N.D., P.D.K., Data Collection or Processing: S.N.D., P.D.K., P.G., Analysis or Interpretation: S.N.D., P.D.K., P.G., P.P.A.K., Literature Search: S.N.D., Writing: S.N.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2023.99075
Eurasian J Emerg Med. 2023;22(1): 49-54

Predictive Performance of the National Early Warning Score 2 for Stratification of Critically Ill COVID-19 Patients

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Abstract

Aim: To validate the ability of National Early Waring Score 2 (NEWS2) for predicting the severity of Coronavirus disease-2019 (COVID-19). In addition, we also intend to examine the impact of pre-existing comorbidities to produce an advanced COVID-19 disease.

Materials and Methods: A multicenter prospective cohort was performed on 108 patients having moderate-intensity COVID-19 infection during October 2020 and November 2021. NEWS2 parameters were recorded on admission to generate an output score, which then classified in accordance with the NEWS2 reference scale into low, medium, and high-risk categories. Each patient was followed till discharge or death for the clinical progression of COVID-19. The measures of validity and area under the curve (AUC) for NEWS2 threshold scores were calculated to predict the clinical deterioration of COVID-19.

Results: Overall, 29.6% patients developed an advanced disease, out of which 21.8% patients died during treatment. NEWS2 score of 6 or more showed the highest sensitivity (78.1%), specificity (94.8%), and the AUC (0.838) for predicting an adverse outcome. Among comorbidities, the majority showed an increased risk of clinical deterioration.

Conclusion: NEWS2 score of 6 or more at baseline showed good predictive ability to stratify patients with poor outcomes who may later require escalated care. However, we recommend more research to confirm our findings.

Keywords: COVID-19, Coronavirus disease-2019, NEWS2, sensitivity

Introduction

The Coronavirus disease-2019 (COVID-19) pandemic is a big challenge for global healthcare systems (1). Although most Severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) patients remained asymptomatic, some of those develops deteriorating disease, which often end up with a fatal outcome (2). The recent estimates indicated that almost 4% of critically ill COVID-19 patients eventually die while receiving intensive care unit (ICU) care (3). Accumulating data suggested that advanced age and pre-existing comorbidities are the main factors involved in the progression of COVID-19. Hence, assessing the risk factors on admission is crucial in determining the possibility of progression in COVID-19 disease (4). Besides, few clinical scoring systems have been evaluated for predicting the clinical deterioration in COVID-19 patients (5).

At the moment, no established method is available for early stratification of high-risk COVID-19 patients. Such risk stratification allows physicians to escalate care for potentially aggressive cases (6). The National Early Waring Score 2 (NEWS2) is a clinical tool used in ICU's to assist health care workers in stratification of high-risk septicemic patients who could be benefited by intensive management and monitoring (7). NEWS2 scale is based on six parameters which includes; temperature, respiratory rate, pulse, blood pressure, consciousness level and oxygenation saturation (8).

Recently, the application of the NEWS2 algorithm for early stratification of severe COVID-19 patients has been proposed (9). The assessment of oxygen and ventilation parameters are the main reasons to recommend NEWS2 in COVID-19 disease compared to some other scoring methods (8).

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Cite this article as: Baig FA, Hamid A. Predictive Performance of the National Early Warning Score 2 for Stratification of Critically Ill COVID-19 Patients. Eurasian J Emerg Med. 2023;22(1): 49-54.

Received: 15.11.2022
Accepted: 18.01.2023

Each NEWS2 parameter is scored in an order of 0 to 3, reflecting the degree of severity. The cumulative NEWS2 score ranges from 0 to 23, which is computed by the addition of all parametric scores. The cumulative score is sub-categorized as; low risk (1 to 4), medium risk (5 to 6) and high risk (≥6) infection (8). However, these risk levels are primarily meant for evaluating the status of patients suffering from sepsis (10).

Nevertheless, there is a dearth of literature on the ability of NEWS2 to predict clinical outcomes in COVID-19, but also the power of NEWS2 scores for stratification of high-risk COVID-19 patients is unclear. Moreover, NEWS2 has been studied mostly in the United Kingdom and its validation in non-caucasian population is a subject of further research. We therefore determined the accuracy of NEWS2 for stratification of risk levels in COVID-19 patients on admission. We also sought to examine the potential of pre-existing comorbidities for clinical deterioration during hospitalization.

Materials and Methods

Study Design and Setting

A multicenter prospective cohort was designed comprising 108 patients with proven COVID-19 infection using SARS-CoV-2 PCR assay. The ethical approval was sought from the Ethic Review Committee Ziauddin University, Karachi, Pakistan (ERC #1701219FHPAT, date: 10.02.2020) in line with the Helsinki Declaration 2013. The subjects were selected from four major tertiary care hospitals located in District East, Karachi, Pakistan. The subjects received in-patient care between October 2020 and November 2021. Written informed consent was obtained from all subjects to use their data. All information were coded and kept confidential.

Participants

The patients were selected by applying non-probability consecutive sampling model. All cases were recently admitted for the treatment of COVID-19. The disease spectrum i.e., mild, moderate, severe and critical was determined on admission in accordance with CDC guidelines, which describes mild disease as no shortness of breath and moderate disease if oxygen saturation (SpO_2) ≥94%. While severe disease is diagnosed when SpO_2 <94%, PaO_2/FiO_2 <300 mmHg and respiratory rate >30 breaths/min whereas, the cases presented with respiratory failure and multi-organ dysfunction are characterized as critical (11). Based on this guideline, our inclusion criteria were newly admitted adult patients with moderate COVID-19 disease. Patients who already developed severe to critical illnesses at the time of admission were excluded from the selection. Also, the cases with mild disease were excluded as they do not require in-patient care.

