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: 20
Issue: 1

www.eajem.com

March
2021

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Official Journal of Emergency Physicians Association of Turkey

EAJEM
Eurasian Journal of Emergency Medicine
Citation abbreviation: Eurasian J Emerg Med

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Printing at: Üniform Basım San. ve Turizm Ltd. Şti. Matbaacılar Sanayi Sitesi 1. Cad. No: 114 34204 Bağcılar, İstanbul, Turkey
Phone: +90 (212) 429 10 00 **Certificate Number:** 42419
Printing Date: March 2021 **ISSN:** 2149-5807 **E-ISSN:** 2149-6048
International scientific journal published quarterly.

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Case Report	1500	200	10	No tables	10 or total of 20 images
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Original Article
DOI: 10.4274/eajem.galenos.2020.95866
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Initial Versus Final Diagnosis in Patients Who Presented to the Emergency Department Without Trauma: A Prospective Cohort Study

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Abstract

Aim: In the emergency department (ED), some patients are discharged after their initial diagnosis and treatment, whereas others are hospitalized for treatment and/or further diagnostic examination. The ED physician usually does not receive feedback regarding diagnostic accuracy, treatment effectiveness, or morbidity or mortality of the patient. In this study, patients in the ED without trauma were followed up to obtain their data.

Materials and Methods: This prospective cohort study includes all patients without trauma who are admitted to the ED of a tertiary hospital during the two-month time frame and were hospitalized in various clinics. Data recorded for each patient are the following: demographic information, vital signs, diagnosis upon admission, diagnosis after hospitalization, length of stay, mortality, and complications.

Results: A total of 740 patients that met the inclusion criteria participated in this study. The mean age was 54 years, wherein 398 patients (53.8%) were male. The initial diagnosis of 22 patients (2.9%) changed after further examinations. The mean age of these patients were 42 years, and 11 patients were male (50%). Emergency invasive intervention was significantly more common among patients with changed diagnosis (cDx) (40.9% vs 4.1%, $p<0.001$). Consequently, the incidence of complications was higher in cDx patients (31.8% vs 10.8%, $p=0.01$).

Conclusion: Majority of patients hospitalized from the ED were treated according to their initial diagnosis until the initial department of hospitalization. We conclude that ED functions at an adequate accuracy despite their high workload.

Keywords: Emergency department, hospitalization, non-traumatic complications, mortality, diagnosis

Introduction

Emergency departments (EDs) are designed to provide continuous medical care to ensure that fast decisions are made in order to prevent patient death and disability. People come to EDs with a great variety of diseases, which translate in to differences in diagnosis and treatment of physical and behavioral problems.

Some patients are discharged following initial diagnosis and treatment, whereas others are hospitalized for treatment and/or further diagnostic examination (1-3). As the ED physician does not follow up with treatment after hospitalization, they usually do not receive feedback regarding the accuracy of their diagnosis, the effectiveness of the treatment, or the morbidity/mortality of the patient. The literature review revealed several studies concerning changed and missed diagnoses among trauma patients (3-6). However, there are only a few articles that concern this issue. Therefore, we aimed to evaluate the demographic characteristics, complications and the initial and final diagnoses of non-traumatic patients that were hospitalized from ED.

Materials and Methods

This prospective cohort study was approved by the local ethics committee (decision no: 521, date:10.12.2014), and was conducted in a tertiary care university hospital ED in accordance with the

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Received: 21.02.2020
Accepted: 02.07.2020

Cite this article as: Mutlu H, Korkut M, Soyuncu S, Bedel C. Initial Versus Final Diagnosis in Patients Who Presented to the Emergency Department Without Trauma: A Prospective Cohort Study. Eurasian J Emerg Med. 2021;20(1):1-5.

Helsinki Declaration Principles. A total of 16,672 patients were treated in the ED during the two-month period, and 740 (4.4%) of these patients were hospitalized (Figure 1). The inclusion criteria were: (a) patients under 18 years old, (b) initial admission to ED, (c) hospitalization. The exclusion criteria were: (a) traumatic injury, (b) hospitalization in a different medical center due to hospital reaching capacity. A form was created for the follow-up and treatment of hospitalized patients, which was filled by the ED physician during treatment. Diagnostic evaluation was recorded by specialist doctors and residents with >3 years' experience. The following data were recorded for each patient: demographic information, vital signs, triage levels, diagnosis at the time of admission, diagnosis after hospitalization, length of stay, mortality and complications during treatment. The triage category of the patients was made (green, yellow, red, black) and the patients were grouped. A change in the initial diagnosis at follow-up was noted. Patients with and without diagnostic changes were compared in terms of parameters. However, the clinical diagnosis may differ from the initial diagnosis, and therefore the main diagnosis was targeted in these cases. The primary outcome of the present study was to determine the initial and final diagnoses of non-traumatic patients that were hospitalized from ED. The second outcome was to investigate the changes in diagnosis and the outcome of these patients.

Statistical Analysis

The data were analyzed using SPSS version 20.0. Demographic data were assessed by descriptive tests, and expressed as percentages, mean ± standard deviation, or median and interquartile range. Chi-square test was used for the comparison of categorical variables. All hypotheses were bi-directional, and significance level was set at 0.05.

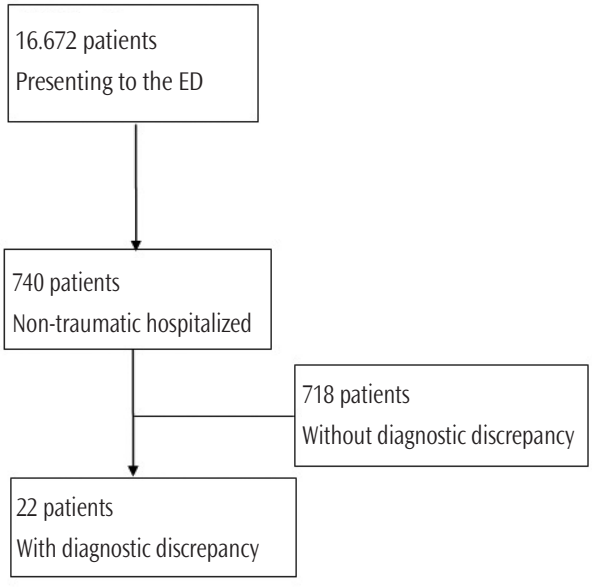

Figure 1. Patient flow chart
ED: Emergency depatment

Results

A total of 740 subjects were included in the study. Mean age was 54 years, 398 patients (53.8%) were male. Median GCS at the time of admission 14.5, and GCS was below 8 for 11 patients (1.4%). Mean hospital length of stay was 7.36±8.55 days, and there were 40 hospital deaths (5.4%). The general characteristics of the subjects are presented in Table 1.

The initial diagnosis of 22 patients (2.9%) was changed after further examinations (cDx). Mean age of cDx patients was 42, and

Table 1. Demographics of study population

Included patients	**740**
Age years (P25-75)	54 (38-68.75)
Male sex, n (%)	398 (53.8%)
GCS <8 at presentation, n (%)	11 (1.4%)
Vital signs, initial	
Systolic blood pressure mmHg, (P25-75)	126 (110-146)
Diastolic blood pressure mmHg, (P25-75)	73 (60-85)
Heart rate beats per minute, (P25-75)	96 (81-125)
Temperature °C, (P25-75)	36.2 (36-36.8)
Oxygen saturation, % (P25-75)	98 (95-99)
Concomitant disease, n (%)	467 (63.1%)
Circumstantial factors	
Waiting time in ED, (min)	188.26±168.76
Time of arrival	
Daytime (08:00-16:00)	304 (41.1%)
Evening (16:00-00:00)	302 (40.8%)
Night time (00:00-08:00)	134 (18.1%)
Emergency intervention	39 (5.3%)
Triage category, n (%)	
1	38 (5.1%)
2	202 (27.3%)
3	483 (65.3%)
4	17 (2.3%)
Primary ICU admission	106 (14.3%)
Medical outcomes	
Complications	85 (11.4%)
In-hospital mortality, n (%)	40 (5.4%)
Length of hospital stay (day)	7.36±8.55

GCS: Glasgow Coma Scale, ED: Emergency department, ICU: Intensive care unit, n: Number

11 were male (50%). Mean length of ED stay was 166.18±87.19 minutes, mean systolic blood pressure was 123.5 mmHg, mean diastolic blood pressure was 73.5 mmHg, and mean length of stay was 7.33±8.62 days. Emergency invasive intervention was significantly more common among cDx patients (40.9% vs 4.1%, p<0.001). Consequently, the incidence of complications was higher in cDx patients (31.8% vs 10.8%, p=0.01). There was no significant difference between the groups in terms of other parameters (p>0.05). The comparison of demographic and etiological data is presented in Table 2. For cDx patients, initial ED diagnosis, diagnosis at the time of discharge, and the clinics that the patients were treated in are presented in Table 3.

Discussion

Majority of ED patients are discharged following initial diagnosis and treatment, whereas others are hospitalized for treatment and/or further diagnostic examination. Since the ED physician does not follow up with the patient after hospitalization, they usually do not receive feedback regarding the accuracy of their diagnosis, the effectiveness of the treatment, or the morbidity/mortality of the patient. The literature review revealed several studies concerning changed and missed diagnoses among trauma patients (4-8). Therefore, we chose to study non-traumatic patients. We aimed to evaluate the demographic characteristics, complications and the initial/final diagnoses of non-traumatic patients that were hospitalized from ED.

A total of 16,672 patients were treated in the ED during the two-month period. This study concerns non-traumatic patients that were treated in an adult ED, thus it does not include patients aged below 16 years. A total of 740 patients were included in the study, overall hospitalization rate was 4.4%. The hospitalization rate of the same hospital was 12.5% in previous years (9). Akpinar et al. (10) found this rate to be 12.8%. Another study conducted among patients hospitalized in the intensive care unit from the ED of a university hospital in the same country found average duration of ED stay to be 300 minutes (11,12). In our study, average stay in ED was 188.26±168.76 minutes. This relatively short average length of stay might be due to the low number of

Table 2. Characteristics of non-trauma patients with- and without changed of diagnosis

	Patients with changed of diagnosis (n=22)	Patients without changed of diagnosis (n=718)	Univariate OR (95% CI)	p-value
Age (years)	42 (32-65)	50.5 (30-67)	-	0.778
Male sex, n (%)	11 (50%)	387 (53.9%)	0.962 (0.412-2.247)	0.829
GCS <8 at presentation	3 (13.6%)	8 (1.1%)	0.801 (0.203-3.291)	0.694
Vital signs, initial				
Systolic blood pressure (mmHg)	123.5 (106.25-140.5)	125 (110-143.25)	-	0.852
Diastolic blood pressure (mmHg)	73.5 (69.75-80)	73 (60-85)	-	0.783
Heart rate (beats per minute)	91.5 (79.5-109)	96 (80-112.25)	-	0.532
Temperature (°C)	36.5 (36-37.08)	36.1 (36-36.7)	-	0.121
Oxygen saturation	98 (96-99)	98 (97-99)	-	0.137
Time of arrival	-	-	0.340 (0.120-0.872)	0.537
Daytime (08:00-16:00)	10 (45.5%)	292 (40.2%)	-	-
Evening (16:00-00:00)	10 (45.5%)	294 (40.9%)	-	-
Night time (00:00-08:00)	2 (9%)	132 (18.4%)	-	-
Emergency intervention	9 (40.9%)	30 (4.1%)	-	<0.001
Primary ICU admission	4 (18.1%)	102 (14.2%)	0.579 (0.136-2.563)	0.579
Medical outcomes				
Complications	7 (31.8%)	78 (10.8%)	3.722 (1.473-9.402)	0.01
In-hospital mortality, n (%)	3 (13.6%)	37 (5.1%)	0.377 (0.108-1.320)	0.104
Length of hospital stay (day)	7.33±8.62	8.55±6.23	-	0.061

GCS: Glasgow Coma Scale, ICU: Intensive care unit, CI: Confidence interval, OR: Odds ratio, n: Number

Table 3. Analysis of patients whose diagnosis was changed			
First diagnosis in ED	**Last diagnosis**	**Mortality**	**Clinics**
ACS	Brain tumour + pulmonary mass	No	Cardiology
ACS	Intestinal perforation	Yes	Cardiology
Cerebrovascular disease	Metabolic disorder	No	Neurology
Cerebrovascular disease	Hypertensive encephalopathy	No	Neurology
Bradycardia	Exacerbations of COPD	No	Cardiology
Cholecystitis	Pneumatosis carcionmatosa	No	General surgery
Choledocholithiasis	Liver cancer	Yes	Internal medicine
Acute renal failure	Acute adrenal insufficiency	No	Internal medicine
Abortion	Ectopic pregnancy	No	Obstetrics and gynaecology
Submandibular abscess	Brain tumour	No	Ear nose throat
Anemia etiology	Mantle cell lymphoma	No	Internal medicine
Etiology of fever	Infective arthritis	No	Infectious diseases
Asthma attack	Bronchiectasis	No	Chest diseases
Anemia etiology	Hemarthroses	No	Infectious diseases
Pulmonary edema	Breast cancer	Yes	Cardiology
Transverse myelitis	Multiple sclerosis	No	Neurology
Lumbar disc herniation	Spinal tumour	No	Neurosurgery
Exacerbations of COPD	Pulmonary mass	No	Chest diseases
Renal abscess	Renal mass	No	Urology
Nonspecific abdominal pain	Portal vein thrombosis	No	Internal medicine
Pyelonephritis	Hemorrhagic ovarian cyst	No	Internal medicine
Acute appendicitis	Inflammatory bowel disease	No	General surgery

ED: Emergency department, ACS: Acute coronary syndrome, COPD: Chronic obstructive pulmonary disease

intensive care unit hospitalizations. The most important factor affecting duration of stay in ED is specialist consultations (13-16). Increasing age and comorbidities require the inclusion of more clinical departments in the treatment. In addition, comorbidities that concern different clinics bring about the requirement of choice between these clinics for hospitalization, leading to prolonged length of stay. In our study, there were 38 (5.1%) Level 1 and 483 (65.3%) Level 3 triage patients, thus, the majority of the subjects were Level 3 triage patients. This factor also contributes to the relatively short average length of ED stay.

The initial diagnoses of 22 subjects (2.9%) were different that the diagnosis at discharge (cDx). Giannakopoulos et al. (4) conducted a similar study, in which they found this rate to be 8.2%, whereas Chen et al. (17) found it to be 12.1%. They also found that 89.6% of cDx patients had life-threatening conditions. In our study, 11 (50%) of cDx patients were male, and the mean age was 42 years. One study found the mean age of cDx patients to be 38.6, and that 69.5% were male (17). Another study found that age and gender were not significant factors in diagnosis change (4).

In our study, the mean length of ED stay (from admission until hospitalization) of cDx patients was 166.18±87.19 minute, and mean length of stay was 7.33±8.62 days. Another study of 976 patients, found the mean length of ED stay and mean length of stay to be 18.5 minutes and 4.3 days, respectively. We believe that the difference in length of ED stay is due to the difference in patients' comorbidities and hospital policies. In our study, most cDx patients had applied between 08:00-16:00 (n=10, 45.5%). However, Chen et al. (17) reported that the most common application time for cDx patients was between 16:00-24:00 (41.5%). In both studies, the smallest number of applications was between 00:00-08:00, as consistent with the literature (18).

Emergency invasive intervention was significantly more common among cDx patients (40.9% vs 4.1%, $p<0.001$). Also, the incidence of complications was higher in cDx patients (31.8% vs 10.8%, $p=0.01$). One study found this rate to be 23.9% (17); however, the shorter length of ED stay in this study may have led to the comparatively low rate. Another study found the rate of

complications to be 5.9% in cDx patients; however, unlike our study, this difference was not significant (17).

The symptom that is the most difficult to distinguish is abdominal and chest pain. Therefore, patients with epigastric pain should be examined for acute coronary syndrome (ACS) (19). In our study, one patient was admitted to the cardiology clinic with potential ACS; however, further examinations revealed intestinal perforation, and the patient died during surgical intervention.

Study Limitations

The limitations of our study are as follows: (a) the limited time frame and the relatively small sample size, (b) exclusion of physical examination findings and symptoms, (c) differences between the diagnosis and treatment methods among clinicians, despite being specialists or senior residents, (d) different treatment and protocols after hospitalization, and not standardizing the physicians making the final diagnosis. The scarcity of relevant literature requires multicenter and prospective studies.

Conclusion

EDs provide intensive medical care, and make up a significant source of hospitalizations. In our study, majority of patients that were hospitalized from the ED were treated with their initial diagnosis and in the initial department of hospitalization. We conclude that the ED performs physical examination, imaging, laboratory and consultation functions at an adequate accuracy despite their high workload.

Ethics

Ethics Committee Approval: Prior to implementation, this study's protocol was approved by Akdeniz University Ethics Committee (decision no: 521, date: 10/12/2014).

Informed Consent: An informed consent form was obtained from each patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.M., S.S., Concept: H.M., M.K., S.S., C.B., Design: H.M., M.K., S.S., C.B., Data Collection or Processing: H.M., M.K., S.S., Analysis or Interpretation: H.M., S.S., C.B., Literature Search: H.M., M.K., S.S., C.B., Writing: H.M., M.K., S.S., C.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
Original Article
DOI: 10.4274/eajem.galenos.2020.69885
Eurasian J Emerg Med. 2021;20(1): 6-11

Factors Affecting Prognosis in Patients with Snakebite

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Abstract

Aim: This study aimed to determine the factors influencing hospitalization durations and discharge status of patients with snakebite, starting from pre-hospital care in the field.

Materials and Methods: A total of 38 patients with snakebite admitted to the emergency medicine department between May 1st, 2013 and August 31st, 2016, participated in the study. Data were evaluated using Statistical Package for the Social Sciences 17.0.

Results: A total of 38 patients were enrolled, of which, 17 (44.7%) were female. Of the 38 patients enrolled, nine patients were in stage 1, 24 in stage 2, and 5 in stage 3. The mean antivenoms given to patients were 3.33±1.29 vials in stage 2 and 4.40±1.14 vials in stage 3. The mean time from bite to antivenom infusion was 80.92±47.57 mins. Hospitalization durations of patients with shorter bite to antivenom infusion intervals (bite-to-needle) were also shorter ($p<0.001$). In addition, overweight patients were found to stay longer in the hospital ($p=0.027$). Patients with low hemoglobin and platelet counts and high creatine kinase (CK) levels were found to stay longer in the hospital ($p<0.05$).

Conclusion: Shorter hospitalization durations of patients with shorter bite-to-needle times show the importance of early administration of antivenom. Moreover, longer hospitalization durations of overweight patients seem to reflect their slow wound-healing times, which may be due to co-morbidities. Low platelet, hemoglobin, and CK are found to be poor prognostic markers in patients with snakebite.

Keywords: Emergency department, snakebite, prognosis

Introduction

As it is throughout the whole world, snakebite is an important cause of morbidity and mortality in Turkey. The estimated number of snakebite victims is 421,000, resulting in 20,000 deaths worldwide (1). More specifically, the annual number of deaths due to snakebites in India was 1,350 in 2004-2009; in the United States, there are five deaths per 7,000-8,000 bites (2,3). Although serious envenoming occurs with snakebites, proper first aid and efficient treatment may help in reducing mortality.

The species *Macrovipera lebetina* and *Vipera barani* comprise most snakes in our region of Turkey (4). These species' toxins cause serious local tissue toxicity due to consumption coagulopathy. Seasonal variations and the rural nature of this entity cause difficulties for obtaining reliable epidemiological data. For this reason, we aimed to investigate in-hospital factors influencing the hospitalisation durations and discharge statuses of snakebite patients, as well as prehospital factors in the field.

Materials and Methods

Patients who were admitted to the emergency department (ED) of Çukurova University Medical School between July 2013 and August 2016 with a history of snakebite were enrolled in the study. The protocol was approved by Çukurova University Faculty of Medicine Noninvasive Clinical Researches Ethics Committee (decision no: 5, date: 05.07.2013).

The exclusion criteria were receiving anticoagulation treatments, having coagulation problems due to chronic diseases and not having fang wounds.

The patients were monitored in the critical care unit of the ED, where their blood samples were obtained for whole blood count,

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Received: 05.05.2020
Accepted: 06.07.2020

Cite this article as: Özbulat M, Açıkalın A, Akday U, Taşkın Ö, Dişel NR, Sebe A. Factors Affecting Prognosis in Patients with Snakebite. Eurasian J Emerg Med. 2021;20(1):6-11.

biochemical and coagulation analyses. Clinical staging is used to standardise the diagnosis, treatment strategies and management and determine the severity of the bite in snake bite patients (5). The stages of the envenoming were assessed according to the local and systemic findings. Table 1 reveals the classification of the staging (5).

Primary wound care and prophylaxis for tetanus were given to the patients, and stage 2 and 3 patients received antivenom. The extremities were immobilised, and the interventions and medications given in the previous hospital were recorded. Prophylaxis for wound infection was given if improper first aid had been performed (e.g. cutting and suction of wound or applying herbal ointments). Fresh frozen plasma (FFP) was given at a dose of 10 mL/kg to patients with coagulation abnormalities and non-regressing tissue oedemas after antivenom infusion.

The body mass indices (BMIs) of the patients were calculated. For the BMI, a result <18.5 kg/m^2 is classified as underweight, 18.5-24.9 kg/m^2 as normal weight, 25-29.9 kg/m^2 as overweight, 30-39.9 kg/m^2 as obese and >40 kg/m^2 as highly obese. The patients were assessed repeatedly for antivenom requirements during hospitalisation and given supplemental vials if needed according to the clinical stages.

Statistical Analysis

The data in our study were analysed using SPSS version 17.0. The normally distributed variables were compared using a t-test and repeated measurement analysis. Variables that were not normally distributed were compared using the Mann-Whitney U test and Friedman test. The χ^2 test was used for categorical variables. The results were expressed as the mean (standard deviation), median (minimum-maximum), n and percentage. A p-value less than 0.05 was considered statistically significant.

Results

Thirty-eight patients (44.7% female) were enrolled in the study. Eight (21.1%) had applied independently after snakebite, so our clinic was the first point of medical contact. The other patients were given different treatments in rural hospitals, from which they were transferred to our ED. The demographics and vital signs of the study patients are summarised in Table 2.

Twenty patients (52.6%) were bitten on the lower extremities, 17 (44.7%) were bitten on the upper extremities and one was bitten on the posterior thoracic region. The first systemic staging of the patients was as follows: nine (23.7%) were stage 1, 24 (63.2%) were stage 2 and five (13.2%) were stage 3.

Thirty-five (92.1%) study patients had improper first-aid interventions, such as a tight tourniquet and/or cutting/suction/bleeding in the prehospital field. Three patients had not received any first aid. Thirty (79%) patients who had infection risks due to cutting and suction were started on prophylactic antibiotics, and nine of them had soft tissue infections. Infection was controlled in all the patients.

The mean time interval between bite and antivenom infusion of the study patients was 80.92±47.57 minutes. When the antivenom doses of the patients were examined, stage 2 patients received 3.33±1.29 vials of antivenom, while stage 3 patients received 4.40±1.14 vials. Of the study patients who received additive vials during hospitalisation, the reason was because they received insufficient vials in the previous hospital in 14

Table 1. Clinical staging of snakebite and treatment (5)

Stage	Findings	Antivenom	Supportive care	Hospitalization/discharging
0	No local or systemic findings (first 8-12 hours)	None	Wound care Tetanus prophylaxis	Discharge after observing 8-12 hours if does not progress to stages 1, 2 or 3
1	Minimal edema around bite without systemic findings	None	Wound care Tetanus prophylaxis	24 hours observation with monitorizing
2	Edeme not exceeding half of the affected extremity, ecchymosis, minimal hematologic abnormalities	Needed	Wound care Tetanus prophylaxis İntravenous crystalloids Cardiac monitorization Analgesics Follow-up for laboratory tests	Intensive care unit hospitalization
3	Edema in the whole extremity, serious pain, compartment syndrome, and serious systemic findings (shock, loss of muscle strength, coagulopathy, spontaneous bleeding, acute renal failure i.e.)	Needed	Wound care Tetanus prophylaxis intravenous crystalloids Cardiac monitorization Analgesics Follow-up for laboratory tests Oxygen Vazopressors if needed	Intensive care unit hospitalization

patients and progressive tissue oedema despite proper treatment in four others. Of the 38 study patients, only one experienced allergy due to antivenom, and anaphylactic shock was managed successfully.

The mean hospitalisation durations of the study patients were as follows: 44.22±26.94 hours in stage 1 patients, 54.73±34.32 hours in stage 2 patients and 70.20±9.17 hours in stage 3 patients. The patients with a shorter time interval between the bite and antivenom infusion (bite-to-needle time) were found to be hospitalised for shorter durations (Table 3).

The relationships between hospitalisation durations and patients' BMIs were examined. The study patients were normal or overweight, and the hospitalisation duration was found to be longer in overweight patients (Table 3). The haematological and biochemical analyses of the study patients revealed that low haemoglobin, low platelets and elevated creatinine kinase (CK) are correlated with long hospitalisation durations (Table 4).

