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

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

Editorial and publication processes of the journal are shaped in accordance with the guidelines of the international organizations such as the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the European Association of Science Editors (EASE). The journal is in conformity with Principles of Transparency and Best Practice in Scholarly Publishing (doaj.org/bestpractice).

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Emergency Medicine

Department of Medical-Surgery Sciences and Translational Mediicne

Chairman Postgraduate School of Emergency Medicine

Faculty of Medicine and Psychology

University of Rome Sapienza

Rome, Italy

E-mail: salvatore.disomma@uniroma1.it

Phone: +39348.3316131

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Original Article	5000 (Structured)	200	50	6	7 or total of 15 images
Review Article	5000	200	50	6	10 or total of 20 images
Case Report	1500	200	10	No tables	10 or total of 20 images
Letter to the Editor	500	N/A	5	No tables	No media
Scientific letter	900	N/A	10	No tables	2 or total of 4 images
Clinical Imaging/ Visual Diagnosis	400	N/A	5	No tables	3 or total of 6 images
History	900	N/A	10	No tables	3 or total of 6 images
Publication ethics	900	N/A	10	No tables	No media

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Books with Single Author: Cohn PF. Silent myocardial ischemia and infarction. 3rd ed. New York: Marcel Dekker; 1993.

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Scientific or Technical Report: Smith P. Golladay K. Payment for durable medical equipment billed during skilled nursing facility stays. Final report. Dallas (TX) Dept. of Health and Human Services (US). Office of Evaluation and Inspections: 1994 Oct. Report No: HHSIGOE 169200860.

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Case Report

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Concerning Nephrotoxicity of Top Guns: Concomitant Pippercillin-tazobactam and Vancomycin with Vancomycin Alone During Treatment of Critically Ill Patients

Sadaf Sheikh[1], Muhammad Akbar Baig[2], Muhammad Azhar Sharafat[3], Umair Javed[2], Muhammad Subhan Khan[2]

[1]Specialist, Emergency Medicine, Sultan Qaboos University Hospital, Muscat, Oman
[2]Department of Emergency Medicine, Aga Khan University Hospital, Karachi, Pakistan
[3]Intern, Civil Hospital Karachi and Dow University of Health Sciences, Karachi, Pakistan

Abstract

Aim: Use of combination antibiotics piperacillin-tazobactam (PTZ) and vancomycin (VAN) is so often used as "top guns" for severe infections in hospitalized patients. VAN's nephrotoxicity is well-known. PTZ has been seen to prolong increased creatinine levels. Reports have surfaced higher rates of acute kidney injury (AKI) among patients treated with combination of PTZ + VAN in the literature. The purpose of this study was to compare the prevalence of AKI with the use of VAN alone and combination of PTZ + VAN treatment at our institution. Our hypothesis was that the combination of PTZ + VAN would be associated with higher prevalence of AKI compared with VAN only.

Materials and Methods: We performed this study to compare the combination of PTZ + VAN and VAN alone in critically ill patients in our hospital from 2016 to 2018. Included patients were stratified by treatment with PTZ + VAN and VAN alone.

Results: A total of 113 patients were included who were treated with PTZ + VAN and VAN alone. Patient demographics, comorbidities, sites of infection, and duration for 48 hours were compared. We found that PTZ + VAN was better than VAN alone in terms of AKI.

Conclusion: The combination of VAN plus PTZ is better use to prevent AKI over VAN monotherapy. Further research in the critically ill population is needed. Recent literature has suggested that the concomitant use of PTZ and VAN is associated with a higher risk of AKI compared with the use of VAN alone. Our study suggested that patients getting combination therapy were sicker hence receiving it as an empiric therapy and it is required to look at the possibility of residual confounding in previous studies.

Keywords: Acute kidney injury, vancomycin, pipercillin-tazobactam

Introduction

Toxic effects caused by antibiotics lead to altered intra-glomerular hemodynamics, tubular cell toxicity, inflammation, crystal nephropathy, rhabdomyolysis, and thrombotic microangiopathy (1). There is a limited published data available on evaluation of prevalence of acute kidney injury (AKI) in the co-administration of piperacillin-tazobactam (PTZ) and vancomycin (VAN). With such prevalent and increasing use of these antibiotic combinations, (2) especially in the emergency department (ED), it is vital to determine any potential for drug-induced comorbidities. It will help develop a thought process among emergency physicians before administrating antibiotics to keep in mind certain essential components such as avoiding further harm, safeguarding patient safety, reducing length of stay in hospital leading to reduced hospital cost. Therefore, we aim to evaluate and compare the prevalence of AKI within 48 hours of completion of therapy with concomitant PTZ and VAN with VAN alone in critically ill patients of an ED of a tertiary care hospital in Karachi, Pakistan.