Each i.e. subject was followed to determine the clinical course of COVID-19 during hospitalization, i.e. of moderate infection to a severe and critical state or death. The demographic data such as age, residence and gender along with presenting symptoms, the vital signs including blood pressure, pulse, respiratory rate and oxygen saturation were recorded at the time of admission. Additionally, the level of consciousness was assessed in accordance with Glasgow Coma Scale (GCS) i.e. GCS >13 for alert.

Procedure

The NEWS2 score was calculated using MDCalc online assessment tool (12). The six parameters, which includes: respiratory rate, oxygen saturation (SpO_2), supplemental oxygen, pulse rate, level of consciousness, and temperature recorded on admission were entered in MDCalc to generate the final scores by an automated preset algorithm. All scores were then organized and distributed among the three NEWS2 categories i.e. 4, 5, and ≥6 indicating low, medium and high-risk levels, respectively.

Statistical Analysis

We classified the outcome according to their clinical spectrum as described in the aforementioned CDC guidelines. Those who remained on a moderate course throughout hospitalization constitute the good outcome or control group while poor outcome or case group was comprised of those participants who progressed to severe or critical disease and those who eventually died. The sensitivity, specificity, positive, negative predictive values, and accuracy for the NEWS2 risk thresholds were estimated to predict worsening of COVID-19. The ROC curve was generated and the area under the curve (AUC) was calculated.

The impact of comorbidities to causing an advanced disease was assessed by relative risk at 95% confidence interval (CI) and the strength of association was determined by p value. The p value <0.05 was considered statistically significant. All statistical analyzes were performed using MedCalc statistical software version 20.

Results

Our data showed that 32 (29.6%) out of 108 cohorts developed an advanced COVID-19 disease during hospitalization, thus classified as a case or poor outcome group. Of which 16 (50%) patients progressed to severe illness, 9 (28.1%) developed critical disease, and 7 (21.8%) died during treatment. We found 76 (70.3%) patients remained on a moderate course and eventually recovered, hence considered as controls or good outcome group. Table 1 shows the number of subjects within the case and control groups based on the clinical outcome. Our demographic data revealed male predominance (n=61). Furthermore, most

participants (75.9%) were aged over 60 years. The minimum age in our series was 18 years, while the maximum age was recorded as 81 years. The overall median age was 67.5 years.

The NEWS2 data showed that scores on admission were ranged from 4 to 14. The median for the score was 9.6. We observed that most patients in the control or good outcome group (89.4%) had an initial NEWS2 score below 6 and some patients (10.5%) were scored 6 or above on admission. Conversely, the majority of subjects (78.1%) in the case or poor outcome category presented with initial scores 6 or more while only few (21.8%) were scored lower than 6 on admission. This accounts for sensitivity (78.1%), specificity (89.4%), positive predictive value (45.1%), and negative predictive value (97.3%) for the score 6 and above. Similarly, the highest accuracy (88.3%) was observed for the scores over 6 to predict deteriorating illness. These validity estimates were also supported by the receiver operating curve that indicated highest AUC (0.838) for scores 6 and above (Figure 1). In comparison, the admission scores 4 and 5 showed low diagnostic value in risk stratification of COVID-19 patients. Table 2 presents the validity estimates of the NEWS2 threshold points for risk assessment on admission.

On the analysis of comorbidities, we found that the overwhelming majority (85%) of cohorts had some forms of pre-existing illness. At 95% CI, increasing age, hypertension, diabetes, renal, hepatic, and cardiovascular disorders showed a greater risk for an advanced disease or poor outcome. These factors were also significantly associated with poor outcomes in COVID-19 on descriptive statistics. However, asthma and chronic obstructive lung disease had higher odds to produce an aggressive disease, but no association with the severity of COVID-19 was observed. Table 3 describes statistical estimates of pre-existing comorbidities with the clinical progression of COVID-19.

Table 1. Distribution of NEWS2 scores among COVID-19 cases and controls

NEWS2 Scores•	COVID-19 disease¶			
	Controls (good outcome group)	Cases (poor outcome group)		
	Moderate disease (n=76)	Severe disease (n=16)	Critical disease (n=9)	Death (n=7)
4	30	2	0	0
5	38	4	1	0
6 and above	8	10	8	7

•NEWS2 cut-off scores for risk levels, ¶Clinical spectrum based on CDC guidelines, COVID-19: Coronavirus disease-2019, NEWS2: National Early Waring Score 2

Table 2. Predictive performance of NEWS2 scores on admission for risk stratification in Coronavirus disease-2019

NEWS2 Scores†	Sensitivity (%)	Specificity (%)	PPV§ (%)	NPV‡ (%)	AUC‡	Accuracy (%)
4	6.2	60.5	1.7	85.3	0.334	55
5	15.6	50	3.3	84.2	0.328	46.5
6 and above	78.1	89.4	45.1	97.3	0.838	88.3

†: NEWS2 cut-off scores for risk levels, §: Positive predictive value, ‡: Negative predictive value, ‡: Area under the curve