Discussion

Snakebite is a serious health problem, especially in tropical regions of the world. Patients can develop long term disability and suffer psychological sequel. The species and poisons vary according to the region, resulting in different clinical findings. The Çukurova region of Turkey is rich with poisonous snakes. *Macrovipera lebetina* and *Vipera barani* are the major poisonous snakes in our region (4). Such species cause local tissue oedema, compartment syndrome, rhabdomyolysis, haemolysis, renal failure and coagulopathy. Local tissue oedema is the major toxicity that occurs after being bitten by our region's snakes, which makes it very important to give proper first aid.

Most feared local complication is compartment syndrome. This situation can lead to permanent disability. However, snakebite patients receiving effective treatment in early period may experience compartment syndrome rarely. The use of tourniquets, which compromise arterial and venous circulation, causes serious oedema and compartment syndrome. In addition to tourniquet use, cutting and suction which were performed by the bystanders also causes damage, and this approach is also still performed in snakebites.

Thirty-eight patients in our study had improper first-aid interventions, while three patients had not received any first aid at all. Nine patients had soft tissue infections despite being started on antibiotics because of cutting and suction of their wounds. All the patients were successfully cured with antibiotics. Delayed treatment in snake bites may cause severe local and systemic serious complications such as necrotizing faciitis and

Table 2. Clinical findings of patients

	Mean ± SD	Min-max
Age	41.7±17.2	18-84
Weight	71.55±12.44	50-90
Height	167.23±7.03	150-180
BMI	25.52±3.84	19-34
Systolic blood pressure	118.94±14.10	70-140
Diastolic blood pressure	72.76±9.20	40-80
Pulse rate	78.86±9.82	61-105
Oxygen saturation	97.57±1.48	94-100
Body temperature	36.52±0.50	35-38

BMI: Body mass index, SD: Standard deviation, min: Minimum, max: Maximum

Table 3. Relation between bite-to-needle time and BMI with hospitalization time

	Hospitalization time	p-value
Bite-to-needle time (minute) 80.92±47.57	(2.25±1.28) (days) (54.0±30.72) (hours)	<0.001
BMI		
Normal weight (n=18)	42.61±26.31 (hours)	0.027
Over weight (n=20)	64.35±31.77 (hours)	

BMI: Body mass index, n: Number

Table 4. Relationship of hospitalization durations and laboratory results

Laboratory results		Hospitalization (Mean ± SD)	p-value
Hb (11.6-15.5 g/dL)	normal	65.20±34.47	0.017*
	low	41.66±21.13	
PLT (156-372 10^3/µL)	normal	74.90±35.10	0.037*
	low	46.60±26.13	
Glucose (70-100 mg/dL)	normal	50.75±23.56	0.617
	high	55.57±34.13	
AST (15-41 U/L)	normal	52.00±30.15	0.272
	elevated	91.00±26.87	
ALT (7-35 U/L)	normal	54.25±31.79	0.530
	elevated	50.50±3.53	
BUN (8-20 mg/dL)	normal	53.44±31.49	0.578
	elevated	65.0±21.21	
Creatinine (0.4-1 mg/dL)	normal	52.91±31.79	0.246
	elevated	67.33±15.53	
CK (38-234 U/L)	normal	46.15±27.81	0.029*
	elevated	71.16±31.53	
Lactate (0.5-2.2 mmol/L)	normal	47.00±31.53	0.056
	elevated	66.14±26.77	
aPTT (20-35 sn)	normal	51.20±30.20	0.069
	elevated	87.33±20.03	
INR (0.85-1.2 INR)	normal	51.29±29.27	0.351
	elevated	66.28±37.47	
PT (11-15 sn)	normal	51.29±29.27	0.351
	elevated	66.28±37.47	

SD: Standard deviation, Hb: Hemoglobin, PLT: Platelet, AST: Aspartate transaminase, ALT: Alanine aminotransferase, BUN: Blood urea nitrogen, CK: Creatinine kinase, APTT: Activated partial thromboplastin time, INR: International normalized ratio, PT: Prothrombin time *: Significant values

mediastinitis. Surgical debridement may be required in these cases. In a study conducted in 2017 in South Africa, Wagener et al. (6), a total of 164 patients included a study, of whom 57 required surgical debridement. Forty-two patients had positive cultures. Thirty-five specimens (83.3%) grew Gram-negative Enterobacteriaceae, the most frequent being Morganella morganii and Proteus species detected by Microbiological analyses. None of our patients required surgical debridement. Celulitis was the most common infection which was controlled by ampiric antibiotic treatment. We believe that our management with profilactic antibiotics in patients with wrong first aid measures helped low serious infection rate (6,7).

In a study conducted in 2001 in Brazil, Ribeiro et al. (8) reported that tourniquet use was related to serious tissue necrosis in *Bothrops jararaca* (Brazilian pit viper) envenoming cases. Pressure immobilisation bandages are recommended in envenoming except for some snake species that can cause local tissue oedema (9,10).

In a study conducted in India in 2008, Suchithra et al. (11) reported that wrong implementation is the major problem in pressure immobilisation. They concluded that this aid causes time loss for snakebite patients. Nearly all the patients' first aid involved a tourniquet in our study; thus, we could not compare tissue necrosis in patients with and without tourniquets.

Of the 38 study patients, the 20 who were overweight were affected more seriously and hospitalised longer (64.35±31.77 hours vs 42.61±26.31). Hyperglysemia, skin and soft tissue infections, are prevalent in the obese patients, which are expected in this population (12). Obesity is found to correlate with prolonged hospitalization which may be due to delayed wound healing and comorbidities of obese patients.

The major problem we realised in snakebite cases was the time loss during applying, referral and transportation to the adequate clinic for treatment. Patients should be evaluated for staging according to the envenomation presentation and given antivenom as quickly as possible. We calculated the time interval between snakebite and antivenom administration to prove the effectiveness of the early administration of antivenom in neutralising the toxic effects of venom. Our patients were evaluated quickly, and antivenom was given at a proper dose after staging. Low bite-to-needle time was correlated with low hospitalisation.

In a study by Sharma et al. (13) conducted in east Nepal in 2004, mortality was found to be correlated with hospital admission time after envenomation. Suchithra et al. (11) also reported a correlation of complication frequency with hospital admission time after envenomation.

There are two strategies on antivenom usage in snakebite treatment, namely, the traditional high-dose versus current low-dose antivenom administrations. Studies conducted in our region reported the effectiveness of low-dose antivenom in the successful treatment of snakebite (14). In their study in India, Das et al. (15) compared the effectiveness of high and low doses in a study and reported that low doses are as effective as high doses and lead to early patient discharge. Stage 2 and three patients were given 3.33±1.29 and 4.40±1.14 vials, respectively, in our study. All the study patients were cured with low doses.

Antivenom may cause serious allergies. As reported in one study, despite premedication, the rate of allergy after antivenom is 17.8% in our region (14). Although no premedication was given to our study patients, only one anaphylactic reaction was observed. The antivenom infusion was stopped, anaphylaxis was treated properly and a quick recovery was achieved. The current antivenoms seem to be less allergic than the old ones were.

The hemotoxic effects of our region's snakes may lead to coagulopathy. FFP was given to the patients in stage 3 in whom expected recovery could not be achieved with antivenom in the treatment of coagulopathy. In 2013, Isbister et al. (16) reported that, in patients with coagulopathy, FFP given as an additive to antivenom helped correct coagulation abnormality but had no effect on early discharge. We also could not find any relationship between FFP usage and hospitalisation duration.

In a study reported in 2016, Li et al. (17) demonstrated that elevated CK and low hemoglobin (Hb) are correlated with snakebite-related acute renal failure. Athappan et al. (18) reported that, intravascular hemolysis, cellulitis, regional lymphadenopathy, more than 2 hours of admission (bite-to-needle time), hypotension, massive bleeding were independent risks for renal disfunction in a series of 159 snakebite patients.

High CK and low Hb may be accepted as markers of serious envenomation, leading to longer hospitalisation. We report the long hospitalisation durations of patients with low platelets and low Hb, as well as elevated CK, which is compatible with the literature. In a study conducted by Ozay et al. (19) in 2005, low platelets were found to lead to more complications as well as longer hospitalisations. The researchers also reported that a platelet level <100,000/mm^3 was a high risk factor.

Study Limitations

The cases of this study were all from The Mediterranean Region. The snake species seen in Turkey are similar in all regions. This study is performed in only one center in The Mediterranean Region which is the major limitation of the study.

Conclusion

There are many harmful, wrong and improperly implemented first-aid measures that cause damage in snakebites. Public education is needed in this matter. The antibiotic usage rate is high because of wrong first aid. The association between shorter bite-to-needle times and shorter hospitalisation durations shows the importance of early administration of antivenom. Low-dose antivenom is effective in snakebite cases and allergy is extremely rare. The long hospitalisation durations in overweight patients may reflect a slower healing process in snakebite cases due to co-morbidities. The long durations of hospitalisation in patients with low platelets, low haemoglobin and elevated CK may lead to interpretation of these markers as poor prognostic indicators.

Ethics

Ethics Committee Approval: This study was approved by Çukurova University Faculty of Medicine Noninvasive Clinical Researches Ethics Committee (decision no: 5, date: 05.07.2013).

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Design: M.Ö., A.A., Data Collection or Processing: M.Ö., A.A., U.A., Ö.T., Analysis or Interpretation: M.Ö., A.A., U.A., N.R.D., A.S., Ö.T., Literature Search: M.Ö., A.A., U.A., N.R.D., A.S., Ö.T., Writing: M.Ö., A.A., U.A., N.R.D., A.S., Ö.T.

Conflict of Interest: The authors declare no conflict of interest.

Financial Disclosure: None declared.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
DOI: 10.4274/eajem.galenos.2020.37039
Original Article
Eurasian J Emerg Med. 2021;20(1): 12-8

Evaluation of the Demographic and Laboratory Data of Patients Diagnosed with Crimean-Congo Hemorrhagic Fever in the Emergency Department and Their Relationship with Morbidity and Mortality

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Abstract

Aim: Crimean-Congo hemorrhagic fever (CCHF) is transmitted by infected ticks or through contaminated blood, tissue, and body fluids. Pathological laboratory results, such as thrombocytopenia, leukopenia, and anemia, along with biochemistry and coagulation parameters, can be used for its diagnosis and the determination of its prognosis.

Materials and Methods: Data of patients over 17 years of age diagnosed with CCHF between 2013 and 2018 were reviewed retrospectively. The complete blood count, liver-renal enzymes, electrolytes, prothrombin time, activated partial thromboplastin time (aPTT), D-dimer values, fibrinogen values, and international normalized ratio (INR) were recorded and analyzed at admission.

Results: Non-survivors had higher levels of alkaline phosphatase, alanine aminotransferase, amylase, aspartate aminotransferase (AST), blood urea nitrogen (BUN), direct bilirubin, gamma-glutamyl transferase, creatinine, potassium, total bilirubin and uric acid ($p<0.05$), whereas creatine kinase (CK), CK-MB, and calcium levels were lower ($p<0.05$). Non-survivors had higher levels of basophil, mean corpuscular hemoglobin concentration, mean corpuscular volume, neutrophil, nucleated red blood cells, platelet distribution width, and white blood cells ($p<0.05$).

Conclusion: Evaluation of routine blood parameters of CCHF patients in the emergency room is a useful tool to accelerate recovery in intensive care and prevent delay in patient treatment. Platelet, aPTT, INR, BUN, and AST values are predictors for mortality.

Keywords: Crimean-Congo hemorrhagic fever, white blood cell, thrombocyte, mortality

Introduction

Crimean-Congo hemorrhagic fever (CCHF) is one of the most common, fatal viral hemorrhagic fevers in the world. It is seen in many countries, especially in Asia, Africa, southeast Europe, and the Middle East (1). CCHF virus causes severe and fatal infection among vertebrae only in humans (2). The cause of CCHF is an RNA virus belonging to the Nairovirus genus from the Bunyaviridae family. The virus is transmitted to humans by infected ticks or by contact with contaminated blood, tissue, and body fluids. The risk of infection as a result of contact with infected blood is 8.7%, especially during the follow-up of patients with bleeding. The risk rises to 33% in the case of needle stick injuries. The highest transmission is observed with a percutaneous injury. The fetal transmission has been reported to a small extent (3). The disease is seen in the spring, summer, and autumn seasons and peak in July (4).

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Received: 17.06.2020
Accepted: 22.07.2020

Cite this article as: Soylu Ü, Demirtaş E, Büyüktuna SA, Korkmaz İ, Tekin YK, Yurtbay S. Evaluation of the Demographic and Laboratory Data of Patients Diagnosed with Crimean-Congo Hemorrhagic Fever in the Emergency Department and Their Relationship with Morbidity and Mortality. Eurasian J Emerg Med. 2021;20(1):12-8.

Thrombocytopenia is a severe laboratory finding in CCHF. The presence of severe thrombocytopenia in the early period can be considered as a clue that the disease may be fatal (5). The direct cytopathic effect of the virus is blamed for liver damage in the disease. Increased liver enzymes, edema in cells, and necrosis occur as a result of the CCHF virus infecting hepatocytes widely. As a result, bleeding occurs as a result of hemophagocytosis and liver dysfunction (6-9). Thrombocytopenia, leukopenia, and neutropenia occur in almost all cases. Severe patients may have anemia. Aspartate transferase (AST), alanine transferase (ALT), lactate dehydrogenase (LDH), and creatinine phosphokinase (CPK) levels are high. Total protein and albumin values may decrease, and prothrombin time (PT) and activated partial thromboplastin time (aPTT) among hemostasis tests are prolonged. Fibrinogen levels may decrease, and fibrin degradation products may increase. In severe patients, bilirubin, urea, and creatine values may increase (10,11).

Using routine laboratory data in determining patients with fatal diseases such as CCHF will help the decision-making process of physicians. To our knowledge, there are studies on this topic in the literature, but there are limited studies with such a large number of cases. In this study, we aimed to investigate the laboratory results and demographic data of the patients who were diagnosed with CCHF in the last five years and to assess their roles in predicting mortality.

Materials and Methods

After the approval of the local ethics committee, the files of patients over the age of 17 who were diagnosed with CCHF between 2013 and 2018 were reviewed retrospectively. Ages, genders, and admission dates were recorded. The investigated admission laboratory parameters were as follows: fasting and postprandial blood glucose, alkaline phosphatase (ALP), ALT, amylase, AST, blood urea nitrogen (BUN), creatine kinase (CK), creatine kinase-MB (CK-MB), direct bilirubin, total bilirubin, gamma-glutamyltransferase (GGT), calcium (Ca), chloride (Cl), potassium (K), sodium (Na), creatinine, uric acid; basophil, eosinophil, hematocrit (HCT), hemoglobin (HGB), lymphocyte, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), monocyte, mean platelet volume (MPV), neutrophil, nucleated red blood cells (NRBC), plasma thromboplastin component (PTC), platelet distribution width (PDW), platelets (PLT), red blood cell (RBC), white blood cell (WBC); PT, aPTT, D-dimer, fibrinogen and international normalized ratio (INR). Patients with missing data were not included in the study.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows version 23.0 (IBM, Armonk, NY, USA), and continuous data were reported as mean ± standard deviation or median, and categorical data were given as number and percentage. Kolmogorov-Smirnov test was used as a test for normality for continuous data, and parametric paired and unpaired t-tests were used. Receiver operating characteristic (ROC) analysis was used to determine the diagnostic efficiency of the laboratory parameters.

Results

Table 1 presents the gender distribution of patients with CCHF according to mortality. No statistically significant difference was observed between the two groups in terms of gender ($p>0.05$). No statistically significant difference was observed in the within-group evaluations. There was no effect of gender on mortality in CCHF patients. When the age was compared in terms of mortality, no statistically significant difference was found between the groups.

The distribution of patients according to the months of admission is given in Figure 1. The highest admission total was recorded as 134 patients in July. Again, the highest mortality was observed in July. No statistically significant difference was found in comparing the mortality of the disease by months ($p>0.05$).

Table 2 shows the comparison of the laboratory data of the survivors and non-survivors. Regarding biochemistry parameters, non-survivors had higher levels of ALP, ALT, Amylase, AST, BUN, direct bilirubin, GGT, creatinine, K, total bilirubin and uric acid levels and this was statistically significant ($p<0.05$). In the non-

Table 1. Comparison of survivors and non-survivors in terms of gender

Gender	**Non-survivors (%)**	**Survivors (%)**	**p**
Female	11 (36.7%)	191 (41.3%)	>0.05
Male	19 (63.3%)	271 (58.7%)	
	p>0.05	**p>0.05**	
Age	59.76±15.89	53.54±15.89	>0.05

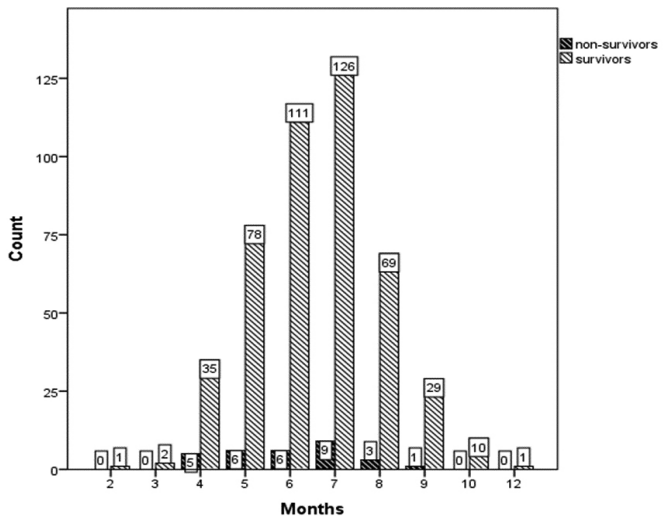

Figure 1. The distribution of patients according to the months of admission

survivor group, CK, CK-MB, and Ca levels were lower, and this was statistically significant ($p<0.05$). No statistically significant difference was found in fasting and postprandial glucose levels, Na and Cl levels between two groups ($p>0.05$). Regarding complete blood count (CBC) parameters, non-survivors had higher levels of basophil, MCHC, MCV, neutrophil, NRBC, PDW, and WBC, and this was statistically significant ($p<0.05$). There was no statistically significant difference in terms of HCT, HGB, MCH, MPV, PDW, RBC, eosinophil, and lymphocyte count between two groups ($p>0.05$). In the non-survivor group, monocyte, PTC, and PLT levels were lower, and this was statistically significant ($p<0.05$). Regarding coagulation parameters, non-survivors had higher levels of aPTT, D-dimer, and INR, and this was statistically significant ($p<0.05$). In the non-survivor group, fibrinogen and PT levels were lower, and this was statistically significant ($p<0.05$).

Table 3 shows the sensitivity, specificity, positive predictive values, negative predictive values, and area under curve values of the laboratory values of the patients according to the ROC analysis. AST and BUN from biochemical parameters, PLT from CBC parameters, and aPTT and INR from coagulation parameters had the highest AUC parameters. Figure 2 shows the ROC analysis charts.

Discussion

Our study, in which we examined a large number of patient populations, revealed that ALT, AST, BUN, creatinine, CK-MB, aPTT, INR, PT, fibrinogen, and PLT could be functional determinants in demonstrating CCHF mortality.

In the studies conducted, no statistically significant difference was found between the survivors and non-survivors in terms of age and gender (12-14). In our study, in accordance with the literature, both groups show similar characteristics in terms of age and gender. Again, in our study, it was observed that the mortality was high in June and July when the disease was prevalent.

When the literature is reviewed, CBC parameters were evaluated in many studies. In a study of 152 patients with CCHF evaluated by Yilmaz et al. (15), admission HGB and PLT values were lower in the severe patient group than in the non-severe group, and this difference was significant (HGB cut-off: 13.5, AUC; 0.61, PLT cut-off: 90,000, AUC: 0.70). They stated that WBC was similar in both groups, and there was no statistical difference. In a study by Hatipoglu et al. (14), they examined the laboratory data of 152 CCHF patients as predictors of mortality. They found that HGB and WBC values were high in patients with mortality, and PLT values were low. In a study conducted by Arslan et al. (16), PLT and HGB values were found to be significantly lower in patients with bleeding compared to the group with no bleeding, and they did not find a statistically significant difference between WBC and CRP values. In the study by Öngörü et al. (12) in which they examined the relationship between coagulation parameters and mortality in CCHF patients, they found that PLT rates were significantly lower in the non-survivors. In the study of evaluating the laboratory and clinical features of CCHF patients as predictors of mortality, Kazancioğlu et al. (17) evaluated a total of 92 patients (77 survivors and 15 non-survivors). They found that the admission levels of HB and WBC did not differ significantly between the non-survivors and survivors. The admission PLT levels were found to be statistically significantly lower in the non-survivors. They found a cut-off value of <30,000 for admission PLT with 85.7% sensitivity and 81.8% specificity (AUC: 0.840). In the severity scoring system of CCHF developed by Bakır et al. (18), PLT decrease and WBC increase are included in the scoring system. In our study, we found many significant differences in CBC parameters, but according to ROC analysis, the PLT cut-off value of <119,500 was the most successful parameter with 79% sensitivity and 83% specificity. These values were also compatible with the literature. Studies reported different opinions with WBC increase. In our study, WBC was significantly higher in the non-survivor group. Again, there are conflicting opinions about HB in the literature. In our study, we found that admission HGB level was not significantly different between the two groups. We think that additional attention should be paid to the lower HGB levels in patients presenting with bleeding.