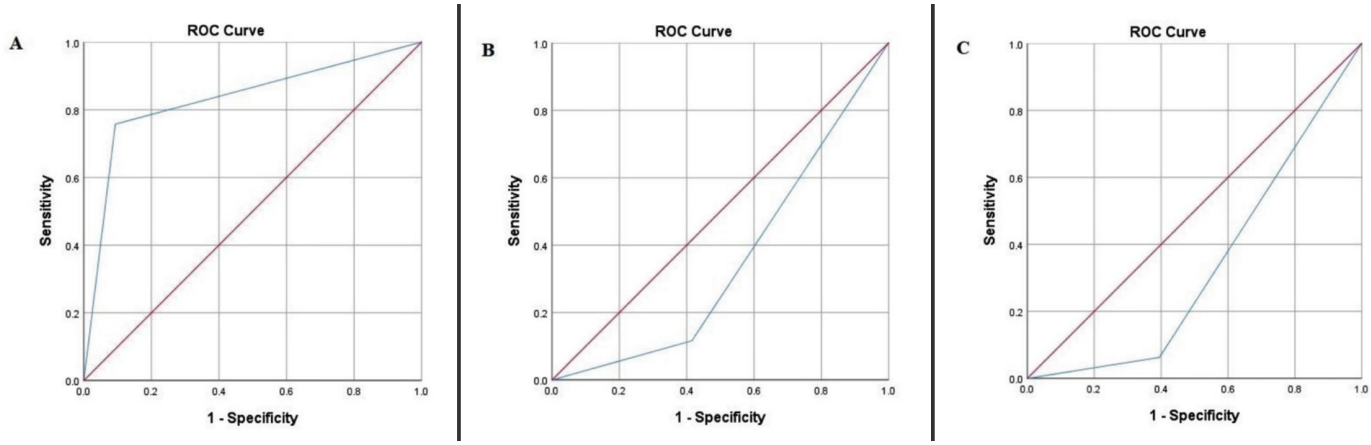

Figure 1. Receiver operating curve (ROC) with reference line (red) comparing the sensitivities for (A) NEWS2 score 6 and above, (B) score 5 and (C) score 4 representing high, medium and low risk of clinical deterioration in Coronavirus disease-2019 patients

Table 3. Association of comorbidities and relative risk estimates for poor outcome in Coronavirus disease-2019 patients			
Factors	**p value***	**Relative risk‡**	**95% CI**
Age	0.0001	3.562	2.085 to 6.085
Hypertension (n=20)	0.007	2.902	1.333 to 6.320
Chronic renal disease (n=18)	0.0006	4.750	1.953 to 11.551
Diabetes (n=17)	0.006	3.392	1.417 to 8.123
Chronic liver disease (n=13)	0.011	3.800	1.345 to 10.732
Cardiovascular disease (n=12)	0.001	7.125	2.062 to 24.613
Asthma (n=5)	0.152	3.562	0.624 to 20.315
Malignancy (n=4)	0.837	0.791	0.0855 to 7.327
Chronic obstructive lung disease (n=3)	0.196	4.750	0.446 to 50.544
*: P value <0.05 is statistically significant, ‡: RR >1.0 represents positive association, CI: Confidence interval			

Discussion

The lack of prognostic indicators for novel COVID-19 is the biggest dilemma of our agile health system. Early warning systems (EWS) are typically employed in critically ill patients by emergency care physicians to identify candidates who could pose a threat of clinical deterioration. To date, several models of EWS have been developed and tested. Out of these, the Royal College of Physicians proposed NEWS2 as a suitable method for risk stratification in COVID-19 patients (13). Therefore, a cohort was designed on patients from various centers that are designated for COVID-19 testing and treatment to evaluate the performance of NEWS2 in early stratification of high-risk COVID-19 patients.

The NEWS2 scale was implemented after the initial assessment of patients who were suitable for admission. Our findings indicated that a score of 6 or more had reasonably good sensitivity (78.1%) and specificity (89.4%) to predict an aggressive course of disease and thus identified those who later required ICU. We also discovered that a minimum score of 6 at baseline had maximum AUC (0.838) for predicting the poor outcome. Furthermore, increasing age, diabetes, chronic renal, hepatic, and cardiovascular impairments are independent factors associated with greater risk of complications.

Since the start of the pandemic, researchers have evaluated numerous factors for prognostic purposes. In early studies, Chinese authors reported that older age, smoking, inflammatory markers such as; neutrophil to lymphocyte ratio, platelet counts, C-reactive protein, procalcitonin, D-dimer could prove useful in the assessment of high-risk COVID-19 patients (14). Another study observed that Sequential Organ Failure Assessment scores traditionally used for characterization of sepsis could also serve as prognosticator for COVID-19 (14). However, it is evident from recent data that adverse outcomes in COVID-19 results from pulmonary complications that are aggravated or triggered by pre-existing comorbidities. Since then studies are focused on factors attributed to progression of COVID-19 (14).

Despite these encouraging reports, the tasks to determine the possibility of clinical deterioration is proving to be extremely challenging. In this context, we have previously attempted to correlate the levels of inflammatory markers with severity of disease; however, most of these laboratory investigations are time consuming, costly, and not readily available in smaller setups. Thus, it is critical to determine alternative methods for stratification of risk in COVID-19 patients (15).

The NEWS score was introduced in 2012 to monitor critically ill patients in the ICU. The NEWS2 is an update to the NEWS score with the addition of parameters such as: oxygen saturation and confusion. National Health System (NHS), United Kingdom has been advocating to implement NEWS2 in the management of COVID-19 patients (8). The basis for this NHS recommendation is the NEWS2 parameters which includes; oxygen saturation and also the benefits of NEWS2 seen in critically ill adults during pre-COVID-19 era (8). Subsequently, a Chinese modification of NEWS2 has been evaluated for triaging COVID-19 patients however, the algorithm had numerous calibration issues which compromised its worth in clinical application (16).

In recent studies, a single center retrospective research conducted in UK found that NEWS2 score of 5 or more during hospitalization can predict clinical deterioration with a greater accuracy (7). Later these findings were also supported by Kostakis et al. (17). Another single center cohort from neighboring India concluded that NEWS2 score of 5 and above at admission has an outstanding discriminatory power (AUC of 0.90; 95% CI: 0.82-0.97) for COVID-19 patients that later required mechanical ventilation or suffered death during hospitalization (6).

Contrary to some of the past studies (6,7), in present research we have documented a higher threshold value (≥6) for predicting worsening of COVID-19 infection, which coincides with NEWS2 risk levels implemented in sepsis. Our finding corroborate with a recent study conducted in neighboring India by Chikhalkar et al. (18) who found that NEWS2 score ≥6 is a statistically significant cut-off value for predicting adverse outcome on admission with 93.24% sensitivity and 98.91% specificity. This observation was also supported by a recent case control investigation (19). Additionally, in agreement to our finding, Rigoni et al. (20) previously recorded NEWS2 score of 6 and above on admission is the best predictor of progressive disease in COVID-19 patients. The author reported 80% sensitivity and 84.3% specificity, with an AUC of 0.822 (20). However, previous authors recommended more research for validation of their findings in view of retrospective design and use of convenience sampling (18,20). In contrast, this research is a multicenter cohort. We have employed CDC criteria for stratification of poor outcomes and for recruitment of the participants. Furthermore, we have validated the performance of NEWS2 cut-offs for risk assessment to predict poor outcomes in COVID-19 disease.

Several studies demonstrated increased risk of clinical deterioration in COVID-19 cases with pre-existing comorbidities (21). On the assessment of our secondary objective, we found that six of the independent factors were significantly associated with worsening condition. However, the risk analysis yielded all factors has increased odds of poor outcome except malignancy. Surprisingly, pulmonary pathologies revealed no association with disease progression. This could be related to the low prevalence of respiratory disorders in our series. Alternatively, the differences in statistical estimates seen in studies might be due to the heterogeneous selection of outcome parameters.

Study Limitations

The results of the present research have better external validity due to prospective and multicenter research design. We have estimated the predictive performance of discrete NEWS2 cut-offs, while most authors evaluated the predictive accuracy of a single threshold value in the COVID-19 setting (6,9). In addition, we have employed the relative risk, which is a more robust test than the odds ratio, used in past studies to determine the adverse outcomes in COVID-19 patients. Moreover, being the first study on NEWS2 from Pakistan, our findings will assist in introducing a new clinical algorithm in local setups for stratification of cases that are expected to get worse overtime. This in turn allows physicians to use our medical resources for those who are on the utmost need.

Besides these strengths, there are some limitations to this study. First, our sample size is lower than some other cohorts. Second, we used clinical history and previous laboratory tests for characterizing comorbidities, and fresh diagnostic investigations were not performed for reassessment of their current status.

Conclusion

NEWS2 score of 6 and above at admission could predict adverse outcomes in COVID-19 patients with high sensitivity (78.1%) and specificity (89.4%). Some of the pre-existing comorbidities are associated with poor outcomes and increased risk of clinical deterioration. We suggest that the NEWS2 score should be assessed in all patients on admission and physicians should be alarmed for the possibility of severe disease in cases with a score greater or equals to 6. However, this conclusion needs to be further validated on a larger scale.

Ethics

Ethics Committee Approval: The study was approved by the Ethic Review Committee Ziauddin University, Karachi, Pakistan (ERC #1701219FHPAT, date: 10.02.2020).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.H., Concept: F.A.B., Design: F.A.B., Data Collection or Processing: A.H., Analysis or Interpretation: F.A.B., A.H., Literature Search: F.A.B., Writing: F.A.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
Case Report
DOI: 10.4274/eajem.galenos.2021.57805
Eurasian J Emerg Med. 2023;22(1): 55-7

Necrotizing Fasciitis as Complication of Combined Use of Bevacizumab with Chemotherapy

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Abstract

Necrotizing fasciitis (NF) is an uncommon, severe, life-threatening soft tissue infection involving the subcutaneous tissue. Immunocompromised and patients with diabetes are at a higher risk of developing NF. One of the pathophysiologic mechanisms of NF is subcutaneous arterie thrombosis and tissue ischemia. Bevacizumab, a agent used in cancer treatment, blocks the activity of the vascular endothelial growth factor receptor. Recently, it is used along with paclitaxel and carboplatin due to an increased survival rate. The frequent use of this combination caused patients to applied to the emergency department (ED) with some side effects. NF is one of the rare side effects of this combination. Here, we present a patient with ovarian cancer who was admitted to the ED with severe leg pain, whose initial examination and tests were normal, and then NF developed within hours and then arrested.

Keywords: Fasciitis, necrotizing, drug therapy, bevacizumab, emergencies

Introduction

Cancer is one of the most common and fatal diseases in the modern era. Current treatment options are traditional chemotherapeutic agents, antiangiogenic therapy, and immunotherapy. Antiangiogenic agents are important for treating many solid tumors. Vascular endothelial growth factor is an important target for therapy as it is the primary mediator in angiogenesis and induced by multiple stimuli in tumor development (1). Bevacizumab, one of the antiangiogenic agents (2,3), shows a significant success rate for treating non-small-cell lung cancer and colorectal, gastric, and ovarian cancer (4). Recently, it is used along with paclitaxel and carboplatin due to the increased non-progressive survival rate in the long term. It is more widely used because of these promising research, but emergency admissions are also increasing due to the various side effects. Necrotizing fasciitis (NF) is reported in a few cases as one of the side effects of bevacizumab treatment. Traditional chemotherapeutic agents can also cause several side effects, and there are cases of NF reported after the combination treatment of bevacizumab and paclitaxel (5,6).