Table 2. Comparison of laboratory data between survivors and non-survivors diagnosed with CCHF

Laboratory parameters (25-75%)	Non-survivors (n=30)	Survivors (n=462)	p
HCT (%)	44.95 (41.6-51.1)	43.65 (40.3-46.9)	0.068
HGB (g/dL)	15.2 (14.4-17.4)	14.7 (13.5-16)	0.073
Lymphocytes (%)	32 (21.8-47.4)	46.9 (34.4-56)	**0.001**
MCH (g/dL)	30.65 (29.1-31.5)	29.90 (28.7-31.1)	**0.091**
MCHC (g/dL)	34.95 (34.4-36.4)	34.60 (33.7-35.3)	**0.028**
MCV (%)	89.75 (86.5-92.4)	87.90 (84.4-91.4)	**0.045**
Monocytes (%)	5.05 (2.3-9.3)	12.03 (9-15.6)	**0.001**
MPV (%)	11.45 (10.7-12.4)	11.05 (10.2-12)	0.127
Neutrophils (%)	84.25 (77.6-89.1)	71.6 (58.8-84.3)	**0.001**
PTC (%)	0.09 (0.05-0.11)	0.16 (0.12-0.2)	**0.001**
PDW (%)	17.05 (15.80-18.70)	16.60 (15-19.10)	**0.014**
PLT (1,000/uL)	81 (40-115)	156 (125-206)	**0.001**
RBC (10^6/uL)	5.2 (4.7-5.92)	5.08 (4.68-5.47)	0.201
WBC (µL)	8.11 (4.04-15.74)	5.53 (4.26-7.56)	**0.004**
Fasting glucose (mg/dL)	160.5 (107-205)	111 (97-135)	0.065
ALP (U/L)	226 (153-279)	87 (67-125)	**0.001**
ALT (U/L)	728 (235-1782)	94.5 (39-181)	**0.001**
Amylase (U/L)	159 (109-300)	76 (57-110)	**0.001**
AST (U/L)	2,397 (626-8,377)	128.5 (48-311)	**0.001**
BUN (mg/dL)	49.78 (34.09-79.73)	16.72 (12.24-22.98)	**0.001**
CK (U/L)	1417.5 (677.5-818)	232 (112-699)	**0.001**
CK-MB (U/L)	78 (44-134)	28.8 (21-43)	**0.001**
Direct bilirubin (U/L)	1.67 (0.07-10.84)	0.19 (0.12-0.35)	**0.001**
GGT (U/L)	213.5 (119-363.5)	57 (25-150)	**0.001**
Ca (mg/dL)	7.7 (7.47-8.97)	8.76 (8.34-9.12)	**0.001**
Cl (mEq/L)	106 (103-110)	105 (102-107)	0.078
Creatinine (mg/dL)	3.05 (1.71-4.74)	0.89 (0.75-1.09)	**0.001**
K (mEq)	4.94 (4.22-5.53)	4.35 (3.98-4.76)	**0.001**
Na (mEq/L)	140 (136-145)	139 (136-141)	0.203
Total bilirubin (U/L)	2.78 (0.83-4.81)	0.54 (0.4-0.94)	**0.001**
Uric acid (mg/dL)	7.7 (6.1-10.4)	4.80 (3.6-6.1)	**0.001**
aPTT (sec)	65.2 (53.9-75.7)	34.6 (30.5-41.2)	0.001
D-Dimer (µg/mL)	24,110 (5,780-6,895)	713 (179-2,692)	0.001
Fibrinogen (mg/dL)	224 (195-257)	345 (292-428)	0.001
INR	1.79 (1.42-2.64)	1.11 (1-1.28)	0.001
PT (sec)	20.9 (16.4-28.8)	13.25 (11.8-14.9)	0.001

CCHF: Crimean-Congo hemorrhagic fever, HCT: Hematocrit, HGB: Hemoglobin, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, MCV: mean corpuscular volume, MPV: Mean platelet volume, PTC: Plasma thromboplastin component, PDW: Platelet distribution width, PLT: Platelets, RBC: Red blood cell, WBC: White blood cell, ALP: Alkaline phosphatase, ALT: alanine transferase, AST: Aspartate transferase, BUN: Blood urea nitrogen, CK: Creatine kinase, CK-MB: Creatine kinase-MB, GGT: Gamma-glutamyltransferase, Ca: Calcium, Cl: chloride, K: Potassium, Na: Sodium, aPTT: Activated partial thromboplastin time, INR: International normalized ratio, PT: prothrombin time, n: Number
Important values are shown in bold

Table 3. Sensitivity, specificity, positive predictive values, negative predictive values and area under curve values of the patients' laboratory values according to ROC analysis

Test result variable(s)	AUC	SE	Asymptotic 95% confidence interval					p	PPV	NPV
			Lower bound	Upper bound	Cut-off	Sensitivity	Specificity			
ALP	**0.849**	[a]0.039	0.773	0.925	144	0.833	0.765	0.000	79.3	80.9
ALT	**0.863**	0.049	0.767	0.958	216	0.833	0.752	0.000	79.3	79.5
Amylase	0.807	0.057	0.695	0.918	124.5	0.778	0.797	0.000	74.1	79.8
AST	**0.911**	0.032	0.848	0.974	620.5	0.833	0.865	0.000	79.2	88.3
BUN	**0.919**	0.021	0.879	0.959	26.20	0.944	0.778	0.000	89.7	81.5
CK	**0.811**	0.040	0.733	0.889	524.5	0.889	0.691	0.000	83.3	70
CK-MB	**0.873**	0.036	0.803	0.944	43.95	0.889	0.752	0.000	80	75.9
GGT	0.754	0.056	0.644	0.864	178	0.722	0.778	0.000	60.7	80.1
Creatinine	**0.910**	0.032	0.848	0.972	2.015	0.833	0.910	0.000	72.4	92.8
Uric acid	**0.840**	0.039	0.764	0.917	6.050	0.833	0.733	0.000	81	74.9
aPTT	**0.932**	0.025	0.883	0.981	48.7	0.893	0.882	0.000	86.2	88.3
D-dimer	**0.816**	0.052	0.715	0.918	5174.5	0.786	0.848	0.000	78.6	84.3
INR	**0.886**	0.035	0.818	0.954	1.4150	0.750	0.862	0.000	75.9	86.5
PT	**0.878**	0.037	0.806	0.950	16.350	0.750	0.857	0.000	75.9	86
Fibrinogen*	**0.831**	0.054	0.726	0.936	257.50	0.904	0.759	0.000	75.9	90.1
Calcium*	0.722	0.062	0.600	0.843	8.1850	0.828	0.621	0.000	62	83
PLT*	**0.865**	0.04	0.774	0.955	119.50	0.790	0.833	0.000	83.3	79.4

ROC: Receiver operating characteristic curve, AUC: Area under the curve, SE: Standard error, PPV: Positive predictive value, NPV: Negative predictive value, ALP: Alkaline phosphatase, ALT: alanine transferase, AST: Aspartate transferase, BUN: Blood urea nitrogen, CK: Creatine kinase, CK-MB: Creatine kinase-MB, GGT: Gamma-glutamyltransferase, [a]PTT: Activated partial thromboplastin time, INR: International normalized ratio, PT: prothrombin time, PLT: Platelets
*: Increasing in fibrinogen and platelets and decrease of the other values were calculated

There are many studies examining biochemical parameters in CCHF. In these studies, especially AST, ALT, ALP, LDH values were found to be higher in severe patients (12-14,16). In the study conducted by Yilmaz et al. (15), no statistically significant difference was found between BUN and creatinine levels between clinically severe and mild groups. In the study of Kazancioğlu et al. (17), admission urea and creatinine levels were found to be significantly higher in the non-survivor group. The sensitivity and specificity of urea for a cut-off value of 27.5 were 92.9% and 58.4%, respectively (AUC=0.760). Similar to these studies, in our study, AST, ALT, ALP, LDH, GGT, CK, CK-MB, BUN, creatinine, and uric acid were higher in the non-survivor group, and these were statistically different parameters. Especially BUN and AST were the biochemical parameters to be considered in the non-survivor group. BUN cut-off value of 26.2 had 94.4% sensitivity and 77.8% specificity. AST cut-off value of 620 had 83% sensitivity and 86% specificity. In another study, Ca levels in children with CCHF were found to be low (18). We also found that Ca levels were significantly lower in the non-survivor group.

Abnormal bleeding time and coagulation parameters can be counted as the most common laboratory findings in patients with CCHF. When we look at the studies in the literature, an increase in aPTT, PT, PTT, and INR, and a decrease in fibrinogen are observed (19-21). In our study, we also found PT, aPTT, INR, and D-dimer increase and fibrinogen decrease in accordance with the literature. Especially aPTT and INR elevation had the highest sensitivity and specificity among these parameters. The aPTT cut-off value of 48.7 had 89.3% sensitivity and 88.2% specificity. INR cut-off value of 1.41 had 75% sensitivity and 86% specificity.

Conclusion

Evaluation of routine blood parameters of CCHF patients in the emergency room is a useful tool to accelerate hospitalization in intensive care and to prevent delay in the treatment of the patient. It should be kept in mind that PLT, aPTT, INR, BUN, and AST values, especially in patients with suspected CCHF, are predictors of mortality.

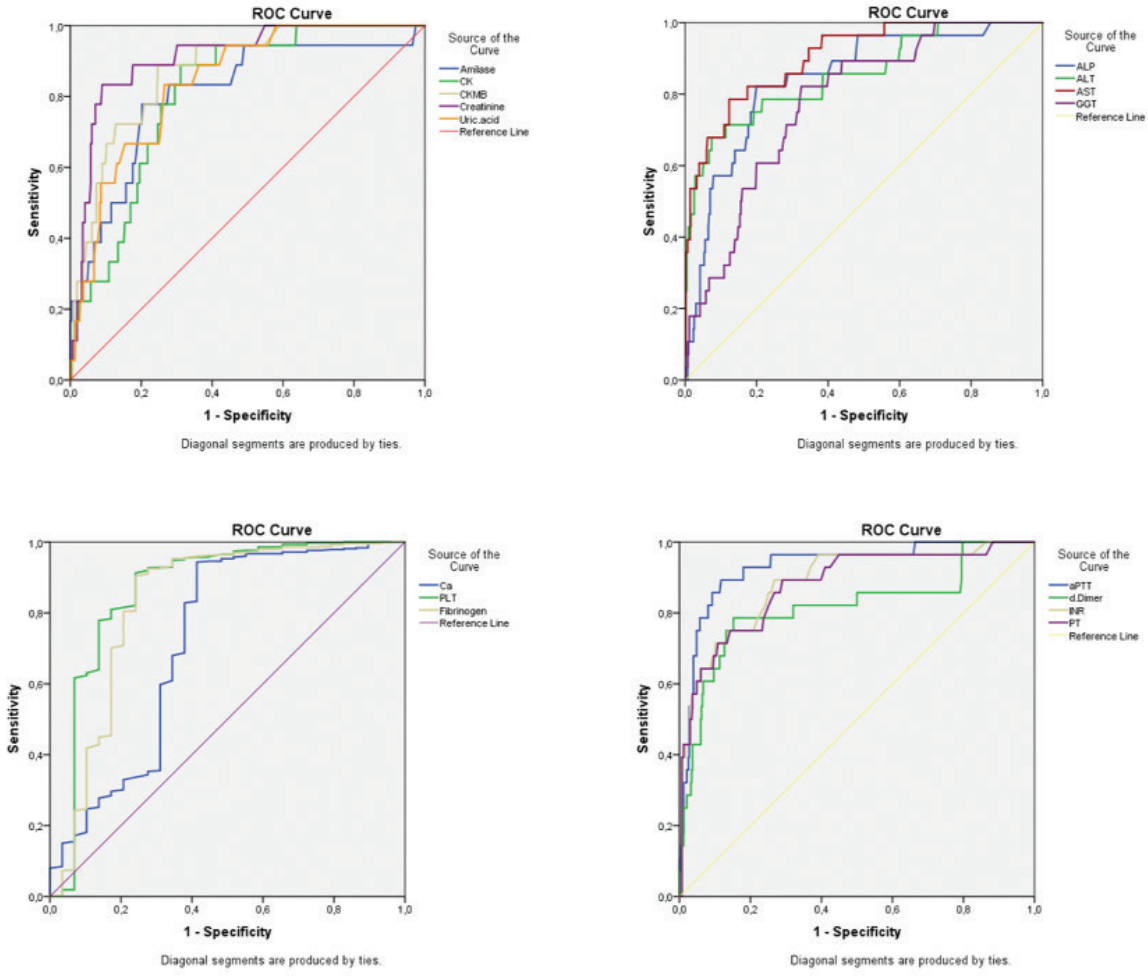

Figure 2. Shows the ROC analysis charts

ROC: Receiver operating characteristic curve, CK: Creatine kinase, CK-MB: Creatine kinase-MB, ALP: Alkaline phosphatase, ALT: Alanine transferase, AST: Aspartate transferase, aPTT: Activated partial thromboplastin time, INR: International normalized ratio, PT: Prothrombin time, PLT: Platelets

Ethics

Ethics Committee Approval: This retrospective study was approved by the institutional human ethics committee [Sivas Cumhuriyet University Ethics Committee (2018-11/06)].

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ü.S., E.D., S.A.B., Y.K.T., Concept: E.D., Y.K.T., Design: E.D., S.A.B., Y.K.T., Data Collection or Processing: İ.K., Y.K.T., S.Y., Analysis or Interpretation: E.D., İ.K., S.Y., Literature Search: E.D., S.A.B., S.Y., Writing: E.D., 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.2020.88942
Eurasian J Emerg Med. 2021;20(1): 19-24

Evaluation of Serum 25-Hydroxyvitamin Vitamin D, Vitamin B12, and Folate Levels in Patients with Benign Paroxysmal Positional Vertigo

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Abstract

Aim: This study aimed to compare 25-hydroxyvitamin D (25-OH Vit D), vitamin B12, and folic acid levels in patients presenting with vertigo diagnosed with benign paroxysmal positional vertigo (BPPV) and healthy volunteer control group without vertigo, and to examine whether they are disease-associated.

Materials and Methods: A total of 190 patients who applied between October to December 2019 diagnosed with BPPV and 149 volunteers without any complaints (control group), who came only for checkup, were included in the study. Serum 25-OH Vit D, vitamin B12, and folic acid levels of all participants were examined.

Results: Of all participants, 209 (61.6%) were male and 130 (38.4%) were female. Out of 94 participants, 25-OH Vit D level was found to be at low levels. Of participants with low 25-OH Vit D levels, 65 (69.1%) were in the BPPV group and 29 (30.9%) were in the control group. Of all participants, 68 had low folic acid levels, wherein 33 (48.5%) were in the control group and 35 (51.5%) were in the BPPV group. The level of vitamin B12 of 2 participants among all participants was below normal values and these 2 participants were in the BPPV group.

Conclusion: In our study, any significant relationship was not found between BPPV and serum vitamin B12 and serum folic acid levels. A significant relationship was determined between BPPV and decreased serum 25-OH Vit D level ($p<0.01$). We identified that low serum 25-OH Vit D levels may be an independent risk factor in the progress of BPPV.

Keywords: Vertigo, benign paroxysmal positional vertigo, 25-OH vitamin D, vitamin B12, folic acid

Introduction

Benign paroxysmal positional vertigo (BPPV) is the most common disease among peripheral vestibular diseases. BPPV, being the most common cause of vertigo in adults (1). BPPV occurs when the otoconia (otolith) breaks away from the utricular or saccular (vestibular end organs) macula, falls into one of the semicircular canals (canalithiasis) or attachesonto the cupula (cupulolithiasis). Clinical complaints occur when the otoconia's sensitivity to gravity increases (2). Cupulolithiasis and canalithiasis are two important mechanisms implicated in the development of BPPV disease. Canalithiasis is responsible for 80% of the cases (3). BPPV is a common disease and its lifetime prevalence is 2.4% (4). The main component of the otolith crystals is calcium carbonate and glycoprotein and these otoconia crystals attach to the hairy cells in the vestibule by protein bonds. It has been proven in studies that the otoconia crystals are the active calcium metabolite of the utricle and the saccule (5-8).

Rat studies have proven that vitamin D dependent calcium channel proteins play a role in active calcium metabolism of vestibular saccule and utricle (9-11).

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Received: 02.12.2019
Accepted: 17.08.2020

Cite this article as: Çelik H, Yardım A, Ertaş A, Varışlı B, Ocak Ö. Evaluation of Serum 25-Hydroxyvitamin Vitamin D, Vitamin B12, and Folate Levels in Patients with Benign Paroxysmal Positional Vertigo. Eurasian J Emerg Med. 2021;20(1):19-24.

Many studies have demonstrated that decrease in bone density, osteopenia and osteoporosis are associated with BPPV. Those studies compared BPPV patients with control groups in terms of 25-Hydroxyvitamin Vitamin D (25-OH Vit D) levels and showed that BPPV patients had lower 25-OH Vit D levels compared to control groups (10,12,13).

Some studies reported both BPPV development and BPPV recurrence to be associated with 25-OH Vit D deficiency. BPPV recurrence is common. BPPV repeats in one of every five cases which occurred in one year, and in one of two cases which occurred in 5 years (14).

Right posterior canal is the most commonly involved canal in BPPV and in 70% of the patient's unilateral involvement is the case (13). Involvement of the right side is attributed to the by the habit of lying on the right side the most. 85-90% of all BPPVs are composed of posterior canal BPPVs, 5-15% are horizontal canal BPPVs and less than 5% are anterior canal BPPVs (15).

Although the etiology of BPPV is not clear, some studies suggest that factors such as internal ear diseases, hormonal factors, female sex, viral diseases, migraine, head and neck traumas, senior age and family history are predisposing in disease formation (16-18).

The prevalence of BPPV in women is explained by the fact that migraine is more common in women and increased BPPV relationship in migraineurs (19).

BPPV carries the word "benign" in its name because vertigo is peripheral and can be treated successfully. It would be wrong to discontinue treatment considering that there would be spontaneous remission. There are studies suggesting that BPPV negatively affects daily life, increases the risk of falling and the frequency of depression, especially in the elderly and recurrent cases (16,20,21).

Clinical studies and rat studies indicate that the calcium metabolism in BPPV patients may be disrupted due to low 25-OH Vit D level (9-13).

In the literature, there are publications pointing out that low vitamin B12 level is associated with the development of BPPV, however there are also studies suggesting otherwise (22,23).

In addition, studies examining the relationship between peripheral vertigo and B12 have found a correlation between low level of vitamin B12 and development of vertigo (24,25).

There are studies investigating the relationship between folic acid level and vertigo, however no studies examining the relationship between folate and BPPV exist in the literature (26).

In this study we aimed to compare 25-OH Vit D, vitamin B12 and folic acid levels between BPPV patients and control group and to investigate the relationship of BPPV with the mentioned substances.

Materials and Methods

Consent of all patients and volunteers included in the study was obtained. We included in the patient group a total of 190 patients (120 males and 70 females) who presented to the outpatient clinics of neurology, otorhinolaryngology, emergency and neurosurgery with the complaint of dizziness and were diagnosed with BPPV in October and November 2019. Otorhinolaryngology specialist performed the Dix-Hallpike maneuver on all the patients who suffered from dizziness. We observed the side, direction, duration and fatigue characteristics of the cases which we determined to have nystagmus and we applied lateral canal test to those without nystagmus. We performed repositioning for canalithiasis and releasing maneuvers for cupulolithiasis for the treatment of patients diagnosed with BPPV. We controlled the patients again within 2-3 days periods and applied the requisite maneuvers as required. Dix-Hallpike and lateral canal tests were performed until nystagmus disappeared.

The control group was composed of 149 healthy volunteers (89 males and 60 females) who presented to the hospital for check-up and who did not receive 25-OH Vit D, B12 and folic acid supplements, had not previously been diagnosed with BPPV, had no complaints of dizziness within the past year, and had no history of trauma in the last 7 days. We performed neurological examination to the entire patient group. We excluded those with pathological findings in neurological examinations, who had unexpected hearing loss in audiometric examination, who had other peripheral or central vertigo other than BPPV, patients who had internal ear surgery, head trauma surgery, drug-induced ototoxicity, dizziness due to drug discontinuation. patients with diagnosed osteoporosis and those using B12, folate, and vitamin D replacement from the study.

Measurement of 25-OH Vitamin D, Vitamin B12, Folate Levels

25-OH Vit D, vitamin B12 and folic acid levels in the serum obtained from the morning blood samples taken from BPPV patients were measured in Mindray Perfect Plus 400 (Germany) biochemistry autoanalyzer by applying electroluminescence method.

We regarded the normal ranges of 25-OH Vit D, vitamin B12 and folate as 10.6-43.4 ng/mL, 211-911 pg/mL, and >5.38 ng/mL respectively. We then statistically compared the data of both groups.

The study was approved by the Ethics Committee of University of Health Sciences Turkey, Erzurum Regional Training and Research Hospital (no: 2019/12-122, date: 07.10.2019). We complied with the principles of the Declaration of Helsinki during the study.

Statistical Analysis

The difference in gender, vitamin D, vitamin B12 and folic acid levels between BPPV and control groups was made using the Mann-Whitney U test, one of the non-parametric tests. We analyzed the age relationships of BPPV and control groups by two independent sample t-tests. We employed SPSS 20.0 package program for all analyses. We regarded $p<0.05$ as statistically significant.

Results

The mean age of the control group was 33.14±13.44, while the mean age of the BPPV group was 43.68±16.04. There was no significant difference between the age and gender variables in the control group and in the BPPV group ($p>0.05$) (Table 1).

The number of patients with BPPV was 190 (56%) and the number of participants in the control group was 149 (44%). Of the male participants included in the study, 120 (57.4%) were in the BPPV group and 89 (42.6%) were in the control group. Of the female participants, 60 (46.2%) were in the control group and 70 (53.8%) were in the BPPV group. There was no significant difference between the gender variable and the progress of BPPV ($p>0.05$) (Table 2). Of the participants included in the study, the mean values of those with low levels of 25-OH Vit D, vitamin B12, and folic acid were 8.15±0.189 (ng/mL), 191.00±20.00 (pg/mL) and 3.73±0.143 (ng/mL) respectively, while these values were found to be as 18.91±0.442 (ng/mL), 457.38±7.15 (pg/mL) and 11.53±0.283 (ng/mL) respectively for those with normal values. Of 94 participants included in the study, 25-OH Vit D level was found to be at low levels. Of the participants with low 25-OH Vit D levels, 65 (69.1%) were in the BPPV group and 29 (30.9%) were in the control group. 25-OH Vit D levels of 245 participants included in the study were found to be at normal values. Of those with normal levels, 120 (49%) were in the control group and 125 (51%) were in the BPPV group (Graphic 1). We determined that the risk of developing BPPV was higher in those with low 25-OH Vit D ($p<0.01$) (Table 3). Of all participants included in the study, 68 had low folic acid levels and 33 (48.5%) of them were in the control group, while 35 (51.5%) of them were in the BPPV group (Table 4). The level of vitamin B12 of two participants among all participants included in the study was below the normal values (Table 5) and these two participants were in the BPPV group. We found that there was no relationship between the low or normal levels of vitamin B12 and folic acid with the prevalence of BPPV ($p>0.05$).

Table 1. Mean values age, vitamin B12, 25-OH D vitamin, folic acid of healthy and BPPV groups

Group statistics		n	Mean	SD	SE (mean)
Age (year)					
	Control	149	33.1477	13.44879	1.10177
	BPPV	190	43.6842	16.04080	1.16372
25-OH vitamin D (ng/mL)					
	Control	149	16.2928	6.66072	0.54567
	BPPV	190	15.6357	8.37392	0.60751
Vitamin B12 (pg/mL)					
	Control	149	453.6779	132.90361	10.88789
	BPPV	190	457.4842	132.57082	9.61770
Folic acid (ng/mL)					
	Control	149	9.5990	5.17374	0.42385
	BPPV	190	10.2671	5.28406	0.38335

BPPV: Benign paroxysmal positional vertigo, SD: Standard deviation, SE: Standard error, n: Number

Table 2. Gender distribution of healthy and BPPV groups

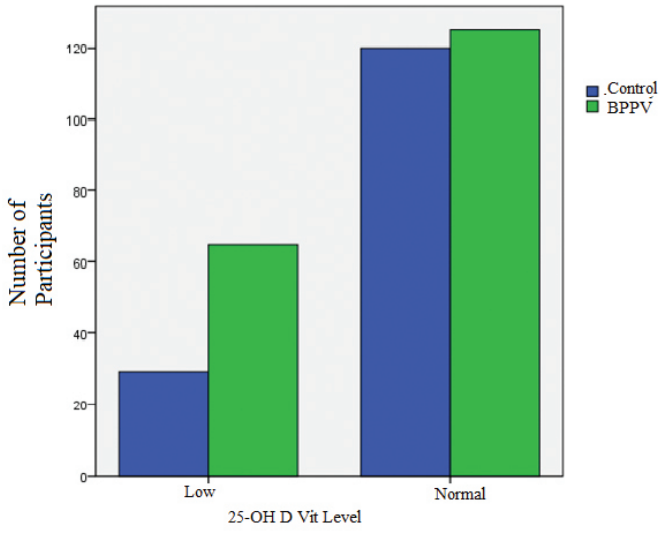
	Control	BPPV	Total	p-value
Male	89 (42.5%)	120 (57.4%)	209	p>0.05
Female	60 (46.1%)	70 (53.8%)	130	
Total	149	190	339	

BPPV: Benign paroxysmal positional vertigo

Table 3. Relationship between 25-OH vitamin D levels and BPPV group and control group					
		Control	**BPPV**	**Total**	**p-value**
25-OH D vitamin levels	Deficiency	29 (30.9%)	65 (69.1%)	94	p<0.01
	Normal	120 (49.0%)	125 (51.0%)	245	
Total		149	190	339	
BPPV: Benign paroxysmal positional vertigo					

Table 4. Relationship between folic acid level and BPPV group and control group					
		Control	**BPPV**	**Total**	**p-value**
Folic acid levels	Deficiency	33 (48.5%)	35 (51.5%)	68	p>0.05
	Normal	116 (42.8%)	155 (57.2%)	271	
Total		149	190	339	
BPPV: Benign paroxysmal positional vertigo					

Table 5. Relationship between vitamin B12 level and BPPV group and control group					
		Control	**BPPV**	**Total**	**p-value**
Vitamin B12 levels	Deficiency	0 (0%)	2 (100%)	2	p>0.05
	Normal	149 (44.2%)	188 (55.8%)	337	
Total		149	190	339	
BPPV: Benign paroxysmal positional vertigo					



Graphic 1. 25-OH vitamin D levels of control and BPPV group
BPPV: Benign paroxysmal positional vertigo

Discussion

The etiology of BPPV is explained by the fact that otoliths break away from the vestibular end organs and fall off or attach to the semicircular canal (2). Utricle and saccule are active calcium metabolites composed of calcium carbonate and glycoproteins (9). Otolith formation needs increased local calcium concentration. Studies have shown the presence of calcium channels such as Calbindine and the plasma membrane calcium pump, which play an important role in calcium absorption from the vestibular endolymph (27). In the studies on rats, it was observed that the expression of calcium-binding proteins in calcium channels in epithelial cells of semicircular canals is increased by 25-OH Vit D (11). Xu et al. (28). found common characteristics between biomineralization of bone and otoliths. They observed that the matrix organization of both tissues had similar characteristics. Studies in the literature have shown that BPPV is more common in women with osteoporosis and osteopenia, and they have frequent recurrences (10,12,16). There are also studies indicating that vitamin D replacement significantly reduces recurrence in BPPV patients (13,14). In our study, we compared the serum 25-OH Vit D levels in the BPPV group and control group, and found that the serum 25-OH Vit D levels of patients with BPPV were significantly lower than the control group (p<0.01). We examined the mean levels of serum 25-OH Vit D of the BPPV patients and the control group without any vestibular complaints and found these mean levels as 15.63±0.60 and 16.29±0.54 respectively. The mean level of 25-OH Vit D in the BPPV group was lower than the control group. The level of decreased serum 25-OH Vit D was found to be likely a risk factor independent from

the age and gender variable for the progress of BPPV. BPPV is the most common recurrent pathogenesis of vertigo in adults, and its prevalence in the general population is 10% (29). In another study, it was reported that 24% of patients abstain from driving their vehicles in the period of BPPV attacks and 18% of them hesitate over going out of their houses (4). Examining the BPPV disease that is commonly seen in the general population under light of literature, the necessity of effective treatment of the disease is better understood. There were no papers investigating the relationship between serum folic acid level and BPPV in the literature. In our study, we found that the low or normal levels of serum vitamin B12 and folic acid are not a risk factor in the progress of BPPV.

Conclusion

In our study, we assume that the low levels of 25-OH Vit D are risk factors independent of age and gender in the progress of BPPV. We did not find a significant relationship between vitamin B12 and folic acid levels with the progress of BPPV. The measurement of 25-OH Vit D levels in patients diagnosed with BPPV and administering replacement treatment may be beneficial. There is scientific evidence in the literature on the fact that replacement treatment may overcome the clinical complaints and may provide a reduction in the recurrence rate (14). Multicenter prospective studies with wider participation are needed to better understand the effect of 25-OH Vit D in BPPV and to prove the need for treatment.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of University of Health Sciences Turkey, Erzurum Regional Training and Research Hospital (no: 2019/12-122, date: 07.10.2019).

Informed Consent: Consent of all patients and volunteers included in the study was obtained

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.Ç., A.Y., A.E., Concept: H.Ç., Ö.O., Design: H.Ç., A.Y., B.V., Data Collection or Processing: H.Ç., A.E., Analysis or Interpretation: A.Y., A.E., B.V., Literature Search: A.Y., A.E., B.V., Ö.O., Writing: H.Ç., B.V.

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.2021.18894
Eurasian J Emerg Med. 2021;20(1): 25-34

Knowledge Level and Beliefs of Patients and Their Relatives about Hypnosis and Their Attitudes toward Use of Hypnosis for Sedation and Analgesia Purposes in the Emergency Department

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Abstract

Aim: To evaluate the knowledge level and beliefs of patients and their relatives about hypnosis and their attitudes toward use of hypnosis for sedation and analgesia purposes in the emergency department.

Materials and Methods: The study was conducted as a two-center study. The total number of participants recruited into the study was 384. A questionnaire including socio-demographic features, sources of information, knowledge and beliefs about hypnosis, and attitudes of participants toward the use of hypnosis in the emergency department in different clinical scenarios was used. Overall results of total study sample and differences between various sub-groups were evaluated.

Results: Mean age of participants was 34.27 years. Two hundred and sixteen (56.3%) participants were male. Television was the source of information with the highest effect on the knowledge of participants about hypnosis. Participants were seen to mostly believe myths about hypnosis. They preferred hypnosis only in the case of the existence or possibility of drug dependence (mean ± standart deviation=3.78±1.979).

Conclusion: Participants were mostly misled by improper sources of information so they were seen to be reluctant to prefer hypnosis in all clinical scenarios other than the existence or possibility of drug dependence.

Keywords: Analgesia, attitude, emergency department, hypnosis, knowledge level, sedation

Introduction

Although the word hypnosis is derived from the Greek “hypnos”, meaning sleep, it is actually a state of highly focused awareness (1). It is an altered, but not decreased, state of consciousness during which an individual is able to have an elevated control over sensory modalities through suggestion and imagination. Hypnotist does not control the patient but guides the patient’s ability to control his or her own sensory state (2). Hypnosis has been used in modern medicine for more than two centuries. Besides, it fulfills nearly all requirements of the ideal emergency department (ED) intervention; it is safe, fast, readily available, cost effective, uses minimal personnel and equipment, and has no risks like infection, prolonged sedation or other risks associated with sedation or medication administration (1,3). Emergency physicians (EP) are presented daily with patients in pain. Provision of safe and quick pain control remains one of their major duties. Hypnosis can be used as an effective adjunct or substitute for analgesic medications when these drugs prove to be ineffective or contraindicated (2). Because there is no physiological or psychological danger unique to hypnosis, it is unlikely that the circumstances surrounding the use of hypnosis in an acute medical situation would lead to any adverse complication. The ED, where patients in pain or with fear are frequently treated,

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Received: 25.12.2020
Accepted: 12.01.2021

Cite this article as: Güneş H, Koyuncu S. Knowledge Level and Beliefs of Patients and Their Relatives about Hypnosis and Their Attitudes toward Use of Hypnosis for Sedation and Analgesia Purposes in the Emergency Department. Eurasian J Emerg Med. 2021;20(1):25-34.

represents one area in which hypnosis could be an effective modality (3). The conditions where hypnosis can be used in ED include providing analgesia for existing pain (e.g. fractures, burns and lacerations), providing analgesia and sedation for painful procedures (e.g. needle sticks, laceration repair, and fracture and joint reductions), reducing acute anxiety, increasing children's cooperation for procedures, and providing analgesia and sedation for obstetric/gynecologic problems and even for myocardial infarction (1,4-8). Well, we have a critical question: Is hypnosis really effective against pain? The answer is yes; imaging studies show that pain under hypnosis is not perceived, rather than simply being experienced with greater tolerance (1). The analgesic effect of hypnosis is not solely a placebo effect which can suppress pain in 20-30% of individuals (2). Placebo appears to work through the endogenous opiate system and can be blocked by naloxone (9). Hypnosis is a modulator of pain, and its analgesic effect been shown to not be blocked by this agent (10). The use of hypnosis, instead of or in combination with drugs, for purposes of sedation and analgesia will be particularly more beneficial in the case of pregnancy, liver or renal insufficiency, or history of drug allergy or abuse. Articles that discuss ED use of hypnosis have sporadically appeared over the past several decades but most of the physicians have been reluctant to use this technique in the practice (2,3,11-16). This is due, in part, to the myths surrounding hypnosis and its association with alternative-complementary medicine. Major barriers to its more common clinical use in ED include lack of training and concerns of EPs about reluctance of patients and their relatives to accept the use of hypnosis. Based on the results of further research, hypnosis could become a powerful and safe non-pharmacologic addition to the EP's arsenal, with the potential to enhance patient care in emergency medicine (EM) (1). First, investigational studies are needed to identify how hypnosis can best be used in EM, and one of the potential study areas is evaluation of the attitude of ED patients and their relatives towards hypnosis. To the best of our knowledge, there are no previous studies investigating the knowledge level and beliefs of ED patients and their relatives about hypnosis and their attitudes towards use of hypnosis for purposes of sedation and analgesia in ED. So, the present study was performed to evaluate this topic.

Materials and Methods

The study was performed on patients and their relatives admitted to Düzce University Hospital Emergency Department in Düzce or Gaziosmanpaşa University Hospital Emergency Department in Tokat. It was conducted, instead of a single-center study, as a two-center study in order to reach more reliable results which reflect the population's knowledge level, beliefs and attitudes more accurately. Düzce and Tokat are 600 km-apart cities one of which is located in the western-half (Düzce) and the other one in the eastern-half of the country (Tokat).

Determination of the Sample Size: The sample size of the study was determined as 384 participants by using sample size calculation formula for known population. The universe of the study population (N) was nearly 600,000 people which was the number of the sum of the population between 18 and 65 years of age living in Düzce and Tokat according to 2016 data provided by Turkish Statistical Institute. When calculating the sample size, the following assumptions were used; confidence interval (CI)=95%, α=0.05, p=0.5 and q=0.5. Half of the participants (n=192) were recruited from Düzce and the other half (n=192) were from Tokat.

Data Collection: The data was gathered using a single-page questionnaire which is provided as a supplement of this paper. It included:

1. Socio-demographic features (e.g. age, gender, previous hypnosis experience, education level, sources of information on hypnosis),
2. Fourteen Likert type statements on knowledge and beliefs about hypnosis - present in the supplemental document - (1 point means absolutely disagree, 2 points mean disagree, 3 points mean mildly disagree, 4 points mean mildly agree, 5 points mean agree and 6 points mean absolutely agree),
3. Seven Likert type statements related to preference of use of hypnosis in ED for purposes of sedation and analgesia (in the case of application to the participant; to a pregnant/breast-feeding/child relative of the participant, or to a relative with liver or renal insufficiency/drug allergy/drug abuse history). (Having the same scoring system with the previous item),
4. A mean value of 3.5 which is the arithmetic mean of 3 and 4 points (the highest disagree point and the lowest agree point, respectively) for Likert type statements was the cut-off value between "agree" and "disagree" decisions. The questionnaire was mostly based on the one used in the study by Johnson and Hauck (17). The questionnaire was applied to participants randomly in order to prevent selection bias. The data collection was completed between March, 2017 and June, 2019.

Inclusion and Exclusion Criteria: The inclusion criteria were as follows: Being a patient admitted to ED or a relative of the patient treated in ED, giving permission and written informed consent to participate in the study. And, the exclusion criteria were as follows: being under 18 or over 65 years of age, illiteracy, blindness, deafness, mental retardation, having an emergent

problem not allowing to fill in the questionnaire or being a patient the clinical condition of whom is unstable or being the relative of such a patient and feeling anxious due to the concerns about the outcome of the patient.

Sub-groups: Participants were grouped in terms of the city the participant lives in, gender, age (young: 18-25 years; younger adults: 26-40 years; middle-aged adults: 41 years and older), education level, occupations and prior hypnosis experience. The differences in the knowledge level and beliefs about hypnosis and attitudes towards its use in the ED for purposes of sedation and analgesia in different clinical scenarios were evaluated. Besides, attitudes of the participants towards use of hypnosis in the emergency department were compared in different city, gender, age, education level, occupation and sources of information groups.

The study had been approved by Local Research Ethics Committee in [Düzce University Non-invasive Health Studies Ethics Committee, (approval number: 2017/46, approval date: 06.03.2017)].

Statistical Analysis

The descriptive statistics of all variables were calculated. The Kolmogorov-Smirnov test was used to evaluate whether the distribution of continuous variables was normal. The results were presented as mean ± standard deviation (SD) for continuous variables, and number (n) and percentages (%) for categorical variables. For normally distributed variables; means of two different groups were compared with Student's t-test; One-Way ANOVA (Bonferroni test) was used for comparison of multiple groups. And, means of previously-hypnotized and non-hypnotized groups were compared with Mann-Whitney U test due to the extremely small number of participants in the previously-hypnotized group. Categorical variables were compared with chi-square test. Statistical analyses were performed using the IBM SPSS Statistics for Windows v.25 (IBM Inc., New York, NY, USA). For all of the statistical tests, a p-value below 0.05 was considered significant.

Results

The first part of the questionnaire was about socio-demographic features. Mean age of the participants was 34.27±12.644 years; 132 (34.4%) participants were between 18 and 25 years old (young group); 136 (35.4%) were between 26 and 40 years old (younger adults), and 115 (29.9%) were 41 years old or older (middle-aged adults); differences among the numbers of the participants in different age groups were found to be non-significant (p=0.473). Gender distribution of the participants were as follows: male: n=216, 56.3%; female: n=167, 43.5%; missing: n=1, 0.3%; difference between the numbers of male and female participants was found to be non-significant (p=0.476). Only 3.4% (n=13,) of the participants had been hypnotized previously; 369 (96.1%) participants had not had any prior hypnosis experience, and 2 (0.5%) patients did not respond to this item. The largest education level group was formed by high school graduates (n=136, 35.4%), and the largest occupation group was wage workers (n=153, 39.8%). Table 1 shows distribution of the participants into the education level and occupation groups.

The source of information having the highest effect on the knowledge of the participants on hypnosis was seemed to be television (no influence: n=153, 39.8%; some influence: n=78,

Table 1. Distribution of the participants in terms of education level and occupation groups

Main parameter	Subgroups	n	%*
Education level	Literate	9	2.3
	Primary school graduate	66	17.2
	Secondary school graduate	47	12.2
	High school graduate	136	35.4
	University graduate	123	32.0
	Missing	3	0.8
Occupation	Wage worker	153	39.8
	Student	74	19.3
	Housewife	58	15.1
	Self employed	54	14.1
	Unemployed	24	6.3
	Retired	21	5.5

n: Number
*The percentages are rounded off to the nearest decimal

20.3%; most influence: n=151, 39.3%; missing: n=2, 0.5%). Table 2 summarizes the sources of information on the knowledge of the participants about hypnosis.

The participants were given 14 Likert type statements about hypnosis and it was seen that means of the answers were above 3.5 for most of the statements which means they agree with the statement. However, most of these statements were about common myths related to hypnosis. Table 3 summarizes the beliefs and thoughts of the participants about these statements.

The last part of the questionnaire included 7 Likert type statements about preference of hypnosis by the participant in different clinical scenarios. It was seen that mean of the participants' responses was higher than 3.5 in one statement only. That statement was "I prefer hypnosis to be applied if drug dependence or possibility of dependence exists (mean ± SD: 3.78±1.979). Table 4 shows the results of the participants' preferences about use of hypnosis in different clinical conditions.

When the attitudes of the participants towards use of hypnosis in ED were compared in terms of the city the participant lives in, gender, age groups, education level, occupation groups and hypnosis experience, it was seen that gender, age group, occupation and hypnosis experience do not have a significant effect on the attitude of the participant towards use of hypnosis. However, the city the participant lives in seemed to affect the preference of the participant in all suggested scenarios except application of hypnosis to the participant's himself or to a breast-

Table 2. Roles of different sources of information on knowledge of the participants about hypnosis

Information source	Effect on knowledge about hypnosis (n - %)			
	No influence	Some influence	Most influence	Missing
Television	153-39.8%	78-20.3%	151-39.3%	2-0.5%
Movies	248-64.6%	71-18.5%	63-16.4%	
Rumors	257-66.9%	73-19.0%	52-13.5%	
Hypnosis shows	293-76.3%	35-9.1 %	54-14.1%	
Clinicians	296-77.1%	33-8.6%	53-13.8%	
Friends	306-79.7%	48-12.5%	28-7.3%	
Teachers	344-89.6%	27-7.0%	11-2.9%	
Other	345-89.8%	28-7.3%	9-2.3%	

n: Number
*The percentages are rounded off to the nearest decimal

Table 3. Thoughts of the participants about some statements related to hypnosis

Statement	Participants' thoughts (mean ± SD)
Hypnotized person has an altered level of consciousness	3.85±1.753
Hypnosis is like sleeping	4.13±1.621
Hypnotized person is totally controlled by the hypnotist	4.13±1.677
Hypnotized person can be made to do something which he or she will not do normally	4.06±1.676
A person can be hypnotized even if he does not want to be	3.31±1.733
Hypnotized person does not feel any pain	3.66±1.709
Hypnotized person can terminate the hypnotic state whenever he wants to do so	2.77±1.671
All secrets of a hypnotized person can be learned by the hypnotist	3.91±1.658
Hypnotized person cannot lie	3.79±1.736
Hypnotized person sometimes do not know what is going on around him or her	4.06±1.550
Hypnotized person forgets what happened during hypnotic state if he is ordered to do so	3.56±1.720
Hypnosis is formed by the person's own imagination	3.34±1.657
Deeply hypnotized ones are likely to forget what happened during hypnotic state	3.78±1.571
Hypnosis makes someone able to do tasks which are normally impossible	3.98±1.617

SD: Standard deviation

feeding relative (p≤0.05 for all scenarios except application to the participant's himself and a breast feeding relative, for the latter two scenarios p=0.061 and p=0.112, respectively). Table 5 includes the attitudes of the participants living in different cities towards the use of hypnosis in ED. Besides, education level seemed to affect the preference of the participants in the case of renal or liver insufficiency (p=0.013) (Table 6).

Discussion

In the current study, which did not include pediatric (below 18 years old) and older adult (older than 65 years of age) populations, the participants were nearly equally distributed among the young, younger adult and middle-aged adult groups. Gender distribution of the participants also was near equal. A really small minority of the participants was seen to have previous personal experience of hypnosis. Nearly all of the participants were at least primary school graduates. Wage workers which included all participants having a paid job formed more than one third of the participants. Most of the participants stated that television somewhat affected their knowledge on hypnosis. The participants were seemed to generally agree with the common myths about hypnosis. A striking finding of the study was that the participants were not likely to prefer hypnosis in any clinical scenario except the existence or possibility of drug dependence. Gender, age, occupation and hypnosis experience were seen to not have a significant effect on the attitude of the participant towards use of hypnosis in ED. Two independent variables only, namely the city the participant lives in and education level of the participant, were seen to affect the preference of the participants in some clinical scenarios.

Distribution of the study population among the young, younger adult and middle-aged adult groups was near equal; each group

Table 4. The participants' attitudes towards the use of hypnosis in different scenarios

Statement	Attitudes of participants (mean ± SD)
I prefer hypnosis to be applied to myself	2.86±1.912
I prefer hypnosis to be applied to a pregnant relative of mine	2.60±1.815
I prefer hypnosis to be applied to my child or a child relative of mine	2.62±1.816
I prefer hypnosis to be applied to a relative with renal or liver insufficiency	2.92±1.842
I prefer hypnosis to be applied to a breast-feeding relative of mine	2.76±1.808
I prefer hypnosis to be applied in the case of drug allergy	3.32±1.929
I prefer hypnosis to be applied if drug dependence or possibility of dependence exists	3.78±1.979

SD: Standard deviation

Table 5. Effect of the city the participant lives in on the preference of hypnosis by the participant

Scenario	City	Mean ± SD	95% CI	p
I prefer hypnosis to be applied to myself	Düzce	3.05±1.960	2.77-3.33	0.061
	Tokat	2.68±1.849	2.41-2.94	
I prefer hypnosis to be applied to a pregnant relative of mine	Düzce	2.79±1.925	2.51-3.06	0.043
	Tokat	2.40±1.677	2.16-2.65	
I prefer hypnosis to be applied to my child	Düzce	2.82±1.913	2.55-3.09	0.029
	Tokat	2.41±1.692	2.17-2.66	
I prefer hypnosis to be applied to a relative with renal or liver insufficiency	Düzce	3.14±1.854	2.87-3.40	0.021
	Tokat	2.70±1.809	2.44-2.96	
I prefer hypnosis to be applied to a breast-feeding relative of mine	Düzce	2.91±1.857	2.64-3.18	0.112
	Tokat	2.61±1.751	2.36-2.86	
I prefer hypnosis to be applied in the case of drug allergy	Düzce	3.67±1.921	3.40-3.95	0.000
	Tokat	2.95±1.872	2.68-3.22	
I prefer hypnosis to be applied if drug dependence or possibility of dependence exists	Düzce	4.07±1.953	3.79-4.35	0.003
	Tokat	3.48±1.965	3.19-3.76	

SD: Standard deviation, CI: Confidence interval

Table 6. Effect of education level on the preference of hypnosis by the participant				
Scenario	**Education level**	**Mean ± SD**	**95% CI**	**p**
I prefer hypnosis to be applied to myself	Literate	1.63±1.768	0.15-3.10	0.461
	Primary school graduate	2.83±1.955	2.33-3.32	
	Secondary school graduate	2.85±2.011	2.25-3.44	
	High school graduate	2.91±1.868	2.59-3.23	
	University graduate	2.93±1.910	2.59-3.28	
I prefer hypnosis to be applied to a pregnant relative of mine	Literate	1.38±10.61	0.49-2.26	0.410
	Primary school graduate	2.50±1.894	2.03-2.97	
	Secondary school graduate	2.60±2.027	1.99-3.21	
	High school graduate	2.64±1.770	2.33-2.95	
	University graduate	2.64±1.733	2.33-2.96	
I prefer hypnosis to be applied to my child	Literate	2.11±2.205	0.42-3.81	0.879
	Primary school graduate	2.54±1.891	2.06-3.02	
	Secondary school graduate	2.78±1.954	2.20-3.36	
	High school graduate	2.63±1.749	2.33-2.93	
	University graduate	2.63±1.785	2.31-2.95	
I prefer hypnosis to be applied to a relative with renal or liver insufficiency	Literate	1.00±0.000	1.00-1.00	0.013
	Primary school graduate	2.72±1.915	2.24-3.20	
	Secondary school graduate	2.78±2.021	2.18-3.38	
	High school graduate	2.91±1.734	2.61-3.21	
	University graduate	3.20±1.837	2.88-3.53	
I prefer hypnosis to be applied to a breast-feeding relative of mine	Literate	1.38±1.061	0.49-2.26	0.108
	Primary school graduate	2.86±1.884	2.39-3.33	
	Secondary school graduate	2.47±1.727	1.95-2.99	
	High school graduate	2.72±1.811	2.41-3.04	
	University graduate	2.96±1.796	2.63-3.28	
I prefer hypnosis to be applied in the case of drug allergy	Literate	1.63±1.188	0.63-2.62	0.157
	Primary school graduate	3.32±1.950	2.83-3.81	
	Secondary school graduate	3.39±2.092	2.77-4.01	
	High school graduate	3.32±1.890	3.00-3.64	
	University graduate	3.43±1.910	3.09-3.77	
I prefer hypnosis to be applied if drug dependence or possibility of dependence exists	Literate	2.89±2.315	1.11-4.67	0.504
	Primary school graduate	3.68±1.977	3.19-4.17	
	Secondary school graduate	3.54±2.126	2.91-4.17	
	High school graduate	3.87±1.904	3.54-4.20	
	University graduate	3.89±1.983	3.54-4.25	
SD: Standard deviation, CI: Confidence interval				

formed approximately one third of the study population. The young group included those participants between 18 and 25 years of age most of whom were students and those graduated school but still had not begun to work in a job. So, it was suggested that their perception of hypnosis might be different from those of the other groups which were formed by younger and middle-aged adults. However, the results did not support this hypothesis because the age groups were seen to not differ in terms of the preference of hypnosis. As far as we know, there are no previous studies evaluating the knowledge level, beliefs and

attitudes of ED patients and their relatives related to hypnosis so we do not have any previous similar reports to compare with the results of the present study. However, Johnson and Hauck (17) conducted a study to evaluate the general public's perception of hypnosis. The study included four different groups formed by the respondents from different backgrounds and age groups. The authors stated that ideas and beliefs of the groups about hypnosis are remarkably consistent. The groups evaluated in the study by Johnson and Hauck (17) had both some similarities and some differences compared to the groups formed with regard to age of the participant in the present study but it is worth mentioning that the results of both studies are similar; different age groups have nearly the same perception of hypnosis. Barling and De Lucchi (18) reported that age did not affect the knowledge level, attitudes and beliefs about clinical hypnosis in both hypnosis-experienced and non-experienced participants. The results of that study also were similar to those of the current study in terms of the effect of age.

Gender distribution of the participants was near equal in the current study, although the number of male participants being higher than that of female participants. It was seen that understanding of hypnosis and ideas about its use in ED did not differ between the genders. In the study by Johnson and Hauck (17), the group a great majority of which was formed by women only stated that they agree to some extent with the statement "I would like to be hypnotized" which indicated that women may be more likely to choose hypnosis to be applied to the participant's herself. Whereas, it was seen, in the present study, that female participants did not differ from males in terms of willingness to application of hypnosis to themselves. Besides, they seemed to think about in the same way with the male participants even in the case of pregnancy or breast-feeding.

A really small minority of the participants stated that they had been hypnotized previously. The authors had suggested that a significant difference would be found between the previously-hypnotized and non-hypnotized groups with regard to their knowledge level and thoughts about hypnosis and attitudes towards its use in ED. However, the results were not as suggested to be; the participants with previous hypnosis experience and those without a personal experience of hypnosis did not differ significantly in terms of their attitudes towards hypnosis. In the study by Barling and De Lucchi (18), it was seen that hypnosis-experienced participants were more knowledgeable and more likely to accept clinical use of hypnosis compared to those without previous hypnosis experience. We suggest that "no significant differences" between the groups, in the present study, might be a result of the extremely small number of hypnosis-experienced participants because there were just 13 participants who had a prior hypnosis experience.

More than half of the participants had graduated from high school, and nearly one third of the participants were university graduates. In the study by Johnson and Hauck (17), 96% of the participants were high school graduates and more than three fourths of them continued their education after high school. So, education level of our participants was lower than that of the participants of the study by Johnson and Hauck (17). Because, the present study was conducted in a developing country and Johnson and Hauck's (17) study was conducted in a developed country, this difference in the education level of the participants is not so surprising. Whereas, nearly 98% of our participants were at least primary school graduates and all of them were literate which makes us to suggest they can understand and accurately interpret information on hypnosis they have gathered from different sources.

The participants were also evaluated with regard to their occupations, and it was seen that more than one third of the participants were wage workers followed by students which formed nearly one fifth of all participants. Wage workers formed the largest group because all participants working in different sectors on fee-earning basis were included in this group. One of the suggestions of the authors was that different occupation groups might exhibit different results but it was seen that occupation groups did not differ in terms of their perception of hypnosis. A possible reason for this result may be accumulation of all fee-earning workers in the same group but there would be more than 20 different occupation groups if more specific groups had been formed and most of these groups would include really small numbers of participants, and that could cause the results to become less reliable even if some significant findings could be detected. Thus, a broader classification was preferred.