Here, we report a patient with NF because of a combination treatment of bevacizumab, carboplatin, and paclitaxel in a patient with ovarian cancer, admitted to the emergency department (ED).

Case Report

A 65-year-old female patient came to ED with pain on the outer side of her left leg and cramps on the left foot dorsum. She described the severity of her pain as 10/10. Her medical history includes hypertensionand ovarian cancer diagnosed 2 months ago with liver metastases, and rectum invasion. Her surgical history includes cholecystectomy, splenectomy, total abdominal salpingoopherectomy, omentectomy, and appendectomy. After surgery, she was started on bevacizumab, paclitaxel, and carboplatin combination therapy. She took her second dose of treatment 10 days ago. Lower extremity physical examination findings were completely normal. Homans test was negative, the extremities were warm, and pulses were equal bilaterally. Lower extremity color Doppler ultrasound (USG) was ordered. Blood flow was evaluated as normal. No deep vein thrombosis and no superficial venous thrombophlebitis were found. In the

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Received: 01.04.2021
Accepted: 07.06.2021

Cite this article as: Emir C, Aktaş C, Aydın AG. Necrotizing Fasciitis as Complication of Combined Use of Bevacizumab with Chemotherapy. Eurasian J Emerg Med. 2023;22(1): 55-7.

superficial USG exam to the left lateral cruris, no pathologies were detected in cutaneous and subcutaneous tissues. Blood tests were unremarkable. As analgesic treatment, the patient was given paracetamol 10 mg/mL intravenous (IV), dexketoprofen 50 mg IV, and tramadol hcl 100 mg IV in ED. After treatment, her pain diminished and since no pathologies were detected and she was discharged.

After 4 h of her discharge, she came to ED with pain, ecchymosis, and edema in her left leg. She was agitated. Blood pressure: 90/60 mmHg, respiratory rate: 16/min, pulse: 98/min, SpO_2: 99%. In the lower extremity examination, her lower 1/3 thigh and lower leg were ecchymotic, edematous, and there was subcutaneous crepitation to palpation. Femoral pulses were present, and distal pulses were weak and palpable. 2-view radiographs of the cruris were ordered; there were subcutaneous air densities lateral to knee joint soft tissue and on the fibula (Figure 1). Lower extremity Doppler USG was performed. subcutaneous fat tissue increased, there was 6 mm effusion between the fat tissue and fascia, with comet artifacts. Left lower extremity computed tomography was performed. Air densities on the femoral vein, saphena magna; on vascular traces through the popliteal fossa, cruris and foot; on distal leg, knee and cruris level were commented as NF (Figures 2, 3). Infectious diseases and orthopedics were consulted. Meropenem 1 gr IV, metronidazole 500 mg IV was given in ED. While planning the patient's hospitalization, the patient was suddenly arrested in the ED and CPR was performed, but the patient was unresponsive.

Discussion

NF most frequently involves the abdominal wall, peritoneal membranes, and lower extremities. NF cases have been reported as more likely to arise in the presence of human immunodeficiency virus infection, diabetes, cancer, alcoholism, vascular insufficiencies, organ transplant - related immunodefiencies, and chronic diseases (7). The use of bevacizumab and paclitaxel were reported as a cause of NF. In 2013, during a safety research conducted for bevacizumab therapy, 52 NF cases and 17 related deaths were reported from November 1997 to September 2012 (8). NF has been recorded as one of the side effects since 2013. The world Health Organization reported 7 NF cases developed after pactikaxel use as a combination therapy with bevacizumab (9). The case we presented supports the literature that bevazicumab and paclitaxel combination therapy increases the risk of developing NF. Although the mechanism is unclear, the progression rate of NF can last days from its beginning or develop quickly in hours ending up with death. In our case, the disease showed a rapid course and resulted in death within a few hours.

Conclusion

Although it is a rare complication, physicians should be reminded of the fact that patients admitted to ED with acute extremity pain and who are taking combined bevacizumab and paclitaxel therapy, carry a risk of having NF with rapid progression and death.

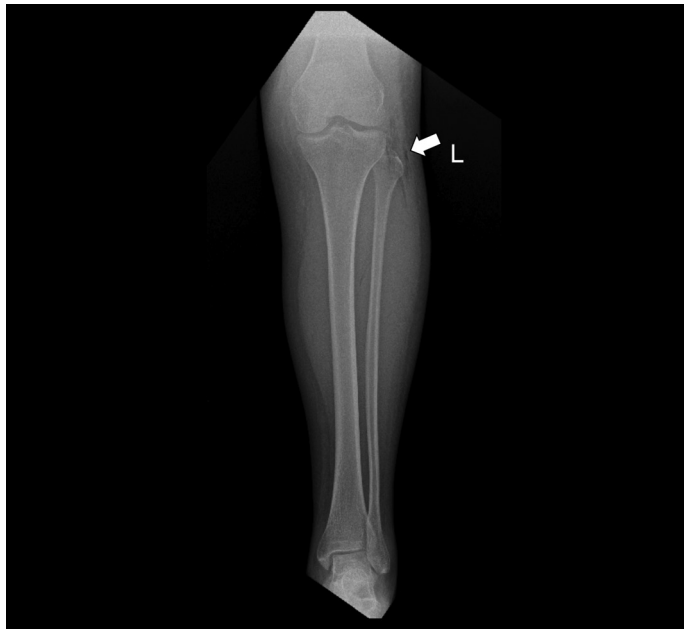

Figure 1. Left knee X-ray. Subcutaneous air densities in the superposed area over the soft tissues and fibula, adjacent to the lateral side of the knee joint