Effect of different information sources on knowledge of the participants about hypnosis was evaluated, and it was seen that the source with the highest effect was television. It was the only information source having more or less effect on the knowledge of more than half of the participants. Television is followed by movies, rumors and stage hypnosis shows. Unfortunately, all of these sources are actually misleading; they rarely provide accurate information. Hypnosis specialists/clinicians and teachers could find a place at the end of the list just before friends and the other sources, respectively. These findings suggest that the participants had not had the chance to acquire accurate information about hypnosis. Barling and De Lucchi (18) also saw that participants who had not been hypnotized previously gathered their knowledge about hypnosis mostly from television or stage shows. We suggest that if educative television programs providing the real facts of hypnosis are made, the population's correct knowledge level can be increased considerably.

After the first part including socio-demographic features and sources of information, the questionnaire included 14 Likert type statements about hypnosis and hypnotized person. This part of the questionnaire aimed to evaluate the knowledge level and beliefs of the participants about hypnosis. Means of the responses of the participants were below 3.5 for 3 statements only. One of these statements -the statement with the lowest mean value- was "Hypnotized person can terminate the hypnotic state whenever he wants to do so". A mean value below 3.5 in this item means the participants believe the hypnotized person cannot terminate the hypnotic state even if he wants to do so. A person believes he or she cannot terminate hypnosis although he wants to do so cannot be supposed to want hypnosis applied to him or her or to a relative. This finding indicates that the participants have fear of "remaining hypnotized forever". The other two parameters with mean scores less than 3.5 were "A person can be hypnotized even if he does not want to be." and "Hypnosis is formed by the person's own imagination." Less than 3.5 points in the former one means the participants mostly believe that a person cannot be hypnotized if he or she does not want to be, and that is true, hypnosis necessitates the patient's cooperation with the hypnotist. Less than 3.5 points in the latter one indicates the participants mostly disagree hypnosis is a function of the participant's own imagination. Actually, this also is partly true because it is not solely a result of imagination but it rather requires more than imagination. All other statements were given mean scores greater than 3.5, and these results collectively show that the participants mostly have a negative perception of hypnosis. For example, they think hypnotized person is totally controlled by the hypnotist, can be made to do something against his or her will and cannot keep his or her own secrets. One of the statements given a mean score greater than 3.5 was "Hypnotized person does not feel any pain". That suggests the participants think hypnosis is effective against pain. There were two other statements with means of greater than 3.5: "Hypnotized person forgets what happened during hypnotic state if he is ordered to do so" and "Deeply hypnotized ones are likely to forget what happened during hypnotic state". It is a positive finding that the participants gave responses which resulted in mean values greater than 3.5 in these statements because these scores may indicate the participants believe hypnosis can make it possible for a patient to forget unpleasant feelings like pain, anxiety and fear occurred during a painful state or procedure. On the other hand, these mean values may also reflect why the participants are afraid of hypnosis because they believe that the hypnotized person is totally controlled by the hypnotist and he or she forgets what happened during hypnotic trance. Combination of these two ideas may result in increased level of fear and anxiety about hypnosis. Finally, one can state that participants mostly do not have a positive perception of hypnosis although some statements resulted in mean scores suggestive of positive feelings about hypnosis. In fact, this is not so surprising because as it was mentioned above sources of information having the greatest influence on the knowledge of the participants about hypnosis were television, movies, rumors and stage shows which mostly provide inaccurate information. Misleading information including myths and misconceptions results in negative feelings and fear of hypnosis (19).

The last part of the questionnaire was about the willingness of the participants to application of hypnosis in ED. It was surprising for the authors to saw that mean of the participants' responses resulted in a value greater than 3.5 in just one statement which was about use of hypnosis in the existence or possibility of drug dependence. The participants seemed to not prefer application of hypnosis instead of drugs even in the case of pregnancy, pediatric age group, renal or liver insufficiency, breast-feeding period and drug allergy. Those results indicate that the participants are really so afraid of hypnosis that they will not approve its application even if the patient has allergy to the analgesic and sedative drugs. We suggest that the reason for the approval of hypnosis instead of drugs in the case of drug dependence can be common use of illegal drugs in Düzce where half of the participants were recruited from. Although Düzce is a small city, because it is located on the road of illegal drug trafficking in Turkey, illegal drug use is relatively more common in Düzce compared to similar small cities (20). Hence, people living in Düzce are familiar with damaging effects of drug dependence on both the person himself and his family; it is a suggested finding that they are going to be more likely to prefer alternative methods in the case or possibility of drug dependence. Since no previous studies, evaluating preference of hypnosis by the ED patients and their relatives, was found in English literature, the results of the present study could not be compared to those of a similar study. However, a study by McIntosh and Hawney (21) showed that patients whose knowledge on hypnosis was gathered primarily from television or stage shows held unfavourable views of hypnosis, and they would not be willing to accept hypnosis-based treatments in general Although that study was not conducted on ED patients or their relatives it provides information on approach of the general population to hypnosis.

It was seen, in the present study, that gender, age, occupation and previous personal hypnosis experience do not significantly affect the attitude of the participant towards use of hypnosis in ED. However, the city the participant lives in seemed to affect the preference of the participant in all suggested scenarios except application of hypnosis to the participant's himself or to a breast-feeding relative. Although, means of the responses

of participants living in Düzce were higher than those of the participants living in Tokat, the only scenario which had a mean value of greater than 3.5 was existence or possibility of drug dependence. In this scenario, mean value of the responses of the participants living in Düzce was 4.07. Actually, mean value of the responses of participants living in Tokat also was really closer to 3.5 (mean: 3.48) but it was still smaller than it. As it was mentioned above, use of illegal drugs and drug dependence is really common in Düzce (20). Thus, it was suggested that people living in Düzce are familiar with the problems related to drug dependence so they supported use of hypnosis in the case of existence or possibility of drug dependence. Education level was the second socio-demographic feature which was seen to affect the preference of the participant but its effect reached statistical significance in only one suggested scenario which is renal or liver insufficiency. It was seen that as the education level of the participant increases the likelihood the participant approves use of hypnosis instead of drugs increases also. However, even the mean value of the responses of university graduates was smaller than 3.5 which indicates hypnosis was not preferred over drugs even by the participants in this "highest education level" group.

Study Limitations

The current study has some limitations: First, it was performed in two centers in different cities but both cities are small ones so a new study conducted in a higher number of centers which also include some centers in metropolises may provide more certain results. Second, the study included ED patients and their relatives but these patients had not needed sedation or analgesia during the visit they participated in the study. However, this may also be considered as strength of the study because the results of the study reflect the opinion of all ED patients and their relatives, and we suggest that it reflects the general public's opinion better. Third, the study did not include pediatric patients. Unlike adults, children in stressful conditions are already considered in the first stage of hypnosis, and so are generally more susceptible to hypnotic suggestions which means they are more hypnotizable (3,22). However, they cannot decide to accept the application of hypnosis by themselves if their parents do not agree with them. Finally, older adults were not included in the study due to the concerns about possible mental and cognitive impairments in this group. Actually, this group is more likely to have renal or liver insufficiency and use multiple drugs which may interact with analgesic and sedative drugs. But, it was not possible, in the ED setting, to reliably determine which patients or relatives above 65 years of age did not have any cognitive impairment so this group was not included in the study.

Conclusion

Television has the highest effect on the participants' knowledge on hypnosis and was followed by movies, rumors and stage hypnosis shows. It seems like these sources resulted in the accumulation of common misleading information in the participants' mind and caused them to approach hypnosis with caution. The participants were seen to be reluctant to prefer hypnosis in any clinical scenario except the existence or possibility of drug dependence. Gender, age, occupation and personal hypnosis experience were seen to not have a significant effect on the attitude of the participant towards hypnosis. The city the participant lives in and education level of the participant were seen to affect the preference of the participants in some clinical scenarios however the effect of education level remained as a "just statistically significant" effect; it did not reach clinical significance because even the most educated group was unwilling to prefer hypnosis. So, the city the participant lives in was the only parameter which seemed to change the overall preference of the study population in at least one clinical scenario which was existence or possibility of drug dependence. Finally, we suggest that, before starting to think about using hypnosis techniques in ED, the population should be educated on hypnosis so that people can get rid of common myths and misconceptions about hypnosis, and the most promising tool which can be used to change the public's view of hypnosis is television which seems to be the main source of misleading information for now.

Acknowledgements

We would like to thank Emine Ayhan Emektar of Balıkesir University School of Medicine Public Health Department for her invaluable contributions to statistical analysis of the study data.

Ethics

Ethics Committee Approval: The study had been approved by Düzce University Non-invasive Health Studies Ethics Committee (approval number: 2017/46, approval date: 06.03.2017).

Informed Consent: Written informed consent had been taken from each participant.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.G., Design: H.G., Data Collection or Processing: H.G., S.K., Analysis or Interpretation: H.G., S.K., Literature Search: H.G., Writing: H.G.

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.2020.50480
Eurasian J Emerg Med. 2021;20(1): 35-8

Retrospective Analysis of Acute Pancreatitis Cases: Diagnostic Accuracy of Amylase or Lipase Alone

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Abstract

Aim: This study aimed to assess the diagnostic accuracy of serum amylase and lipase in acute pancreatitis and perform its cost analysis to check if one alone is sufficient for a more cost-effective diagnostic process.

Materials and Methods: This was a retrospective study conducted in a hospital with a 335,000 annual number of emergency department (ED) visits. All patients to whom both amylase and lipase test were performed in 2019 were analyzed. Patients with three or more times the normal range elevation of either the amylase (>300 U/L) or lipase (>195 U/L) were included into the study. Sensitivity of those enzymes in diagnosing acute pancreatitis was calculated. Cost measurement of amylase and lipase was also determined.

Results: The number of patients with both enzyme levels measured for any reason at ED was 53,944 in a year. A total of 130 patients who met the inclusion criteria were analyzed. Wherein, 108 had elevated levels of both enzymes. Moreover, 22 of these patients had amylase lower than the three fold of the normal range with a significantly high lipase. No patient had elevated amylase with normal lipase levels. Sensitivity of serum amylase and lipase was 84% and 100%, respectively. If lipase is measured only for all patients whose amylase and lipase were measured, potential saving is calculated as 71,745 TL (10,298 USD) annually.

Conclusion: "Lipase only" measurement is recommended in terms of diagnostic accuracy and cost effectiveness in differential diagnosis for acute pancreatitis.

Keywords: Acute pancreatitis, amylase, lipase, cost, accuracy

Introduction

Acute pancreatitis (AP) is an inflammatory condition of pancreas most commonly caused by bile stones and excessive alcohol use. It is a very common gastrointestinal disorder with an incidence of 38/100,000 (1). However, recent studies showed an increase in the annual incidence and also the number of hospital admissions thus AP leading to a huge physical and financial burden (2).

According to guidelines of American College of Gastroenterology (ACG) diagnosis of AP is established by the presence of two of the three following criteria: abdominal pain consistent with the disease, serum amylase and/or lipase greater than three times the upper limit of normal, and/or characteristic findings from abdominal imaging (3). Although typically, pain of AP is defined as a constant severe pain at the epigastric region that radiates to back, pain is a subjective criteria and it may not be possible to obtain a typical history from elderly and dementia patients. On the other hand, despite contrast-enhanced computed tomography (CECT) of the abdomen is considered as the gold standard for the diagnosis, it can be normal at the early phase and it is recommended to be reserved for patients in whom the diagnosis is unclear or who fail to improve clinically within the first 48-72 h after hospital admission or to evaluate complications (3,4). Therefore, during the acute phase in the emergency department (ED) the only objective diagnostic tool for the diagnosis of AP is amylase and lipase.

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Received: 01.10.2020
Accepted: 26.11.2020

Cite this article as: Çıkrıkçı Işık G, Çinpolat R, Çevik Y. Retrospective Analysis of Acute Pancreatitis Cases: Diagnostic Accuracy of Amylase or Lipase Alone. Eurasian J Emerg Med. 2021;20(1):35-8.

Amylase and lipase are enzymes made primarily by the pancreas and released into the digestive tract to aid in the digestion of starch and fats, respectively. They often rise in parallel and used to confirm the diagnosis of pancreatitis, irrespective of the etiology and levels of the enzymes have no correlation with the severity of the disease (5). According to a Cochrane review both appear to have similar sensitivities (0.72 for amylase, 0.79 for lipase) and specificities (0.93 for amylase and 0.89 for lipase), however some recent guidelines recommend the use of lipase over amylase (6,7). On the other hand, co-ordering of both tests has shown little to no increase in the diagnostic accuracy, but it is increasing the costs (7).

The aim of the study was to assess the diagnostic accuracy of the serum amylase and lipase in AP and perform a cost analysis of those enzymes to find out if one alone was sufficient for more cost-effective diagnostic process.

Materials and Methods

This was a retrospective cross-sectional study conducted in a training and research hospital with a 335,000 annual number of ED visits. Ethics committee approval was obtained for the study from University of Health Sciences Turkey, Ankara Keçiören Training and Research Hospital Clinical Researches Ethics Committee (no: 2012-KAEK-15/2112, date: 10.06.2020). All the patients to whom both amylase and lipase test were performed between January 2019 and January 2020 in the emergency department were analyzed. Those total number was used for cost-analysis. Patients who had an elevation of three or more times the normal range of either amylase (>300 U/L) or lipase (>195 U/L) were included into the study. The number of patients with increased enzyme levels was used for sensitivity and specificity analyses. Patients with high enzyme levels were diagnosed with AP according to the guidelines of ACG that mentioned above. Those cases with the missing data were excluded (Flow chart 1). Hospital data registration system was used to collect data included demography, clinical presentation, laboratory studies, radiological investigation and underlying etiology.

Recorded blood sample analysis at presentation included serum amylase [reference range (RR): 28-100 U/L], serum lipase (RR: 0-65 U/L), liver function tests (alanine amino transferase, aspartate amino transferase, gamma glutamyl transferase, alkaline phosphatase, lactate dehydrogenase, total bilirubin, urea, creatinine, electrolytes, calcium level and complete blood count.

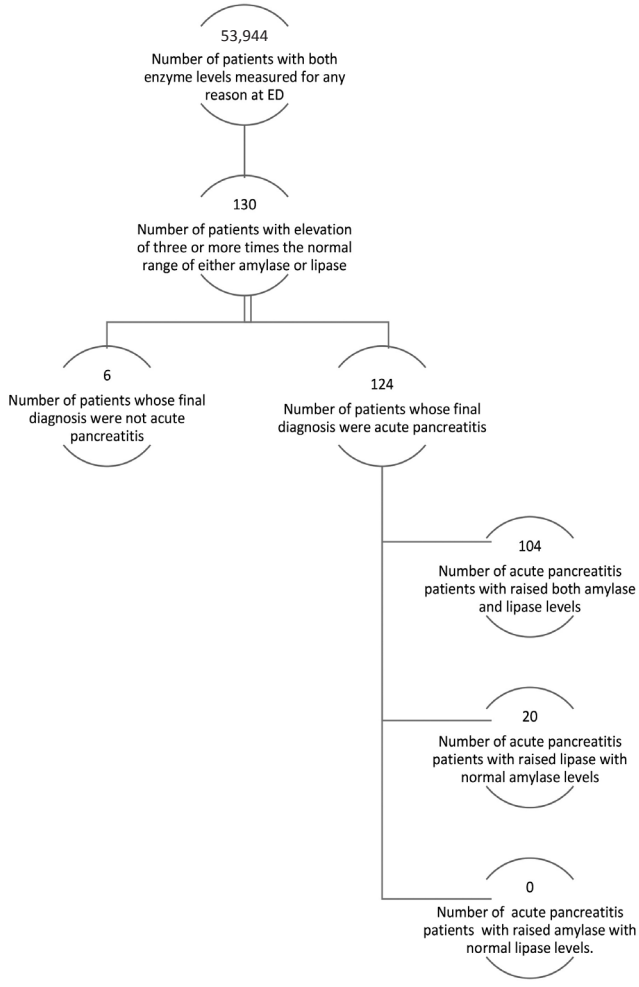
Patients underwent radiological investigation to identify the etiology. An abdominal ultrasonography (USG) was usually the initial radiologic tool, and in cases of clinical suspicion abdominal CECT was performed. According to our hospital policy, patients with confirmed common bile duct stones, or presence of cholangitis together with AP; referred to another hospital to perform endoscopic retrograde cholangio-pancreatography.

Cost Analysis

The cost of a single pancreatic enzyme level was 1.33 Turkish Liras (₺) for amylase and 2₺ for lipase. The cost of both amylase and lipase levels when measured together were 3.33₺.

Statistical Analysis

The statistical analysis was performed using the Statistical Package for the Social Sciences, version 22.0 (SPSS Inc., Chicago, IL, USA). Following a determination of whether or not they were normally distributed using the Shapiro-Wilk test, continuous variables were presented as the median and [interquartile range (IQR): 25-75%]. The descriptive analyses were presented using frequency tables for the ordinal variables. Patients who did not have AP, but had an elevation of three or more times



Flow chart 1. Distribution of the patients analysed

ED: Emergency department

the normal range of amylase or lipase were included in the specificity analysis. Sensitivity of those enzymes in diagnosing AP were calculated. Cost measurement of amylase and lipase was determined.

Results

Number of patients with both enzyme levels measured for any reason at ED were 53,944 in a year. There were only 15 patients with only amylase measurement in this period and there was any patient with only lipase measurement.

Total of 130 patients who had an elevation of three or more times the normal range of either amylase or lipase were included in to the study. Eighty (61.5%) of the patient were female with a median age of 58 (IQR: 44-77). Both amylase and lipase tests were performed for those patients in the ED. Radiologic investigation were performed either with USG or CECT to 73.8% of patients at ED. At six of those 130 patients final diagnosis were not AP (chronic pancreatitis 1; pancreas cancer 2; acute gastroenteritis 1; gastric perforation 2). Eighty-three (63.8%) were diagnosed with acute biliary pancreatitis and 41 (31.5%) were diagnosed with acute non-biliary pancreatitis. Majority of the patients admitted to gastroenterology department. General characteristics of the study population summarized in Table 1.

Majority of the patients had raised levels of both amylase and lipase (n=108, 83%) At 22 of those patients amylase was lower than the three fold of the normal range but lipase was significantly high. There was no patient with raised amylase with normal lipase levels. (Table 2). Considering the patients diagnosed with AP in this study, sensitivity of serum amylase was 84% and sensitivity of serum lipase was %100.

Cost of measuring both amylase and lipase in patients with AP in a year period was 419.5₺, compared to 252₺ if serum lipase was measured alone. That means 167.58₺ saving in a year for patients whose end diagnosis was AP. When all the patients with both enzyme levels were measured (n=53,944) taken into account, annual potential saving might reach to 71,745₺ [9,775 USD ($)].

Discussion

This study showed us there was a tendency of measuring both pancreatic enzymes together in the emergency department. However, this caused a huge financial burden. It was demonstrated here that lipase was more sensitive and sufficient alone for the diagnosis of AP. By measuring lipase levels only, 71,745₺ (9,775$) could be saved annually according to this study. However, those numbers underestimate the true costs because we were included only the patient at the ED and this was a single centered study. Therefore, it is obvious if lipase tested only, the cost savings will be much more at the national level.

Table 1. Characteristics of the study population (n=130)

Characteristics	Number
Gender	
Female	80
Male	50
Age	58 (IQR 44 -77)*
Laboratory investigation at ED	
Both amylase and lipase	130
Radiological investigations at ED	
Abdominal USG	77
Abdominal CECT	15
Both abdominal USG and abdominal CECT	4
None	34
Final diagnosis	
Acute biliary pancreatitis	83
Acute non-biliary pancreatitis	41
Other	6
Outcome	
Discharged	5
Admitted to gastroenterology department	110
Admitted to other departments	3
Admitted to intensive care unit	3
Referred to another hospital	9

ED: Emergency department, USG: Ultrasonography, CECT: Contrast-enhanced computed tomography, IQR: Inter quartile range, n: Number
*Median (IQR: 25-75)

Table 2. Conditions that caused raised levels of amylase and lipase

	Raised amylase and lipase levels (n=108)	Raised lipase with normal amylase levels (n=22)	Raised amylase with normal lipase levels (n=0)
Acute biliary pancreatitis	76 (70.4%)	7 (31.8%)	0
Acute non-biliary pancreatitis	28 (25.9%)	13 (59.1%)	0
Other diagnosis	4 (3.7%)	2 (9%)	0

n: Number

Although serum amylase and lipase are still the most commonly obtained biochemical markers for the evaluation of AP in the ED, clinical utility of testing those enzymes is conflictive. Our study showed that pancreatic enzymes ordered very often in ED settings. However, it was demonstrated that routine measurements of those enzymes were unhelpful in the diagnosis of acute abdominal pain unless there was clinical suspicion of AP (8).

Another ongoing debate in this regard is whether it is necessary to measure amylase and lipase together. Many studies in recent years concluded that serum pancreatic lipase is a more accurate biomarker of AP than serum amylase (5,6,9). In 2016, The American Society for Clinical Pathology Choosing Wisely® recommended not to test for amylase in cases of suspected AP and advocated for testing with lipase alone (10). However, despite those evidence-based guidelines, unnecessary laboratory testing remains a persistent issue.

Health care spending in Turkey has increased from 11.3% of government budget in 2002, to 16.3% in 2019 (11). Increasing growth rate in health care expenses is a problem for many countries and, governments and private sector experts concede that this growth cannot be sustained in the long term (12). Therefore, aim must be the prevention of unnecessary tests and procedures under the guidance of evidence-based medicine to reduce the financial burden in health. Methods such as changing order sets to only order lipase, electronic health record alerts and education campaign to providers should be used to reduce the unnecessary amylase testing in AP (12,13).

Study Limitations

This study has some limitations. First, this was a single centered study and included only the patients visited the emergency department, but not the other inpatient clinics. Second, recurrent enzyme measurements were not investigated. Therefore, it is weak to estimate the true costs.

Conclusion

In conclusion, "lipase only" measurement is recommended in terms of diagnostic accuracy and cost effectiveness in the differential diagnosis of AP. Educational and awareness campaign with the decoupling of amylase from electronic order sets might be helpful to reduce unnecessary amylase testing.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained for the study from University of Health Sciences Turkey, Ankara Keçiören Training and Research Hospital Clinical Researches Ethics Committee (no: 2012-KAEK-15/2112, date: 10.06.2020).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: R.Ç., Y.Ç., Concept: G.Ç.I., Y.Ç., Design: G.Ç.I., Y.Ç., Data Collection or Processing: R.Ç., Analysis or Interpretation: G.Ç.I., R.Ç., Literature Search: G.Ç.I., Y.Ç., Writing: G.Ç.I.

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.2020.29494
Eurasian J Emerg Med. 2021;20(1): 39-42

Effect of Ipratropium Inhalation on Pupil Dilatation in Rats

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Abstract

Aim: This study aimed to investigate the effect of inhaled ipratropium on pupil diameter when applied directly to the eye in a closed environment.

Materials and Methods: A total of 14, 8-week-old and 350-g weight Sprague-Dawley rats were obtained from Yeditepe University Laboratory of Experimental Animals for research. At constant temperature (22 ºC±3 ºC) and 12-hour light/dark cycle, the rats had access to standard food and water. A total of 7 rats were exposed to ipratropium, whereas 7 rats were given saline nebular. Pupil diameters and pupillary-orbital diameter ratios were compared before and 2 hours after drug exposure.

Pupil diameters and pupillary-orbital diameter ratios measured before and 2 hours after ipratropium inhalation were compared in the computer environment after 4288 × 2848 pixel magnification.

Results: No significant difference was observed in the pupil/orbital diameter ratios in either right or left eyes after treatment compared to baseline values ($p>0.05$, for both). No significant difference was found in Delta rates. The numerical data fitted the normal distribution.

Conclusion: In our study, no significant difference was determined in diameter changes that would advocate a more careful action in the case of anisocoria development in patients receiving ipropropium treatment and perform a detailed neurological examination and request neurology consultation as soon as possible. Anisocoria or changes in pupil diameters encountered in both pupils may not always be associated with drug use.

Keywords: Pupil diameter, nebulized ipratropium, anisocoria

Introduction

Obstructive pulmonary diseases are important health problems in our country and all over the world. Besides the preventive measures, it is necessary to know the mechanism of action and side effects of the drugs used. Asthma is a reversible chronic inflammatory disease of the respiratory tract resulting from increased bronchial hypersensitivity. Although inhalation beta-2 agonists and systemic corticosteroids are used in treatment, it has been reported that beta-2 agonists and inhalation quarternary ammonium derivative ipratropium bromide and atropine can also be used (1,2). Chronic obstructive pulmonary disease (COPD) is characterized by chronic inflammation in the airways, diffuse alveolar damage, and airway collapse and increase in respiratory work resulting from the loss of elasticity. Beta agonists and anticholinergic drugs are used during attacks. Due to their lipophilic quarternary ammonium structure, systemic absorption and toxicity in the inhalation use are lower in anticholinergics than in beta 2 agonists. The main mechanism of action of anticholinergic drugs such as ipratropium, oxitropium and tiotropium bromide is the blockade of the acetylcholine effect via M_3 receptors on airways in COPD patients (3).

The M_3 receptor is the major mediator of the muscarinic receptors in bronchoconstriction, mucus secretion and mucociliary clearance. M_3 stimulation activates phospholipase which causes an increase in inositoltriphosphate (IP_3) and intracellular calcium.

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Received: 18.01.2020
Accepted: 02.07.2020

Cite this article as: Akça HŞ, İhtiyar B, Kokulu K, Algın A, Özdemir S, Eroğlu SE, Aksel G. Effect of Ipratropium Inhalation on Pupil Dilatation in Rats. Eurasian J Emerg Med. 2021;20(1):39-42.

Ipratropium is a non-selective antimuscarinic agent. However, in acute asthma, Ipratropium is more effective on the bronchi than other antimuscarinics. Antimuscarinics have a low oral absorption and they cannot cross the blood brain barrier (4).

Retinal vascularity lacks sympathetic innervation. Circulating hormones and local factors are the main determinants of retinal blood flow. Activation of central nervous system increases the level of circulating adrenaline and stimulates beta receptors in the retinal arterioles by increasing retinal blood flow (5). In obstructive airway diseases, inhaled ipratropium can block muscarinic receptors and cause pupil dilatation with local parasympatholytic effect (6,7).

Mydriasis, cycloplegia, blur in vision, dryness in eyes may be observed due to local absorption of ipropropium. Unilateral or bilateral mydriasis has been reported due to leakage or due to improper placement of direct contact or face mask (8,9).

In vivo studies have shown that beta 1, 2, 3 specific receptor agonists as well as beta agonists are effective in retinal vasodilatation. In these studies, the intravenous form of drug was used (10-13).

Clinical studies were carried out in the Emergency Medicine clinic of the University of Health Sciences Turkey, Ümraniye Training and Research Hospital, İstanbul. Except for clinical trials and case reports, there was no study to determine whether experimentally inhaled ipratropium had any effect on pupil dilation.

Aim

The aim of this study was to investigate the effect of inhaled ipratropium on pupil diameter when applied directly onto the eye in a closed environment.

Materials and Methods

A total of 14, 8-week-old and 350-g weight Sprague dawley rats were obtained from Yeditepe University Faculty of Medicine Experimental Research Center. At constant temperature (22±3 ºC) and 12-hour light/dark cycle, the rats had access to standard feed and water. Seven rats were exposed to ipratropium while seven rats were given saline nebular. Pupil diameters and pupillary-orbital diameter ratios were compared before exposure and 2 hours after exposure to the drug.

In a closed environment, ipratropium nebular was inhaled at a dose of 1.5 mg/kg. The control group received the same dose of saline inhalation. The use of masks was not possible in rats. There was no mask for the rats. Ipratropium was given with the help of nebulizer in the closed area covered with glass, which the rats could easily move, we could observe from the outside. Thus, direct eye contact was achieved. Saline administration to the control group was performed with the same method. The rat pupil diameters were measured using original high-resolution nikon digital fundus camera (1.5 ft, 0.45 mm) at the same temperature (22±3 ºC) and lightened environment. Photos were obtained and recorded in the same heat and light environment at a 90º angle at a distance of 30 cm to the orbit. Pupil diameters and pupillary-orbital diameter ratios measured before and 2 hours after inhalation ipratropium administration were compared in the computer environment after 4288x2848 pixel magnification. The same method was applied for the control group.

Statistical Analysis

Collected data analysis was performed by using SPSS software (version 20.0, SPSS Inc., Chicago, Illinois). The Shapiro-Wilk test was used to evaluate distribution of continuous variables. Normally distributed continuous variables were compared with Student's t-test, while non-normal distributed continuous variables were compared with Mann-Whitney U test. Pupil diameters of rats before and second hours were compared with paired t-test and/or Wilcoxon tests. The results were evaluated at 95% confidence interval and a p-value of <0.05 was considered as statistically significant.

Ethics committee was given by Yeditepe Experimental Research Center where the study was conducted. No treatment was applied to the subject rats after drug exposure.

Results

There were also significant differences in the pupil diameters of the rats at the 0th hour measurements. For this reason, we thought that we would get reliable results with the ratio of pupil diameter/orbital diameter and delta value.

An increase in the mean right pupil diameter was observed at the 2nd hour compared to the baseline in the ipratropium group, but this difference was not statistically significant ($p=0.09$). Although there was an increase in left pupil diameter, no statistically significant difference was found ($p=0.05$). There was no significant difference in pupil diameter ratios in either the right or the left eyes after treatment compared to baseline values ($p>0.05$, for both). There was a significant difference in pupil/orbital ratio in right ($p=0.014$) and left ($p=0.016$) eye, but not in delta values. Madication and Control Group Pupil Diameter, Orbital Diameter and Delta Ratios are specified in the table (Table 1).

There was no significant difference in Delta rates (right pupil $p=0.67$, left pupil $p=0.95$). The numerical data fitted the normal distribution.

Table 1. Medication and control group pupil diameter, orbital diameter and delta ratios (p<0.05)			
Data	**Iratropium group**	**Control group**	**p**
Right pupil 0th hour average diameter (pixel)	7.0±1.7	5.5±1	0.07
Right pupil/right orbit 0 hours (%)	16.7±4	12±2.6	0.02
Left pupil 0th hour average diameter (pixel)	7±1.7	5.5±1	0.07
Left pupil/left orbit 0 hours (%)	16.4±3.6	12±2.3	0.017
Right pupil 2nd hr average diameter (pixel)	7.6±1.7	6±1.5	0.09
Right pupil/right orbita 2nd hour (%)	17.2±2.6	13±2.7	0.014
Left pupil 2nd hour averagediameter (pixel)	7.8±1.8	5.8±1.4	0.05
Left pupil/left orbita 2nd hour (%)	16.8±3.2	12.4±2.5	0.016
Delta right pupil	0.5±3.5	1.1±1.6	0.67
Delta left pupil	0.4±3.4	0.5±1.4	0.95

Discussion

Anticholinergic drugs are more effective in COPD than in asthma (3). The significant side effects of inhaled anticholinergics are mouth dryness and cough. Metallic taste and urinary obstruction may occur rarely. Headache, nervousness, irritability, dizziness, nausea, constipation, tachycardia and rashes can also be seen. Paradoxical bronchospasm may occur due to the preservative ingredients in the nebulizer ipratropium (2,3,14-16).

Only 1% of ipropathium is absorbed; therefore, it has a wide therapeutic range. There are different reportsregarding the effect initiation time and maximum duration of effect in different papers. According to some authors, the bronchodilator effect starts at 30 to 120 minutes, lasts for 4-8 hours, and the half-life is 3.2 hours (2,17-19).

According to some reports, the aerosol reaches its maximum effect after 30-60 minutes of application and its effect lasts for 3-6 hours (20-25).

The most technically feasible inhalation doses of metered dose aerosol are 1.5 mg/kg/day in rats and 1.8 mg/kg/day in rabbits. There was no adverse effect on the reproductive system. Ipratropium bromide solution in water (0.05 mg/kg) was locally well tolerated when administered to rats by inhalation (single administration for 4 hours). In repeated dose toxicity studies, ipratropium bromide was locally well tolerated (26).

In our study, ipratropium was given at a dose of 1.5 mg/kg/day. No rat died during or after the procedure. Decapitation was not performed in rats; there was no change in pupillary diameter or the ratio and no other side effects were observed either. Two hours after drug administration, the pupil diameter and the pupil diameter/orbital diameter ratios and delta values were measured and evaluated. As the size of the orbital diameters may vary slightly, the ratio of the pupil diameter to the orbital diameter was also included in our data. Although large-scale studies are not sufficient, there is no *in vivo* study comparing the changes in pupil diameter after inhaled ipratropium. Inhaled ipratropium contact with the eye in aerosol form may sometimes present with mydriasis and sometimes anisocoria. This may be due to mask mismatch, patient discordance, or mask shape. Mydriasis due to aerosol leakage has been reported in cases receiving ipratropium treatment. These cases were mostly published as case reports. The normal mental status and absence of any speech disorder or hemiparesis has led to exclusion of a possible herniation diagnosis (25-30).

To date, there is an insufficient number of clinical studies on the effect of inhaled ipratropium on pupil dilatation. In the case reports, it was emphasized that the patients receiving ipratropium treatment could experience anisocoria or change in pupildiameters in both pupils, and therefore, unnecessary examination should be avoided.

In our study, no significant difference in diameter changes were determined that would advocate that we should be more careful in the case of anisocoria development in patients receiving ipropropium treatment and to perform a detailed neurological examination and request neurology consultation as soon as possible. Anisocoria or changes in pupil diameters that we may encounter in both pupils may not always be associated with drug use.

Conclusion

Our study is important in terms of demonstrating that significant pupil dilatation does not occur due to ipratropium inhalation in rats.

In addition to clinical studies, it is necessary to conduct large-scale experimental animal studies and detailed studies for long-term side effects.

Ethics

Ethics Committee Approval: Ethics committee was given by Yeditepe Experimental Research Center where the study was conducted (decision no: 693, date: 19.09.2018). No treatment was applied to the subject rats after drug exposure.

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.Ş.A., S.E.E., S.Ö., B.İ., Concept: S.E.E., A.A., G.A., Design: H.Ş.A., S.Ö., K.K., A.A., Data Collection or Processing: H.Ş.A., B.İ., S.E.E., G.A., Analysis or Interpretation: B.İ., G.A., K.K., A.A., Literature Search: H.Ş.A., S.E.E., S.Ö., B.İ., Writing: H.Ş.A., K.K., B.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.2020.82621
Eurasian J Emerg Med. 2021;20(1): 43-8

Anxiety Level in Pre-hospital Emergency Medical Services Personnel During Coronavirus Disease-2019 Pandemic

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Abstract

Aim: This study aimed to determine the anxiety level in pre-hospital emergency medical services personnel (PHEMSPs) and investigate the factors that potentially affect the anxiety level during the pandemic.

Materials and Methods: This cross-sectional survey was conducted with PHEMSPs during the Coronavirus Disease-2019 (COVID-19) pandemic. A 60-item survey, including socio-demographic characteristics, anxiety-related demographic factors, and State-Trait Anxiety Inventory (STAI) scale scores was used.

Results: Among 586 PHEMSPs participating in the study, 50.5% were female, with median age of 30 years. The mean STAI-S value was 42.2, and the median STAI-T value was 48. The anxiety levels of female PHEMSPs (STAI-S=51 and STAI-T=44.14) were higher than male (STAI-S=44 and, STAI-T=40.26). The anxiety level of patients with chronic diseases (STAI-S=56 and, STAI-T=45.77) was significantly higher than those without chronic diseases. State anxiety scores in married individuals (STAI-S=49) were higher than those unmarried individuals.

Conclusion: Clearly, people who provide this service should be psychologically healthy to efficiently provide healthcare for the benefit of the people. All types of media assume a great responsibility in reducing the unrest or anxiety that may occur in humans, especially because of their potential to reach many parts of the society.

Keywords: STAI, SARS CoV-2, outbreak

Introduction

In December 2019, cases of pneumonia of unknown cause emerged in Wuhan, Hubei, China (1). A new type of coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) had been identified as the etiological agent causing pneumonia (2). Although this new type of coronavirus was first seen only in China, it has rapidly spread across the world, especially in countries in the continents of Europe and America, and the World Health Organization has defined this outbreak as the coronavirus disease-19 (COVID-19) pandemic.

As the number of infections increased, the lack of precise information about the virus in the media and the thought that currently available resources may be insufficient caused intense anxiety among health care workers (3,4). Faced with this large-scale infectious public health incident, health workers have been under both physical and psychological stress (5).

Prehospital emergency medical services personnel (PHEMSPs) are a community that provides service 24/7.They have crucial high-risk duties and responsibilities that involve intensive work rates, and they work under pressure and stress (6). The incidence of mortality, fatal accidents and injuries, musculo skeletal system complications, anxiety, and sleep problems were found to be higher in PHEMSPs than in other health care workers (7).

To the best of our knowledge, no study has measured the level of anxiety in PHEMSPs during the COVID-19 pandemic. This study was performed to determine the level of anxiety in PHEMSPs during the pandemic. In addition, this study aimed to investigate factors that potentially affect the level of anxiety, such as age, concomitant chronic disease, marital status, and child status.

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Received: 05.08.2020
Accepted: 20.10.2020

Cite this article as: Mutlu H, Sert ET, Kokulu K, Sarıtaş A. Anxiety Level in Pre-hospital Emergency Medical Services Personnel during Coronavirus Disease-2019 Pandemic. Eurasian J Emerg Med. 2021;20(1):43-8.

Materials and Methods

This cross-sectional survey was conducted with PHEMSPs working in Aksaray and Konya during the COVID-19 pandemic (from April 21st, 2020 to April 27th, 2020). The study was approved by the Local Ethics Committee of Aksaray University Human Researches (no: 2020-03/54, date: 24.04.2020) and the Ministry of Health of the Republic of Turkey (2020-05-13T13_55_01). A total of 1357 PHEMSPs are currently performing their duties; 278 are employed in Aksaray and 1,079 in Konya. Participation in the study was voluntary, and 586 PHEMSPs who completed the questionnaire participated in the study. Data was collected via an online survey over the Internet. PHEMSPs who agreed to participate in the study were sent a link through social media (WhatsApp, Twitter, and Facebook) and were asked to complete the survey. Participants were allowed to drop out of the study at any time. The survey was anonymous and information kept confidential. Participants were instructed to complete the survey and answer all questions. The survey comprised 60 items including sociodemographic characteristics (age, gender, marital status, child status, living with family, education level, and occupational status), health, social and demographic factors that are thought to be related to anxiety (smoking, presence/absence of chronic diseases, whether the workplace measures are adequate, workplace satisfaction, and compliance with measures taken for the pandemic), and State-Trait Anxiety Inventory (STAI) scale scores.

The STAI consists of two parts, each with 20 questions. While the stateanxiety (STAI-S) scale aims to measure anxiety at a given time, the trait anxiety (STAI-T) scale measures long-term anxiety levels. All items are evaluated using a 4-point Likert scale. There are 10 reversed phrases inSTAI-S and 7 in STAI-T. In the evaluation process, points between 1 and 4 were scored as negative (reducing the total anxiety score) or positive (increasing the total anxiety score) according to the selected option. As a constant value, 50 for the STAI-S and 35 for the STAI-T were added to the obtained scores. The most recent value obtained was taken as the anxiety score of the individual. Accordingly, the highest value was 80 and the lowest value was 20. Values of 20-35 indicated little anxiety, 36-41 indicated moderate anxiety, and 42-80 indicated high anxiety. The State-Trait Anxiety Inventory (STAI FORM TX-1, TX-2) was developed by Spielberger et al. Turkish validity and reliability of the scale was performed by Öner and Le Comte (8).

Statistical Analysis

All statistical analyses were performed using SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Among the trait variables, those that were normally distributed were presented as the average ± standard deviation and those that were non-normally distributed were presented as the median (interquartile range). The compatibility of trait variables to normal distribution was evaluated using the Kolmogorov-Smirnov test. Categorical data was expressed as n (%). In the comparison of the trait data between the two groups, the Mann-Whitney U test was used for non-normally distributed trait data and independent sample t-test was used for normally distributed trait data. The chi-square test or Fisher's exact test (as applicable) was used to compare categorical variables. In the comparison of the trait variables among three groups, One-Way analysis of variance was used for normally distributed trait data and the Kruskal-Wallis H test was used for non-normally distributed trait data. Posthoc Bonferroni correction was used for subgroup comparisons. The relationship between age, working time, and number of suspected patients evaluated daily and anxiety scale scores were evaluated using Spearman correlation.

Results

Among 586 PHEMSPs participatingin the study, 49.5% (n=290) were male and 50.5% (n=296) were female, and the median age was 30 (25-36) years. Two hundred and eighty-seven (49.0%) PHEMSPs were emergency medical technicians and 196 (33.4%) were paramedics. In addition, 423 (72.2%) lived with their family, whereas 163 (27.8%) consisted of those who would live separately from their family during the pandemic. The mean STAI-S value of PHEMSPs was 42.2±8.6, and the median STAI-T value was 48 (39-56). The distribution of participants according to sociodemographic and professional characteristics is given in Table 1.

The anxiety levels of female PHEMSPs (STAI-S=51 (44.25-57.0), STAI-T=44.14±8.15) were higher than those of male PHEMSPs [STAI-S=44 (35-52), STAI-T= 40.26±8.62] ($p<0.001$). The anxiety level of patients with chronic diseases (STAI-S=56 (49.25-59.0), STAI-T=45.77±8.31) was significantly higher than those without chronic diseases ($p<0.001$). State anxiety scores in married individuals [STAI-S=49 (40-57)] were higher than those in unmarried individuals ($p=0.03$). The distribution of anxiety scores according to sociodemographic characteristics is shown in Table 2.

There was no statistically significant relationship between STAI-S scores and participant age ($r=0.032$, $p=0.45$). There was also no statistically significant relationship between STAI-T scores and participant age ($r=0.01$, $p=0.82$). There was no statistically significant relationship between the participants' working time and the STAI-S and STAI-T scores ($r=0.067$, $p=0.11$ and $r=-0.02$, $p=0.64$, respectively). There was a significant, positive, weak correlation between the STAI-S score and the number of suspected patients assessed daily ($r=0.243$, $p<0.001$).

Table 1. The distribution of participants by socio-demographic and professional characteristics	
Variables	
Age, year, median (IQR)	30 (25-36)
Gender, n (%)	
Male	290 (49.5%)
Female	296 (50.5%)
Marital status, n (%)	
Married	387 (66.0%)
Unmarried	199 (34.0)
Child status, n (%)	
Yes	343 (58.5%)
No	243 (41.5%)
Living with the family	
Yes	423 (72.2%)
No	163 (27.8)
Occupation	
Physician	14 (2.4%)
Paramedic	196 (33.4%)
Emergency medical technician	287 (49.0%)
Nursing	27 (4.6%)
Driver	42 (7.2%)
Another	20 (3.4%)
Smoking	
Never used	276 (47.1%)
Used and left	95 (16.2%)
Actively using	214 (36.5%)
Number of COVID-19 suspected patients evaluated daily median (IQR)	3 (2-5)
Chronic disease	
Yes	48 (8.2%)
No	538 (91.8%)
State anxiety score, median (IQR)	48 (39-56)
Trait anxiety score, mean ± SD	42.2±8.6
IQR: Interquartile range, COVID-19: Coronavirus disease-19, SD: Standard deviation, n: Number	

Furthermore, a significant, positive, very weak correlation was found between the STAI-T score and the number of suspected patients evaluated daily ($r=0.086$, $p<0.04$).

The STAI-S and STAI-T scores of the participants were significantly different among groups formed according to their compliance with measures taken due to the pandemic ($p<0.001$) (Table 3).

Discussion

As of April 21st, 2020, the initiation date of our study, the total number of cases in Turkey was reportedly 95,591 and the number of deaths was 2,259 (9). We believed that the increase in the number of cases and deaths would increase the level of anxiety in healthcare workers as well as in the entire community. In this study, we observed that the anxiety level of PHEMSPs during the COVID-19 pandemic had increased; in addition, the anxiety levels in women, those who have children, those with chronic diseases, those living with their family, and those who do not comply with the measures taken due to the COVID-19 pandemic have increased further. In the COVID-19 pandemic, the frontline unit is undoubtedly PHEMSPs. Therefore, their anxiety levels are considered to be high.

In healthcare workers, psychological conditions such as anxiety and symptoms of depression, insomnia, denial, anger, and fear as well as post-traumatic stress disorder increase during pandemics or infectious disease outbreaks (10-12). Studies conducted during outbreaks such as the severe acute respiratory syndrome (SARS) and H1N1 revealed depression in 3.7% of all individuals and 9.6% of those affected by infection (13). In another study, 17.3% of healthcare workers who were actively working in hospitalized services of patients with SARS during the SARS outbreak reported mental symptoms (14,15).

The COVID-19 pandemic has caused increased fear across the world. Not knowing when the pandemic will end, not knowing the exact method of treatment, constant changes in information in the press about its effects, suggestions to stay at home during the pandemic, and the decline in social relations have negatively affected everyone's mental health (16).

The fact that health workers who are directly involved in the diagnosis, treatment, and care of patients with COVID-19 have close contact with infected patients results in fear, affective disorders, sleep problems, psychological adaptation, and similar concerns about mental health, such as depression and anxiety (17,18). Kang et al. (5) reported that the anxiety levels of healthcare workers that work in Wuhan has increased due to overwork, high risk of infection, isolation, inability to meet with family, and discrimination. Styra et al. (19) reported that in hospital employees working in Toronto during the SARS epidemic had increased anxiety levels and post-traumatic stress disorder. However, they reported that this increase was less in those who cared for patients with SARS compared with that in those who did not. Similar to findings reported in the literature, we found that PHEMSPs who were the first to contact patients with COVID-19 had high state and trait anxiety levels.

In our study, the state and trait anxiety levels in female PHEMSPs were higher than those in male PHEMSPs, which suggests that the psychiatric effect of COVID-19 are greater in female healthcare workers. Alexander et al. (20) have previously shown that anxiety

Table 2. Relationship between anxiety scores and sociodemographic characteristics				
	STAI-S score	**p-value**	**STAI-T score**	**p-value**
Gender				
Male	44 (35-52)	**<0.001**	40.26±8.62	**<0.001**
Female	51 (44.25-57.0)		44.14±8.15	
Marital status				
Married	49 (40-57)	**0.03**	42.03±8.55	0.45
Unmarried	47 (39-54)		42.59±8.70	
Child status				
Yes	49 (39-57)	**0.05**	42.14±8.32	0.78
No	47 (39-54)		42.34±9.0	
Living with the family				
Yes	49 (40-56)	0.16	40.62±7.51	0.68
No	46 (39-53)		43.30±6.45	
Occupation				
Physician	46 (39.75-55.21)	0.52	42 (36)	0.75
Nurse	48 (40-55)		43 (37)	
Health officer	49 (41-56)		42 (36)	
Emergency medical technician	51 (30-61)		43 (34)	
Medical secretary	42 (37.50-55,25)		42.50 (39)	
Security	44 (32-56.75)		39 (32.25)	
Smoking				
Never used	48.50 (41-56)	0.56	42.5 (38.75-46)	0.39
Used and left	48 (37-57)		38 (34-47)	
Actively using	48 (37.75-54.25)		42 (36-46)	
Chronic disease				
Yes	56 (49.25-59.0)	**<0.001**	45.77±8.31	**0.003**
No	48 (39-54)		41.91± 8.56	

STAI-S: State anxiety scale; STAI-T: Trait anxiety scale
Significant p-values are shown in bold.

disorders and depressive disorders are more common in women. Many studies have shown that female PHEMSPs have a higher level of anxiety than men (21,22). Anxiety disorder was found to be three times higher in women than in men during the COVID-19 pandemic (4). Liu et al. (23) reported that female gender is the most important determinant of post-traumatic stress disorder after the COVID-19 pandemic in China. As with all these studies and our study, the level of anxiety in women is higher than that in men.

Studies show that patients with COVID-19 with comorbidities have poor prognosis (24). Zhou et al. (25) reported that advanced age and concomitant chronic diseases are the most important risk factors for COVID-19 mortality. Additionally, the risk of developing the disease increases in patients with chronic diseases (26). In our study, we found that the level of anxiety was higher in PHEMSPs with chronic diseases than in those who did not have chronic diseases. Visual and printed media, including social media, have reported that those with chronic diseases have a higher risk of contracting COVID-19 and that the course of the disease may be poor. We believe that such explanations contribute to increased anxiety levels in patients with chronic diseases.

Study Limitations

The present study has several limitations: those who did not have access to the internet and could not use a smart phone were not included. There was a selection bias: because the survey was completed online, the pre-pandemic levels of anxiety in PHEMSPs who filled the survey were unknown. Another limitation was the small number of cases for a disease affecting the entire world. An

Table 3. Relationship between the anxiety scale scores and the groups categorized for their compliance with COVID-19 related measures

Compliance with the COVID-19 related measures	n (%)	STAI-S score	p-value	STAI-T score	p-value
Incompatible	2 (0.3%)	59.5 (54-65)	<0.001	41.5 (38-45)	<0.001
Somewhat compliant	30 (5.1%)	55 (49-60)		47 (42.5-49.5)	
Very compliant	184 (31.4%)	50 (43-56.75)		43 (39-49)	
Completely compliant	370 (63.1%)	47 (36.75-54)[1,2]		41 (35-47)[3,4]	

STAI-S: State anxiety scale; STAI-T: Trait anxiety scale, n: Number
[1]There is a statistically significant difference when compared with somewhat compliant group (corrected p=0.001)
[2]There is a statistically significant difference when compared with very compliant group (corrected p=0.006)
[3]There is a statistically significant difference when compared with somewhat compliant group (corrected p=0.004)
[4]There is a statistically significant difference when compared with very compliant group (corrected p=0.01)

advantage of this study is that it is the first study to measure the anxiety level of PHEMSPs during the pandemic.