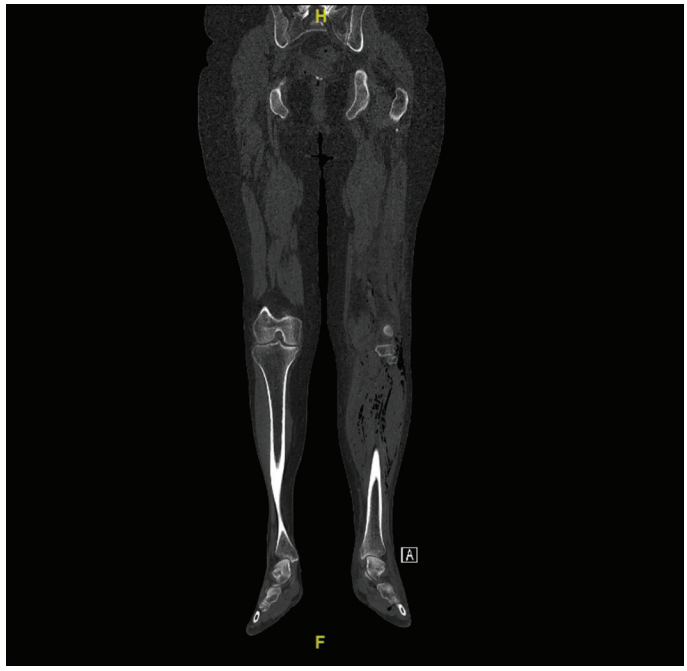

Figure 2. Lower extremity computed tomography. Air densities at the knee and cruris levels

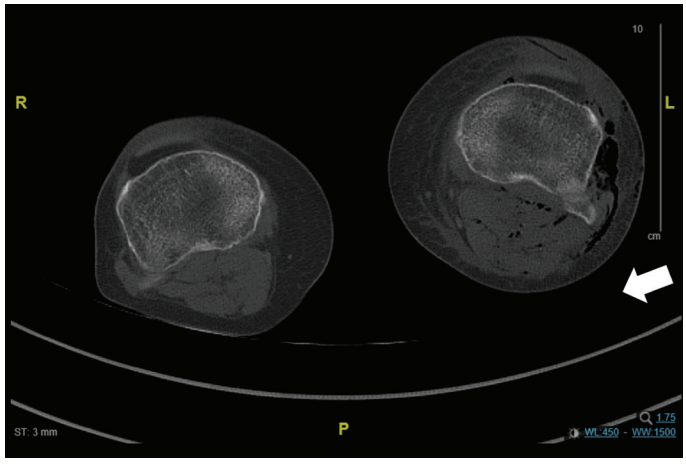

Figure 3. Lower extremity computed tomography

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Design: C.A., Data Collection or Processing: C.E., Literature Search: A.G.A., Writing: C.E.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
DOI: 10.4274/eajem.galenos.2021.05902
Case Report
Eurasian J Emerg Med. 2023;22(1): 58-61

Development of Pituitary Apoplexy in a Patient with Meningioma and Pituitary Macroadenoma: A Case Report

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Abstract

Although pituitary adenomas and meningiomas are among the commonly encountered benign tumors, the co-existence of these tumors is rare. One of the most important complications of pituitary adenomas is the development of apoplexy, often resulting in death if left untreated. In this article, we present a patient admitted to the emergency department with complaints of sudden-onset headache, nausea, vomiting, and optic nerve paralysis. On examination, the case was found to have parietal lobe meningioma and pituitary adenoma. Therefore, the case underwent emergent transsphenoidal surgery considering pituitary apoplexy and was treated with l-thyroxine and hydrocortisone in the post-operative period. Although the co-existence of a pituitary adenoma and a meningioma is known in the literature, such a co-existence with apoplexy is the first case to be described in the literature.

Keywords: Apoplexy, hypophysis, meningioma, pituitary adenoma

Introduction

Pituitary apoplexy is one of the major complications of pituitary adenomas and is known to be one of the endocrinological emergencies manifesting itself with headache, visual impairment, hypopituitarism, and cranial nerve paralysis. If untreated medically and/or surgically, pituitary apoplexy can result in death. The frequency of apoplexy ranges between 2 and 12% in patients with pituitary adenomas (1). Apoplexy generally develops suddenly at the base of a non-functional or functional pituitary adenoma, triggered by hypertension, anticoagulant therapy, increased intracranial pressure, and major surgery, and sometimes also occurs idiopathically due to necrosis triggered by dynamic tests and sometimes owing to hemorrhages, and thus resulting in a rapid increase in the size of the pituitary gland (1,2). Apoplexy may also lead to deaths if it goes untreated surgically and/or conservatively medically.

Meningiomas are tumors with a commonly often benign nature and originating from arachnoidal cap cells by constituting 13%-26% of intracranial tumors (3). Meningiomas are generally seen in later periods of life and among women (3). Complete surgical excision is the standard treatment, and radiotherapy can also be administered for treating atypical, recurrent, or malignant meningiomas (3).

Although the number of meningiomas is limited, the cases of meningiomas co-existent with functional or non-functional pituitary adenomas have been reported in the literature (4-6). Some cases of meningiomas, especially those originating from the region of the diaphragmatic sella, may present with an appearance similar to pituitary adenomas and cause diagnostic confusion (4-6).

In our report, we presented a case detected with a pituitary macroadenoma and a right parietal lobe meningioma in

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Cite this article as: Yılmaz H, Adıbelli Z, Akkuş C, Demirci H, Mızrak B, Duran C. Development of Pituitary Apoplexy in a Patient with Meningioma and Pituitary Macroadenoma: A Case Report. Eurasian J Emerg Med. 2023;22(1): 58-61.