Conclusion

It is obvious that people who provide this service should be psychologically healthy so that people can benefit from healthcare provision more efficiently. This is even more important in pandemics, during which the need for healthcare workers reaches a peak. All types of media assume a great responsibility in reducing the unrest or anxiety that may occur in humans, especially because of their potential to reach many parts of the society.

Ethics

Ethics Committee Approval: The study was approved by the Local Ethics Committee of Aksaray University Human Researches (no: 2020-03/54, date: 24.04.2020) and the Ministry of Health of the Republic of Turkey (2020-05-13T13_55_01).

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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.2021.78309
Eurasian J Emerg Med. 2021;20(1): 49-55

Analysis of Childhood Physical Violence Cases Presented to the Emergency Department

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Abstract

Aim: To examine the demographic and epidemiological characteristics of children who were exposed to physical violence.

Materials and Methods: Data of patients younger than 18 years admitted due to physical violence exposure to the Emergency Medicine Clinic in a tertiary university hospital were retrospectively reviewed.

Results: A total of 120 cases met the study criteria. The median age of patients was 15 (4-18) years and 70.8% of them were male. The female/male (F/M) ratio was 35/85. Emergency admissions due to physical exposure were made most frequently in July (n=16, 13.3%), where in 57.5% were made between 16:00 and 23:59. The most common injury site was the head (n=39, 32.5%) followed by the extremities (n=21, 17.5%). Moreover, 87.5% of patients had minor injuries according to Injury Severity Score levels.

Conclusion: Most of pediatric forensic cases were male adolescents. Education about a safe environment should be provided by taking protective measures to reduce the incidence of these cases. In addition, awareness activities in which parents and children can participate effectively should be supported and expanded by social institutions.

Keywords: Emergency service, physical violence, pediatric patient

Introduction

Exposure to physical violence and assault are significant public health problems. In the last decade, there has been an increase in the visits to the emergency service associated with such childhood injuries and pediatric abuse cases worldwide (1,2). In 2017, the World Health Organization estimated that around one billion minors aged between 2 and 17 were exposed to physical, emotional, or sexual abuse. Childhood injury is among the leading causes of death worldwide, constituting approximately 40% of all childhood deaths (3).

Various studies conducted in Turkey have reported prevalence rates of pediatric forensic assault cases varying between 6.1% and 19% (4).

Pediatric forensic cases constitute a particular group in terms of management and processes due to the differences in children's anatomical, physiological, and psychological profiles. It is essential to characterize the types of pediatric forensic cases presenting to the emergency service concerning sex, age, and diagnosis (5,6). Most studies performed on children and adolescents focus on only specific anatomical areas, a single injury mechanism (gunshot injuries, sexual assault, non-accidental trauma), or all pediatric forensic cases collectively (7,8).

Childhood exposure to physical violence has further importance in pediatric cases where a good case history cannot be taken (9). The Glasgow Coma Scale (GCS) and Injury Severity Score (ISS) can evaluate trauma in children. GCS is also used for pre-verbal children. ISS is an anatomical score and is appropriate for patients with multiple injuries (10).

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Received: 14.12.2020
Accepted: 29.01.2021

Cite this article as: Akpınar G. Analysis of Childhood Physical Violence Cases Presented to the Emergency Department. Eurasian J Emerg Med. 2021;20(1):49-55.

Very few articles have been published on the types of pediatric forensic cases or these patients' characteristics in Turkey. To develop protocols, standards, and education programs regarding the approaches and precautions concerned with forensic cases in Turkey, the types of pediatric forensic cases, and the contributing factors need to be defined. Moreover, being informed about the pediatric forensic cases frequently encountered in emergency services and the demographic characteristics of these children would also increase the awareness of health officers employed in emergency services (4). To contribute to the literature, we aimed to determine the demographic and epidemiological characteristics of the cases presenting to our emergency service due to child exposure to physical violence and compare these with the literature data.

Materials and Methods

Design and Setting

Study data were obtained by retrospectively reviewing the data of patients younger than 18 years who presented to the emergency medical clinic with the complaint of exposure to physical violence between 01/01/2015-31/12/2019, accessed via the hospital information processing system and archived records. An ethics approval was obtained from Düzce University Ethics Committee (approval number: 2020/223, date: 19/10/2020).

Study Population

The patients' age, sex, GCS, ISS, presentation time, cause of the incident, and site of injury data were evaluated. Statistical correlations between these parameters and mortality were determined.

Patients who presented to the Emergency Medicine Department outside the study period (01/01/2015-31/01/2019) or had insufficient data were excluded from the study.

Statistical Data Analysis

The normality condition was tested using the Shapiro-Wilk test for continuous variables. Differences between two groups were analyzed using the Mann-Whitney U test, differences between three or more groups were analyzed using the Kruskal-Wallis test. Correlations between two categorical variables were investigated using the Pearson chi-square and Fisher's Exact tests. Continuous variables were reported as median (Interquartile range) and minimum (min)-maximum (max) values. Categorical variables were presented as percentages. IBM SPSS Statistics for Windows, Version 23 (Armonk, NY: IBM Corp) was used for all statistical analyses. The level of significance was defined as $p<0.05$.

Results

Between 2015 and 2019, 120 children presented to the emergency service due to exposure to physical violence. The patients' median age was 15 (4-18) years, and 70.8% were male. The female/male (F/M) ratio was 35/85. Of the presentations, 57.5% were made between the hours 4:00 p.m-11:59 p.m. (Table 1).

The number of cases, which varied between one and three between 2011 and 2015, rose to 25-27 between 2015 and 2018. However, it declined to five in 2019. Cases were encountered most frequently in the summer (n=39, 32.5%) and least frequently in the winter (n=13, 10.8%). Emergency presentations due to exposure to physical violence were most frequent in July (n=16 13.3%), followed by April (n=14, 11.7%). The number of cases was 12 for Wednesdays and varied between 17th-19th on the other days of the week (Figure 1).

General body trauma (GBT) was determined in 43.3% of the patients. The most common injury site was the head (n=39, 32.5%), followed by the extremities (n=21, 17.55%). Of the patients, 77.5% were diagnosed with soft tissue trauma (STT), 10.83% with ecchymosis (n=10) or hematoma (n=3). One patient

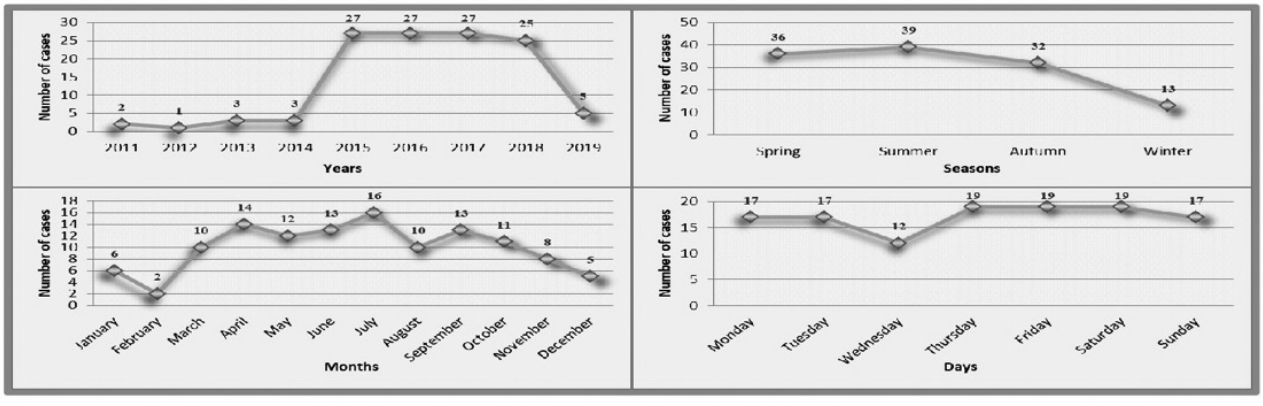

Figure 1. The number of emergency presentations due to exposure to physical violence by years, seasons, months and days

was determined to have multiple trauma involving ecchymosis and incision. Consultations were requested for 24 (20%) patients. The ear-nose-throat (ENT) clinic was consulted the most commonly (n=10, 41.7%).

Table 1. Demographic characteristics and time of presentation

	Median (IQR) / n	Min-max / %
Age	15 (4)	4-18
Sex		
Female	35	29.2
Male	85	70.8
Time of presentation		
00:00 a.m. - 07:59 a.m.	19	15.8
08:00 a.m. - 03:59 p.m.	32	26.7
4:00 p.m. - 11:59 p.m.	69	57.5

IQR: Interquartile range, n: Number, min: Minimum, max: Maximum

According to ISS levels, minor injuries (ISS ≤3) were determined in the patients at a rate of 87.5%, and moderate injuries (ISS; 4-8) at 12.5%, with no patients with an ISS ≥9.

The evaluation of the patients' conditions based on sex revealed a significant difference between females and males in terms of the site of injury (p=0.013). Follow-up analysis determined that injuries to the head area caused this difference. Injuries to the head area showed higher rates than expected in males than females (n=34, 87.2%). Diagnosis, consultation status, and ISS characteristics were not significantly different across sexes (respectively; p=0.126, p=0.132, p=0.226).

Analyses did not determine significant differences in site of injury, diagnosis, consultation status, ISS characteristics based on patient age (respectively; p=0.600, p=0.247, p=0.674, p=0.346, Table 2).

Table 2. Review of the patients' conditions based on demographic characteristics

	Total n (%)	Sex, n (%)		p	Age median (IQR)	p
		Female (n=35)	Male (n=85)			
Site of injury						
Head	39 (32.5)	5 (12.8)	34 (87.2)	0.013	16 (6)	0.600
Chest	5 (4.17)	3 (60)	2 (40)		16 (10.5)	
Abdomena	3 (2.5)	0 (0)	3 (100)		12 (0)	
Extremity	21 (17.5)	9 (42.9)	12 (57.1)		17 (4)	
GBT	52 (43.3)	18 (34.6)	34 (65.4)		16 (3.8)	
Diagnosis						
Ecchymosis, hematom[a]	13 (10.83)	1 (7.7)	12 (92.3)	0.126	17 (1.5)	0.247
Fracture	9 (7.5)	1 (11.1)	8 (88.9)		17 (1.5)	
Incision	4 (3.33)	1 (25)	3 (75)		16.5 (7.8)	
STT	93 (77.5)	32 (34.4)	61 (65.6)		16 (5)	
Multiple trauma[a]	1 (0.83)	0 (0)	1 (100)		15	
Consultation						
No	96 (80)	31 (32.3)	65 (67.7)	0.132	16 (4)	0.674
Yes	24 (20)	4 (16.7)	20 (83.3)		16 (4.8)	
Plastic surgery	1 (4.2)	0 (0)	1 (5)		15 (-)	
Orthopedics	5 (20.8)	1 (25)	4 (20)		17 (5)	
ENT	10 (41.7)	2 (50)	8 (40)		16.5 (3.3)	
Ophthalmology	3 (12.5)	1 (25)	2 (10)		11 (-)	
Pediatric surgery	2 (8.3)	0 (0)	2 (10)		14 (-)	
Neurosurgery	3 (12.5)	0 (0)	3 (15)		17 (-)	
ISS						
3 or less	105 (87.5)	33 (94.3)	72 (84.7)	0.226	16 (5)	0.346
4-8	15 (12.5)	2 (5.7)	13 (15.3)		17 (2)	

STT: Soft tissue trauma, IQR: Interquartile range, GBT: General body trauma, ENT: Ear-nose-throat, ISS: Injury Severity Score, n: Number
[a]: Group not included in the analysis due to an insufficient number of samples

At least one injury site was significantly different in terms of ISS (p<0.001). Using follow-up analysis, GBT was identified as the group that caused this significant difference. GBT was associated with significantly higher rates of minor injuries than expected when compared with other injury sites. Patients with GBT did not demonstrate any moderate injuries.

A significant difference was determined between the diagnosis groups in terms of ISS (p<0.001). It was concluded based on follow-up analyses that this difference was primarily caused by the diagnosis of fracture, followed by the diagnosis of STT. Patients determined to have fractures showed more effective rates (n=9, 100%) of moderate injuries than expected compared with the other groups. Meanwhile, no moderate injuries were detected in patients with STT, as opposed to the expected prevalence.

Significantly more moderate injuries were found in patients for whom a consultation was requested (n=14, 93.3%) compared with others (p<0.001, Table 3).

For patients who presented to the emergency service due to physical violence exposure, the lowest treatment cost was 15.5₺, while the highest cost was 743.62₺. The sites of injury associated with the highest median costs were the abdomen (369.79₺) and chest (283.88₺ -357.1₺), and the diagnoses associated with the highest median costs were incisions 251.34₺ (57.4)₺ and STT (189.45₺ (304.5)₺. In patients for whom consultations were requested, the departments associated with the highest median costs were ophthalmology (max: 575.37₺) and ENT (max: 516.59₺).

In the analyses performed concerning injury, diagnosis types, consultation status, and ISS evaluations, no significant differences were determined between the variable groups in terms of cost (respectively; p=0.321, p=0.170, p=0.297, p=0.255, Table 4).

Discussion

Emergency services have an essential role in identifying forensic events, which are among the most preventable health problems

Table 3. Review of ISS based on the patients' sites of injury, diagnoses, and the departments consulted

	Total n (%)	ISS - n (%)		p
		3 or less (n=105)	4-8 (n=15)	
Site of injury				
Head	39 (32.5)	27 (69.2)	12 (30.8)	<0.001
Chest	5 (4.17)	5 (100)	0 (0)	
Abdomen[a]	3 (2.5)	3 (100)	0 (0)	
Extremity	21 (17.5)	18 (85.7)	3 (14.3)	
GBT	52 (43.3)	52 (100)	0 (0)	
Diagnosis				
Ecchymosis, hematoma	13 (10.83)	8 (61.5)	5 (38.5)	<0.001
Fracture	9 (7.5)	0 (0)	9 (100)	
Incision	4 (3.33)	3 (75)	1 (25)	
STT	93 (77.5)	93 (100)	0 (0)	
Multiple trauma[a]	1 (0.83)	1 (100)	0 (0)	
Consultation				
No	96 (80)	95 (99)	1 (1)	<0.001
Yes	24 (20)	10 (9.5)	14 (93.3)	
Plastic surgery	1 (4.2)	1 (10)	0 (0)	
Orthopedics	5 (20.8)	2 (20)	3 (21.4)	
ENT	10 (41.7)	3 (30)	7 (50)	
Ophthalmology	3 (12.5)	0 (0)	3 (21.4)	
Pediatric surgery	2 (8.3)	2 (20)	0 (0)	
Neurosurgery	3 (12.5)	2 (20)	1 (7.1)	

STT: Soft tissue trauma, IQR: Interquartile range, GBT: General body trauma, ENT: Ear-nose-throat, ISS: Injury Severity Score, n: Number
[a]: Group not included in the analysis due to insufficient number of samples

Table 4. Cost analysis based on the patients' sites of injury, diagnoses, and the departments consulted				
	Total n (%)	Costs (₺)		p
		Median (IQR)	Min-max	
Site of injury				
Head	39 (32.5)	191.09 (236.9)	15.50-575.37	0.321
Chest	5 (4.17)	283.88 (357.1)	129.44-680.62	
Abdomen[a]	3 (2.5)	369.79 (-)	106.61-475.85	
Extremity	21 (17.5)	111.00 (322.7)	15.50-487.51	
GBT	52 (43.3)	159.55 (269.5)	15.50-743.62	
Diagnosis				
Ecchymosis, hematoma	13 (10.83)	133.55 (287.2)	15.50-575.37	0.170
Fracture	9 (7.5)	109.34 (96.3)	27.30-350.00	
Incision	4 (3.33)	251.34 (57.4)	245.36-320.96	
STT	93 (77.5)	189.45 (304.5)	15.50-743.62	
Multiple trauma[a]	1 (0.83)	191.09 (236.9)	15.50-575.37	
Consultation				
No	96 (80)	164.74 (254.9)	15.5-743.62	0.297
Yes	24 (20)	230.65 (303.6)	27.3-575.37	
Plastic surgery	1 (4.2)	149.80	149.80	
Orthopedics	5 (20.8)	191.51 (342)	107.66-487.51	
ENT	10 (41.7)	116.43 (319)	27.3-516.59	
Ophthalmology	3 (12.5)	320.96 (-)	183.05-575.37	
Pediatric surgery	2 (8.3)	422.82 (-)	369.79-475.85	
Neurosurgery	3 (12.5)	350 (-)	101.15-406.45	
ISS				
≤3	105 (87.5)	189.45 (299)	15.5-743.62	0.255
4-8	15 (12.5)	116.2 (220.6)	27.3-575.37	

STT: Soft tissue trauma, IQR: Interquartile range, GBT: General body trauma, ENT: Ear-nose-throat, ISS: Injury Severity Score, n: Number, Min: Minumum, max: Maximum
[a]: Group not included in the analysis due to insufficient number of samples

for children. No studies have been conducted exclusively on exposure to physical violence injuries in pediatric forensic cases, particularly in the pediatric age group. We think that our study will contribute to the demographic data of our country in this domain. Various consequent injuries were detected in patients in the pediatric age group who presented with the complaint of exposure to physical violence, the most common of which was STT. Injuries to the head area showed higher rates than expected in males than females (n=34, 87.2%). A significant difference was determined between diagnosis groups in terms of ISS ($p<0.001$). Patients determined to have fractures showed significantly higher rates (n=9, 100%) of moderate injuries.

Meanwhile, no moderate injuries were detected in patients with STT, as opposed to the expected prevalence. GBT was evaluated as a minor injury at significantly higher rates than expected compared with other injury sites. No moderate injuries were encountered in patients with GBT.

Assault-related injuries are a significant cause of morbidity and mortality in the youth. Of these injuries, 30% are caused by exposure to physical violence by peers. According to the Centers for Disease Control and Prevention (CDC), exposure to physical violence is the second leading cause of death for those aged between 15-19 years and the fourth leading cause of death in those aged between 10-14 years (11). Meanwhile, in the 0-18 age group, the primary cause of non-fatal traumatic injury is non-intentional injuries (12). In the present study, the F/M ratio was 35/85, and no deaths associated with physical violence were encountered. This can be due to the absence of political conflict and the low population in our region.

In studies conducted in our country, intentional injuries constituted the second-largest trauma group after traffic accidents with a rate of 21.6%. Among intentional injuries, exposure to physical violence was the most common cause (62.5%). Exposure to physical violence was determined to comprise 13.5% of all forensic cases. Most of the patients exposed to such trauma were male (70.0%). In another study conducted in our country, most of the forensic medicine reports of male patients involved the ages 15-18 years, while this age range was 7-14 for female cases; and the majority of forensic cases younger than 18 years were males (58.1%). A recent national study reported more male pediatric forensic cases and that the most common age range was 7-10 years (13-15). In the present study, 120 child patients presented to the emergency service. The patients' median age was 15 (4-18) years, and 70.8% were male. The F/M ratio was 35:85. These values were consistent with other studies. The fact that individuals are highly influenced by their friends and environment during adolescence, and act without much thought, prioritizing their sense of independence, may lead to behaviors associated with exposure to physical violence. Particularly in boys, this situation was reported to increase the likelihood of exposure to physical violence (13).

In a study by Kalkan et al. (14), the cases' seasonal distribution revealed that the majority of the cases (45.5%) presented in the summer, with 38.8% in August. In our study, 57.5% of the presentations were made between 4:00 p.m. - 11:59 a.m. Cases were encountered most frequently in the summer (n=39, 32.5%) and least frequently in the winter (n=13, 10.8%). Due to physical violence exposure, emergency presentations were most frequent in July (n=16 13.3%), followed by April (n=14, 11.7%). We reason that the schools being closed and children spending more time outside during the summer contribute to the increase in exposure to physical violence in the summer.

According to the CDC data, non-fatal injuries are more common in boys than in girls in the 1-19 age range (16). Males were exposed more to behaviors reinforcing masculinity and risky situations that might result in early death. On the other hand, females were the primary victims of domestic physical violence. Close partners comprised 40% of the main perpetrators of female exposure to physical violence (17). Our study could not obtain adequate data regarding the perpetrators of physical violence due to the lack of relevant data in the system.

Many studies have reported the head-neck and upper extremities to be the body parts that are injured the most commonly. Again, in single-site trauma, head-neck is the most common site of injury (18,19). In the study by Kalkan et al. (14), almost half of the patients (49.3%) had trauma in the head-neck area, and 23.6% in the lower extremities. The upper extremities were the third, and the abdomen was the fourth area. Further, the head-neck area (34.4%) was affected the most commonly in single-site trauma. In the present study, 43.3% of the patients were determined to have GBT. The injuries were most common in the head area (n=39, 32.5%), followed by the extremities (n=21, 17.5%). STT was present in 77.5% of the patients, and there was a significant difference between females and males in terms of the site of injury (p=0.013). Injuries to the head area showed unexpectedly higher rates in males than females (n=34, 87.2%).

Various scoring systems are being used to determine the severity of trauma and predict mortality in trauma cases. Some of these scoring systems were constructed based on physiological parameters; some were constructed based on anatomical localization, and others using both (20). GCS is a physiological scoring system. It is used widely worldwide in the evaluation of the state of consciousness and identification of coma (21). ISS is an anatomical scoring system. It is computed by dividing the body into six areas (head-neck, face, thorax, abdomen, extremities, other). The score varies between 1-75, and a score of 16 or higher indicates significant trauma (22). When Kalkan et al. (14) evaluated their cases concerning trauma severity, the injury was found to be non-life-threatening in most cases. Basic medical intervention was sufficient, and bone fractures did not occur. They did not have any cases resulting in death.

Most of the cases were evaluated as minor or moderate injury. This situation was interpreted as the most important factor explaining the low hospitalization rates and the 0.0% mortality rate (14). There was a significant difference between the diagnosis groups in terms of ISS ($p<0.001$) in our study. Based on follow-up analysis, this difference was caused primarily by the fracture diagnosis, followed by the STT diagnosis. Patients determined to have fractures (n=9, F=1, M=8) showed more significant rates (100%) of moderate injuries than expected compared with others. Meanwhile, as opposed to the expected prevalence, no moderate injuries were detected in patients with STT.

Significantly more moderate injuries were determined in patients for whom a consultation was requested (n=14, 93.3%) compared with others ($p<0.001$). In our study, consultations were requested for 24 (M/F: 20/4) patients, most commonly from the ENT clinic (n=10, 41.7%) and the orthopedics clinic (n=5, 20.8%), in descending order of frequency.

Childhood injuries exert significant pressure on families, societies, and health systems. The first step in reducing this injury burden is identifying the causative risk factors and devising strategies to eliminate these (23). Apart from the psychosocial effects of injuries, their burden on national expenditure is remarkably high. The annual economic burden of all Canadian

citizens' injuries was estimated at 26.8 billion dollars (24). In the present study, for patients who presented to the emergency service due to physical violence, the lowest treatment cost was 15.5₺, while the highest cost was 743.62₺. The injury sites associated with the highest median costs were the abdomen (369.79₺) and chest (283.88₺ -357.1₺), while the diagnoses associated with the highest median costs were incisions 251.34₺ (57.4)₺ and STT (189.45₺ (304.5)₺.

Study Limitations

The study's retrospective design and the inclusion of the limited number of patients based on the data present in the hospital records.

Conclusion

Most of the physical violence cases were adolescents. It is essential to determine the characteristics associated with the injuries and trauma profiles. Such data can be used to bolster the interventions aimed at fostering a safe environment for children. Epidemiological data obtained in such studies should be considered when instituting preventive measures against injuries and constructing injury control programs.

Acknowledgements

I would like to thank everyone who contributed to this study.

Ethics

Ethics Committee Approval: An ethics approval was obtained from Düzce University Ethics Committee (approval number: 2020/223, date: 19/10/2020).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Financial Disclosure: This study did not receive financial support.

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EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2020.38257
Eurasian J Emerg Med. 2021;20(1): 56-60

COVID-19: Transport Operation from an Endemic Area

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Abstract

Aim: Turkish Government launched an operation to transport the Turks living in Wuhan, China to Turkey because of coronavirus disease-19 (COVID-19) pandemia. In this study, the transport method, medical measures taken and quarantine process were evaluated.

Materials and Methods: Turkish citizens living in China had reported to the Turkish Embassy in Beijing that they wanted to return to Turkey. Thereupon Turkish Embassy in Beijing contacted the Ministry of Foreign Affairs of Turkey, and it was decided to transport Turkish citizens from China to Turkey. The governments of Georgia, Bulgaria, Azerbaijan, and Albania, who were aware of this development, requested the Ministry of Foreign Affairs of Turkey for their own citizens to be included in this transport.

Results: A total of 42 people were transported from city Wuhan to Turkey. Among them, 27 were citizen of Turkey, 6 were citizens of Azerbaijan, 4 were dual citizens of China and Turkey, 3 were citizens of Georgia, 1 was citizen of Bulgaria and 1 was citizen of Albania.

Conclusion: It suggests that there is a serious outbreak, as COVID-19 disease transmits from human-to-human and spread rapidly worldwide. Therefore, taking this outbreak seriously and taking all necessary measures will reduce the spread of COVID-19.

Keywords: COVID-19, patient transport, prehospital

Introduction

On December 31st 2019, the World Health Organization (WHO) China Country Office was informed of cases of pneumonia of unknown etiology detected in the city of Wuhan in Hubei Province, China. The Chinese authorities identified a new type of coronavirus (2019-nCoV), which was isolated on January 7th 2020. The disease then began to appear outside of China (Thailand, Japan, and Korea, respectively) (1). The WHO agreed that the outbreak met the criteria for a Public Health Emergency of International Concern (PHEIC) on January 30th 2020 (2). On February 11th 2020, the WHO named the disease COVID-19, short for "coronavirus disease 2019" (3). By March 11th 2020, a total of 4,290 patients had died in 113 countries (4).

COVID-19 spread rapidly in China and was soon seen in other countries (5). It was also confirmed that the disease was being transmitted from humans to humans (6). The Chinese government took some measures to control the outbreak. On January 23rd 2020, the government quarantined the city of Wuhan. Many cities in China have closed their public transportation systems (5). Later, the United States government canceled all flights from China (7). Turkey stopped all flights arriving from China until the end of January.

With the COVID-19 pandemic, aircraft and helicopter ambulances, as well as land ambulances, have had to deal with COVID-19 patients, a situation that they had not experienced before. There were no established guidelines on COVID-19 patient transport and information on this subject is still limited. In addition, it is known that aeromedical crew members are at higher risk than hospital staff (8).

The Turkish government launched an operation to transport the Turks living in Wuhan, China, back to Turkey. In this study,

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Received: 13.05.2020
Accepted: 08.10.2020

Cite this article as: Şan İ, Korkut S, Usul E, Bekgöz B, Kayıpmaz AE. COVID-19: Transport Operation from an Endemic Area. Eurasian J Emerg Med. 2021;20(1):56-60.

the transport method, the applied medical measures, and the quarantine process are evaluated.

Materials and Methods

Turkish citizens living in China had reported to the Turkish Embassy in Beijing that they wanted to return to Turkey. The Turkish Embassy in Beijing then contacted the Ministry of Foreign Affairs of Turkey, and it was decided to transport Turkish citizens from China to Turkey. The governments of Georgia, Bulgaria, Azerbaijan, and Albania, who were aware of this development, requested that the Ministry of Foreign Affairs of Turkey also include their own citizens in this transport, a request that the Turkish government accepted.

To transfer Turks and their Chinese spouses to Turkey, an Airbus A400M cargo aircraft of the Turkish Armed Forces was adapted for passenger transfer. A total of 75 passenger seats were mounted on this plane. In addition, the necessary materials were placed in the back of the aircraft (Table 1). For this operation, a total of 19 personnel, including four pilots, six crew members, two doctors (infectious disease specialists), one paramedic, three nurses, two press members, and one Foreign Ministry staff member were assigned. The Science Board of the Ministry of Health of Turkey decided to keep the passengers, medical staff, and aircraft crew under quarantine for 14 days after transport. A hospital building that was recently closed for service and was empty at that time was used for the quarantine. All of the medical equipment of that hospital was reviewed, all necessary medicines and medical supplies were provided, and doctors and nurses were assigned for patient follow-up. It was decided to transfer the passengers from the airport to this hospital by land ambulances. For this transfer, 10 ambulances and seven multi-stretcher ambulances (capable of transferring four patients at once) were prepared.

The plane took off from Ankara Etimesgut Military Airport on January 31st, 2020 at 08:30 a.m. to fly to Wuhan. The flight lasted 16 hours and 30 minutes (with 1 hour and 30 minutes for refueling at Ulaanbaatar Cengiz Han Airport in Mongolia). The plane landed at Wuhan Tianhe International Airport (WUH) airport on February 1st, 2020 at 00:48 p.m.

When the plane landed at the airport, the passengers had not yet arrived. Passengers were brought to the airport in two buses with capacity for 50 people, with one seat distance between them. The windows of the buses were kept open to allow ventilation. After the passport procedures were completed, the passengers arrived at the airport at 05:30 a.m. They were then transferred from the waiting room to the plane by a bus carrying 75 people, making two trips. The windows of this bus were also kept open to allow ventilation. The bus parked 100 meters from the plane.

During the bus transfer, passengers wore normal surgical masks and did not wear protective clothing. One infection specialist and two nurses entered the bus and examined the passengers there. No pathology was detected in the examination of the passengers and vital signs were normal. A body temperature above 37 °C was not detected in any passengers.

It was learned from the technical staff of the aircraft that the air flow would be from front to back and there was no negative pressure on the plane (Figure 1). It was therefore decided to board passengers from the rear cargo door of the plane. After the examinations on the bus were completed, the plane's rear cargo door was opened to the passengers. A total of 100 seats were placed on the plane. The seating plan consisted of 25 rows and 6 seats per row. One seat (120 cm) was left empty beside each passenger (Figure 1). Passengers were instructed by one paramedic and one nurse in a practical way about how to wear D-type protective clothing, glasses, gloves, and N95 masks. Each passenger was allowed onto the plane after putting on their personal protective suit and mask. Pilots, crew, and medical personnel were wearing D-type protective equipment, N95 masks, and glasses. The passengers, who would get off the plane first, were seated in the back of the plane. The aircraft crew and medical staff sat behind the passengers. Passengers were asked if they had any complaints and their body temperatures were measured at 1-hour intervals.

Passengers ate at different times on the plane. Starting from the first row, the passengers in each row ate at the same time. During the trip, passengers were allowed to take off their masks only while eating. Their masks were changed after each meal or when they went to the toilet. Hand washing and use of disinfectants were mandatory after eating or using the toilet. The plane landed at Ankara Etimesgut Military Airport at 9:20 p.m. A final

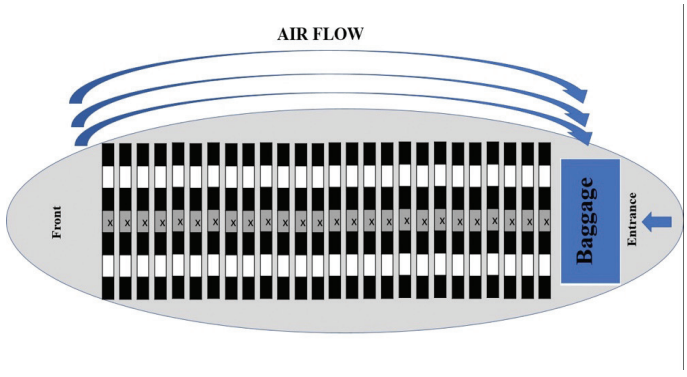

Figure 1. Seating arrangement of passengers and air flow in aircraft

Black seats: Seats for passengers, white seats: empty seats, x: corridor

examination and body temperature control were performed before landing.

When the plane landed, ambulances were waiting 100 meters from the location where the plane would be parked. Ambulance personnel also wore D-type protective clothing, glasses, gloves, and N95 masks. After the plane was parked, patient transfer started from the rear cargo door. Each ambulance had a number and transported the passengers assigned to them. Ambulances were positioned 10 meters from the rear cargo door of the plane. Passengers were then taken off the plane one by one, taken to ambulances, and transported to the hospital (Figure 2).

When the ambulances arrived at the hospital, the hospital staff welcomed the passengers. Hospital personnel also wore D-type protective clothing, glasses, gloves, and N95 masks. Each passenger was taken to a room prepared for follow-up purposes. Each room was allocated for one passenger. Families were followed in rooms with a maximum of two people (mother and child).

The clothes of the ambulance team that completed the transfer were placed in medical waste bags and thrown into a medical waste bin. The ambulances were disinfected before they were assigned to any other cases. For sterilization, solutions containing H_2O_2 and Ag^+ were sprayed with a Dismist® S2 device (Human Health Technology, 2019). After spraying the solution for 15 minutes for each ambulance, the solution was allowed to settle for 2 hours and 15 minutes. After this process was over, ambulances were ventilated with fresh air for 30 minutes.

The patients were followed in the hospital for 14 days. Nurses wore D-type protective clothing, gloves, glasses, and masks when entering the rooms. Vital findings were examined four times each day. Since there were no clear guidelines for COVID-19 at the beginning of the pandemic, a commission of infection specialists was established within the Ankara Provincial Health Directorate during this period. Follow-up and treatment process decisions for the patients were made by this commission. Since this commission considered the passengers coming from abroad as high risk, they recommended taking swab samples from them every 3 days. Since this commission recommended that the patients be followed for 14 days, the quarantine period was determined as 14 days.

Figure 2. Transporting patients from plane to ambulance

A nasal swab sample was taken from the passengers on the day of hospitalization and then every 3 days. The last nasal swab was performed on the day of discharge. The quarantine was terminated for the passengers who did not have coronavirus in swab samples and who did not develop disease findings and fever.

The Non-Invasive Ethics Committee of the University of Health Sciences approved our study with number 2020/93, date: 25.02.2020.

Results

A total of 42 people were transported from the city of Wuhan to Turkey. Among them, 27 were citizens of Turkey, six were citizens of Azerbaijan, four were dual citizens of China and Turkey, three were citizens of Georgia, one was a citizen of Bulgaria, and one was a citizen of Albania. While 22 of the transported individuals were male, 20 were female. The mean age was 30.1±10.6 years.

The transported passengers did not have serious comorbidities. While one passenger had diabetes mellitus and hypothyroidism, one had rheumatoid arthritis, and another had diabetes mellitus and chronic gastritis.

The vital findings of the passengers were normal (Table 1).

Discussion

The rapid spread of COVID-19 is likely to be driven by the phenomenon of superspreading. Superspreading describes heightened transmission of a disease to at least eight contacts and has been observed for several infectious diseases including Severe acute respiratory syndrome, Middle East respiratory syndrome and influenza. Another reason for the rapid spread of COVID-19 is that modern air travel allows passengers to traverse the globe in less than a day (9). Thus, Turkey blocked all flights from China. However, a special transport flight was organized because Turks living in China wanted to return to Turkey.

Emergency medical services (EMS) play a vital role in responding to requests for assistance, triaging patients, and providing

Table 1. The vital findings of the passengers		
	Mean ± SD	**Min-max**
Age	30.2±12.1	29.5 (3.0-62.0)
Systolic arterial pressure (mmHg)	125.2±15.5	125.0 (90.0-155.0)
Diastolic arterial pressure (mmHg)	74.6±9.6	75.0 (60.0-95.0)
Fever (^{0}C)	36.5±0.3	36.5 (36.0-37.2)
Pulse (min)	78.9±12.6	79.0 (60.0-112.0)
SpO_2 (%)	96.6±1.5	96.0 (95.0-99.0)
SD: Standard deviation, min: Minimum, max: Maximum		

emergency medical treatment and transport for ill persons. Unlike patient care in the controlled environment of a healthcare facility, care and transport by EMS present unique challenges because of the nature of the setting, enclosed space during transport, frequent need for rapid medical decision-making, interventions with limited information, and a varying range of patient acuity and jurisdictional healthcare resources (10). In this study, however, operational planning was performed in the early period, the personnel were informed, and necessary measures were taken.

According to the WHO, a patient with acute respiratory illness and a history of travel to a country that has reported local transmission of COVID-19, a patient with acute respiratory illness who has come into contact with a confirmed or probable case of COVID-19, or a patient with severe acute respiratory infection who requires hospitalization constitutes a suspected case of COVID-19 (11). The passengers transported from Wuhan to Turkey had no symptoms and did not meet this definition.

According to one study, the mean incubation period of 2019-nCoV was 5.2 days [95% confidence interval (CI): 4.1-7.0] (12). In another study the mean incubation period was estimated to be 6.4 days (95% CI: 5.6-7.7) among travelers from Wuhan, China (13). Studies have reported that the disease is transmitted from humans to humans (14,15). On the day of transport, there were still no COVID-19 cases in Turkey. The incubation period of the disease was reported to be 14 days in the guidelines of the Science Board of the Ministry of Health of Turkey, and the patients reported here were regularly screened for COVID-19, as it was recommended to take a throat swab sample every 3 days. In the literature, it appears that each country has its own guidelines. For example, after an operation to transport citizens home from Italy, South Korea applied quarantine for 14 days and administered throat swabs every 2 days (8).

In a study on the transport of patients with Lassa fever, it was stated that the transport of those patients was possible only with the correct use of necessary medical and technical equipment and personal protective equipment (16). Due to this information, no risks were taken and both aircraft personnel and ambulance crew used disposable examination gloves, disposable isolation gowns, N95 masks, and protective glasses according to the Centers for Disease Control and Prevention recommendations.

Since COVID-19 was suspected during a flight from Israel to Germany, two seats were left empty between passengers (17). The WHO recommends a distance of at least 1 meter for protection from COVID-19 transmission (18). In our organization, in accordance with the literature and the WHO recommendations, passengers were seated on the plane while leaving 1 seat (120 cm) empty between them.

In a study describing the transport process of patients affected by a tsunami, it was emphasized that pre-operative organization was very important for the success of the transport (19). We also conducted detailed pre-operation planning in our study. Before the operation, all details such as the necessary equipment, how to use the equipment, the necessary meals and drinks for the passengers, the seating plan, the number of personnel to be sufficient according to the number of passengers, where the passengers would be quarantined, and the ambulances to be used for transport from the aircraft to the quarantine buildings were considered. In another study on the transport of COVID-19 patients, the seating plan was determined while considering even the airflow on the plane (17). In our planning, since the airflow on the plane was from front to back, the boarding of the passengers onto the plane and the seating plan were arranged accordingly.

Conclusion

In this paper, we have presented the details of the organization of a very successful large transfer of Turkish people from Wuhan back to Turkey. In epidemics and pandemics, taking the necessary precautions in the transport of passengers by plane during evacuations from risky areas is very important to prevent the spread of infectious diseases such as COVID-19.

Ethics

Ethics Committee Approval: The Non-Invasive Ethics Committee of the University of Health Sciences approved our study with number 2020/93, date: 25.02.2020.

Informed Consent: Since this study does not contain the data of the patients, informed consent is not necessary.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Design: İ.Ş., B.B., Data Collection or Processing: E.U., Analysis or Interpretation: A.E.K., Literature Search: S.K., Writing: B.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
DOI: 10.4274/eajem.galenos.2021.79663
Letter to the Editor
Eurasian J Emerg Med. 2021;20(1): 61-2

Impact of Personal Protective Equipment on Intravascular Access Effectiveness

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To the Editor,

A year ago, the world faced the problem of infections with the new SARS-CoV-2 coronavirus, which quickly became a pandemic. The risk of infection for emergency medical personnel is relatively high, so in the era of a pandemic, the best solution would be for medical personnel to provide medical assistance to patients in pre-hospital conditions, when wearing full personal protective equipment (PPE) for aerosol generating procedures (AGPs) (1,2). However, as many studies show, the use of protective suits may reduce the effectiveness of the procedures performed, both in terms of the effectiveness of a procedure and the extension of its time (3-5). In many clinical situations where drugs must be administered quickly or fluid resuscitation is started, prompt intravascular access is a priority for emergency care. However, in the case of a collapsed vascular bed, and the use of prophylactic double gloves, accessing it can be difficult or even impossible. Then an alternative to peripheral intravenous access (PIV) could be intraosseous access (IO). As indicated by many studies, the intraosseous access is a full-fledged intravascular access, through which we can administer both drugs to the patient and use fluid resuscitation or transfuse blood and blood products.

According to the research by Castle et al. (6) the mean length of the procedure for obtaining intraosseous access with PPE AGP was 36±9.8 seconds and was statistically significantly shorter than with obtaining intravascular access (126.9±39.8; $p<0.05$). A similar relationship is also showed by Lamhaut et al. (7), where the procedure time was 65±17s for IO and 104±30s for PIV, respectively. In turn, Szarpak et al. (8) Comparing the IO access using bone injection gun and Jamshidi with and without PPE AGP, they showed that the use of PPE AGP compared to the procedure without PPE AGP did not significantly extend the duration of the procedure (29.5±13.2 vs 22±7 s, $p=0.063$). However, accessing with Jamshidi needle was associated with a statistically significantly longer duration of the procedure with PPE-AGP than without PPE-AGP (69.5±34.2 s vs 35±8 s, $p<0.001$).

In conclusion, as the presented results show, the using of intraosseous punctures as the basic form of intravascular access in the aspect of COVID-19 patients and any other infectious disease is reasonable.

Keywords: Intravascular access, intraosseous access, personal protective equipment, SARS-CoV-2, COVID-19

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Received: 09.12.2020
Accepted: 11.02.2021

Cite this article as: Drozd A, Evrin T, Kosior D, Borkowska G, Wozniak S, Gasecka A, Katipoğlu B, Szarpak L. Eurasian J Emerg Med. 2021;20(1):61-2.

Ethics

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.D., T.E., D.K., G.B., S.W., A.G., B.K., L.S., Design: A.D., T.E., D.K., G.B., S.W., A.G., B.K., L.S., Data Collection or Processing: A.D., T.E., D.K., G.B., S.W., A.G., B.K., L.S., Analysis or Interpretation: A.D., T.E., D.K., G.B., S.W., A.G., B.K., L.K., Literature Search: A.D., T.E., D.K., G.B., S.W., A.G., B.K., L.K., Writing: A.D., T.E., D.K., G.B., S.W., A.G., B.K., L.S.

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.2020.43827
Case Report
Eurasian J Emerg Med. 2021;20(1): 63-4

False Positive Computed Tomography Imaging for Coronavirus-2019

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Abstract

A 79-year-old female patient presented to the emergency unit with cough and severe shortness of breath. Due to a bilateral multilobular ground glass density result from thoracic tomography, the patient was admitted to intensive care with the preliminary diagnosis of corona virus-2019 (COVID-19), and a continuous positive airway pressure was applied. A polymerase chain reaction (PCR) test was performed, and treatment with hydroxychloroquine and azithromycin was initiated. At the same time, the patient with an arterial blood pressure of 190/100 mm/hg was administered with diuretic treatment to reduce lung congestion. The follow-up computed tomography of the patient showed rapid recovery, and ground glass appearances had completely resolved. The PCR was negative and the patient was diagnosed with acute lung edema. The treatment was prescribed, and the patient was discharged from the hospital. Thoracic tomography findings are useful in early period for COVID-19 diagnosis; however, it may show similar results as other diseases that cause respiratory failure and lead to misleading interpretations.

Keywords: COVID-19, Sars-CoV-2, computed tomography

Introduction

Diverse experiences are being shared by scientists in many countries on the diagnostic evaluations of the Coronavirus-2019 (COVID-19) pandemic, which emerged in the Wuhan province of China and affected the whole world. Although polymerase chain reaction (PCR) is valuable in terms of diagnosis, it is also challenging to diagnose due to false negativity in early diagnosis. However, even though PCR is negative in thorax computed tomography (CT), there are many articles that report that peripheral and scattered bilateral consolidated areas are quite significant in early diagnosis of COVID-19 (1-3). We believe that CT will play an important role in the epidemic, which is also seen in our country, in the early diagnosis of patients, isolating the contacts and controlling the spread. While 91% of patients infected with COVID-19 apply with pneumonia, 3.4% of them can be seen in the Acute Respiratory Distress Syndrome (ARDS) table and 1.1% in the shock table (4). In this sense, it was determined as the main target to start the drug protocol, which was established in the light of shared treatment regimens in the world, together with supportive treatment in the early period by making rapid evaluations in the diagnosis (5).

Case Report

A 79-year-old woman is brought to our emergency department by ambulance with shortness of breath and respiratory distress after a sudden cough. Vital signs of the patient who had aortic stenosis in her history and stated that her daughter was working as a nurse in COVID-19 pandemic hospital was noted as SpO_2: 81% TA: 190/90, fever: 36.3 °C. In her physical examination, she had a skin with sweaty skin, and Ronkus and rough rales in the lungs. The patient's blood gas was Ph: 7.1 and PO_2: 62 and PCO_2: 78.6 complete blood counts were 16000/µL. Continuous Positive Airway Pressure (CPAP) was applied to the patient with severe respiratory distress by non-invasive mechanical ventilation. CRP, renal function tests and liver function tests parameters were within normal limits. Troponin I: 17,800 (0,000-16,000) was slightly above the upper value. When the thorax CT of the patient with sudden onset cough and respiratory distress was taken, hydroxychloroquine, influvir and azithromycin treatment was initiated by considering PCR, which is considered significant in terms of COVID-19 infection in both ac parenchyma, and widespread ground glass density and consolidated areas holding

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Received: 19.05.2020
Accepted: 10.07.2020

Cite this article as: Akküçük MH, Karadaş MA, Seviner M, Demir TA, Kılıçlı Doğanay E. False Positive Computed Tomography Imaging for Coronavirus-2019. Eurasian J Emerg Med. 2021;20(1):63-4.

all segments on the left (Figure 1). In addition, diuretics were given to the patient, who was hypertensive, to reduce lung congestion. After 8 hours of intermittent CPAP support, blood gas and oxygenation improved, and the patient was followed up with nasal oxygen. Upon the clinical recovery of the patient who was taken into service on the 2nd day, pro Bnp was sent to evaluate other differential diagnoses and control CT was planned. The patient's pro-bnp was very high (6800 µ/L), and there was no pathological finding other than minimal pleural effusion in the control CT taken on the 3rd day (Figure 2). The patient, who had a negative COVID-19 PCR test, was treated and followed up by cardiology. On the 3rd day, the patient recovered and was discharged with an outpatient treatment.

Discussion

There are many experiences in the literature about the characteristic features of pneumonia CT findings caused by COVID-19 (1,3,6). In the light of this information, high concentration on pandemic may cause us to ignore other emergency diagnoses. In addition, given hydroxychrorocinin and azithromycin may cause morbidity and mortality due to cardiac side effects (7). Patients infected with COVID-19 may come on the shock table due to ARDS and myocardial involvement, and acute lung edema may also come with a similar clinic (1). In addition, physical examination and other differential examinations are less frequent with the concern of minimizing contact during the pandemic period. In this period, we wanted to remind that thorax CT image, which is not in the diagnostic algorithm but which we frequently use for differential diagnosis due to a pandemic, may be very similar and may be confused with COVID-19 pneumonia. Although CT is a powerful diagnostic method while performing COVID-19 diagnosis and treatment, we think it is useful to re-examine with PCR and clinic.

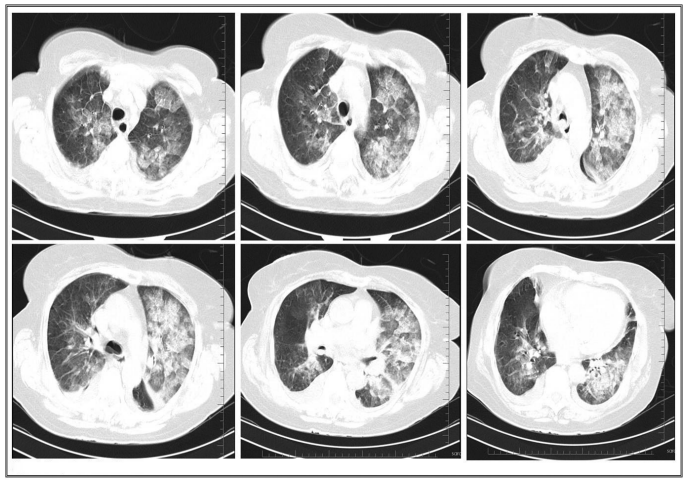

Figure 1. The patient's first CT scan

CT: Computed tomography

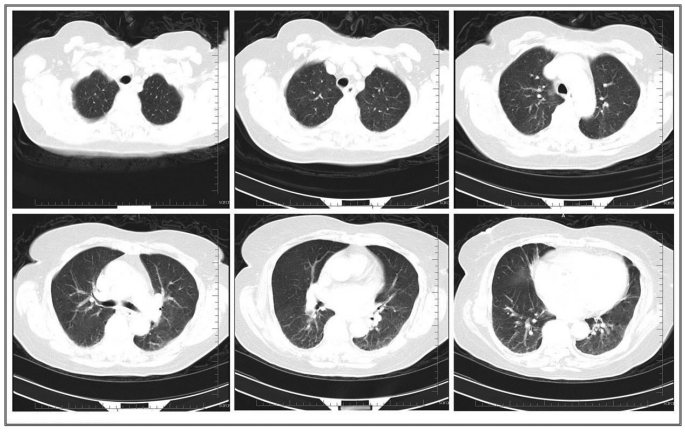

Figure 2. The patient's 3rd day CT

CT: Computed tomography

Ethics

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: M.H.A., M.A.K., M.S., T.A.D., E.K.D., Design: M.H.A., M.A.K., M.S., T.A.D., E.K.D., Data Collection or Processing: M.H.A., M.A.K., M.S., T.A.D., E.K.D., Analysis or Interpretation: M.H.A., M.A.K., M.S., T.A.D., E.K.D., Literature Search: M.H.A., M.A.K., M.S., T.A.D., E.K.D., Writing: M.H.A., M.A.K., M.S., T.A.D., E.K.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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