Received: 19.06.2021
Accepted: 06.08.2021

emergency examinations performed due to the clinic of pituitary apoplexy, where hypopituitarism developed after surgical debulking by the transsphenoidal route.

Case Report

A 72-year-old female patient was found to develop severe headache with sudden onset, nausea, vomiting, vision loss in the left eye, and left-eyelid ptosis on cranial computerized tomography (CT) performed nearly three months ago (on 8th October 2020). On CT examination, an extra-axially located calcific meningioma on the right side of the cranium was determined (Figures 1A, B). Additionally, a peripherally located extra-axial meningioma in size of 12x11 mm was detected in the lateral part of the parietal lobe on cranial magnetic resonance imaging (MRI). A 22 mm adenoma, the borders of which could not be distinguished, was also identified within the pituitary gland (Figures 2A-D). At once, considering pituitary adenoma and apoplexy in the case, an emergent pituitary decompression surgery was performed by the transsphenoidal route under the coverage of steroids, and during the surgery, the pressurized hematoma or adenoma was observed to be evacuated after the dura incision. The histopathological examination of the hypophysectomy material of the case, where postoperative hypopituitarism was detected and steroid therapy was continued, revealed that the lesion was completely necrotic. Through the medical history, it was determined that the case had been diagnosed with low-grade non-Hodgkin lymphoma (NHL) 34 years ago, received chemotherapy due to the recurrence twice 34 and 12 years ago, undergone hysterectomy 30 years ago, had hypothyroidism for 25 years, and so received the treatment with levothyroxine 50 µg/day po recently, and had chronic hepatitis B infection for 18 years and thus been treated with entecavir of 0.5 mg tb 1x1 po lately. The medical history also revealed that the case had hypertension for 10 years, and most recently received a combination therapy of perindopril/indapamide 4 mg/1.25 mg 1x1 po with amlodipine of 5 mg 1x1 po, as well as receiving metformin 2x850 mg po due to type 2 diabetes mellitus (T2DM) for the last seven years. The patient having received hydrocortisone treatment of 3x10 mg po within the latest period was admitted to our department. On physical examination, the case (height: 162 cm, weight: 72 kg, and body mass index: 27.4 kg/m^2), was found to be conscious, cooperative, and full of motor functions. Blood pressure and visual field examination of the case were observed to be within the normal limits. Given the re-examination of the specimens prepared in the pathology unit, it was detected that while the preparations were inappropriate for healthy histopathological evaluation due to necrosis, the background was composed of the cells with monotonous appearance not constituting a distinct pattern, and these cells were stained with synaptophysin in immunohistochemical examination (Figures 3A, B). Therefore, the case was followed up in the outpatient clinic with the current treatment.

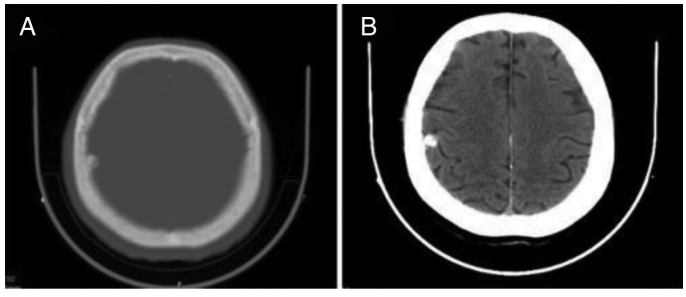

Figure 1. The extra-axially located calcific nodular mass lesion (calcific meningioma) is present on the right side of the bone window (A) and parenchymal window images (B) taken through unenhanced computerized tomography

Discussion

In this report, we present a case developing pituitary apoplexy at the base of a pituitary adenoma and a simultaneous meningioma detected in the right parietal region. To our knowledge, no reports, including the co-existence of pituitary apoplexy and a meningioma, were encountered in the literature. Albeit their rarity, pituitary adenomas and meningiomas can be seen together. In some cases, both conditions can be found together as a collision tumor (7). Since adenomas and meningiomas are

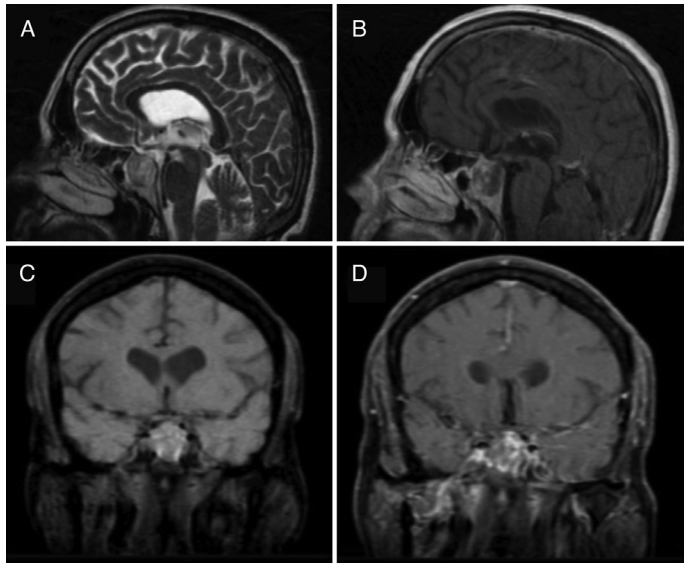

Figure 2. A) T2-weighted sagittal section. Magnetic resonance imaging (MRI) shows the heterogeneous enlargement of the pituitary gland, (B) T1-weighted contrast-enhanced sagittal, and (C) T1-weighted non-contrast coronal section. MRI shows the enlargement of the pituitary gland with heterogeneous hyperintense hemorrhagic areas, and (D) T1-weighted contrast-enhanced coronal section. MRI shows the heterogeneous contrast enhancement of the enlarged pituitary gland

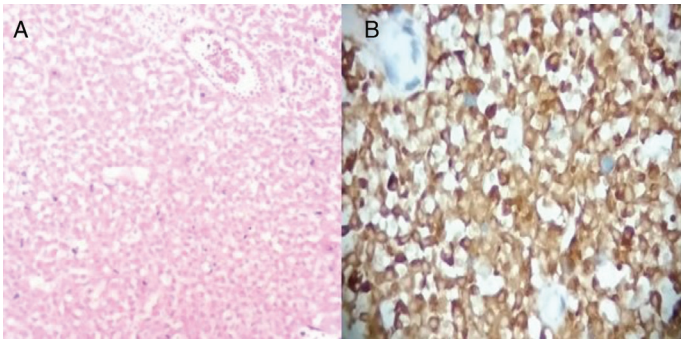

Figure 3. A) The area containing necrobiotic cells surrounded by necrotic tissue and thrombus-including venule (x20 magnification, stained with hematoxylin and eosin), and (B) diffuse synaptophysin positivity in cells. The vessel wall was negatively stained (x40 magnification)

often required to be removed by transsphenoidal surgery and craniotomy, respectively, the preoperative differential diagnoses of pituitary adenomas and meningiomas, particularly arising from diaphragmatic or tuberculum sella, are so important (6). It has been reported that contrast-enhanced dynamic pituitary MRI can be beneficial in the differential diagnosis of these two conditions (5). The meningioma in our case was detected in the parietal region, and thus, there was no diagnostic confusion. The reason for the co-existence of a meningioma and a pituitary adenoma has yet to be fully elucidated. In a study comparing 57 cases with pituitary adenoma-related meningiomas with those sporadic pituitary adenomas and sporadic meningiomas, Zhu et al. (8) reported that the lower expression of the multiple endocrine neoplasia type 1 gene is central to pituitary adenoma-related meningiomas by upregulating the mammalian target of the rapamycin (mTOR) signaling pathway, and that the treatment with rapamycin, an mTOR inhibitor, can be used by increasing apoptosis in treating pituitary adenomas in the future.

In our case, such clinically pre-existing symptoms as headache, problems of vision, and galactorrhea were absent. Additionally, our case was deprived of other clinical findings suggesting Cushing's syndrome or acromegaly, and probably the adenoma in our case was also non-functional. On pathological examination, it was determined that the base was composed of cells with a monotonous appearance not forming a distinct pattern. The immunohistochemical examination also revealed that these cells were stained with synaptophysin. Even so, no immunostaining could be performed for pituitary hormones due to necrotic tissues. The presence of necrotic tissues in the surgical material was also compatible with apoplexy. In her history, our case was determined to have been diagnosed with NHL, as in a remission state. Base on the literature, NHL exhibits sometimes an adenoma-like image by leading to the pituitary infiltration (9); however, there was no finding suggesting the lymphoma infiltration in the pathological examination of our case.

The prevalence of apoplexy ranges between 2-12% in patients with pituitary adenomas (1). Apoplexy is an emergency-requiring condition developing usually with hypertension, anticoagulant therapy, etc. at the base of a non-functional or functional pituitary adenoma, or developing sometimes idiopathically, occurring suddenly after the necrosis or hemorrhages, and resulting in a rapid increase in the size of the pituitary gland; it may also result in deaths if untreated surgically and/or conservatively medically (1,2). Her history revealed that our case had a medical history of hypertension and T2DM, and so receiving three antihypertensive drugs and one oral antidiabetic medication per day due to these diseases. The case also received L-thyroxine therapy for the pre-existing hypothyroidism. When diagnosed with apoplexy, the case underwent transsphenoidal surgery under the coverage of steroids and as the continuation therapy, hydrocortisone combined with L-thyroxine was continued.

Our case had a history of NHL existing for many years and currently in remission. Based on the literature, various cases rarely developing apoplexy in the lymphoma background have been reported (10). However, in our case, there was no lymphoma infiltration in the postoperative tissue, and immunostaining with synaptophysin was consistent with the pituitary adenoma.

Conclusion

In conclusion, in the report, we presented a case developing the pituitary apoplexy at the base of a pituitary adenoma and a parietal meningioma. Although the co-existence of a pituitary adenoma and a meningioma is known in the literature, such a co-existence with apoplexy is the first case to be described in the literature.

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices - Concept - Design - Data Collection or Processing - Analysis or Interpretation - Literature Search - Writing: H.Y., Z.A., C.A., H.D., B.M., C.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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DOI: 10.4274/eajem.galenos.2023.e001

Erratum

Eurasian J Emerg Med. 2023;22(1): 62

DOI: 10.4274/eajem.galenos.2021.65477

Pourahmad A, Karimi S, Elfil M, Babaniamansour S, Aliniagerdroudbari E, Baratloo A. The Accuracy of CPSS, LAPSS and MASS in Terms of Early Acute Ischemic Stroke Diagnosis. Eurasian J Emerg Med. 2022;21(1):50-5.

The mistake has been made inadvertently by the author.

The 5th institution on page 50 of the related article has been corrected by the author as below.

The incorrect 5th institution

[5]Research Center for Trauma in Police Operation, Directorate of Health, Rescue and Treatment, Police Headquarter, Tehran, Iran

The corrected 5th institution

[5]Research Center for Trauma in Police Operation**s**, Directorate of Health, Rescue **&** Treatment, Police Headquarter, Tehran, Iran