Aims and Hypothesis

Specific Aim: The primary aim of this study was to find prevalence of AKI, within 48 hours of completion of therapy of concomitant PTZ and VAN versus VAN alone amongst critically ill patients,

Corresponding Author: Sadaf Sheikh MD, Department of Emergency Medicine, Aga Khan University Hospital, Karachi, Pakistan
Phone: +0092 306 2567638 **E-mail:** sheikh.sadaf@gmail.com **ORCID ID:** orcid.org/0000-0001-7457-0012

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where antibiotics were initiated in the emergency room followed by ward admission in our hospital.

Secondary aims included AKI severity and time to AKI with outcomes such as length of stay and mortality.

Specific Hypothesis: Among adult patients there will be an increased prevalence of AKI within 48 hours of therapy with PTZ and VAN versus those treated with VAN alone.

Materials and Methods

Study Design

This was a retrospective cross sectional single-center study in critically ill patients admitted to a tertiary care hospital. Critically ill patients with sepsis who received VAN alone and those received combination therapy were identified from hospital's electronic medical records. Patients with normal renal function were defined as having an estimated glomerular filtration rate >60 mL/min. Patients received PTZ at a daily dose of 4.5 gram intravenously every 8 hours, and VAN 1 gram every 12 hours. Patients aged ≥18 years who had received a minimum of 48 hours of antibiotic treatment and who had a baseline serum creatinine (SCr) level measured within 24 hours of admission and whose SCr levels were checked daily or every other day, were included. An increase of ≥50% in SCr level from baseline or an absolute increase of ≥0.3 mg/dL in SCr level during antibiotic therapy or in the 72 hours after discontinuation of treatment would be considered AKI (2-10).

Study Duration: The data of past 1 year (January 2016 - December 2018) were collected to understand the trends and consequences of antibiotic use in this population.

Study Setting: Retrospective review of records of patients presenting to the ED.

Eligibility Criteria

- **Inclusion Criteria:**

1. All adult patients aged 18 years and older who were admitted in ED with sepsis. File codes for review: Sepsis and AKI
2. Initiation of concomitant therapy for 48 hours with an order for PTZ and VAN or VAN
3. Baseline SCr analyzed within 24 hours of admission
4. Patients with combination therapy if the PTZ was started within 48 hours of VAN

- **Exclusion Criteria:**

1. Patients on combination therapy already prior to ED visit
2. End stage renal disease or having a baseline raised SCr >1.5 mg/dL
3. Patients receiving hemodialysis or renal replacement therapy
4. Presence of shock
5. Mechanical ventilation
6. Chronic Liver disease
7. All pregnant women and patients having any history of an allergic reaction against a beta-lactam drug

Data Collection Procedure: A data collector was appointed who reviewed the electronic medical records system for all eligible adult patients presenting to the ED. All baseline socio-demographics (age, gender), suspected source of infection (skin and soft tissue infection, respiratory tract infection, intra-abdominal infection, urinary tract infection, empiric therapy, endocarditis, central nervous system infection, bone and joint infection, neutropenic fever) and SCr level measured in ED visit were be noted. The cases were divided into two groups as receiving PTZ and VAN or VAN alone.

Sample Size Calculation

An anticipated sample size of minimum 60 patients in VAN alone and 53 patients in PTZ + VAN were included rendering the total sample to be 113. Sample size was calculated by using OpenEpi software. The confidence interval was set to 95% with statistical power of 80% based on the estimates of a 41.3% rate of AKI in the PTZ + VAN and 15.7% in the VAN alone (3).

Patients from a sample in the PTZ + VAN group were consecutively selected from the most recent administration date until the minimum number of patients needed to meet the required sample size were included.

Ethical Review Committee Approval: The study was granted an exemption from the Ethical Review Committee of the Aga Khan University before initiation. All of the data collected remained confidential and properly stored as ethics review committee guidelines at the institution suggested. ERC approval granted by the Aga Khan University (protocol no: 2019-0880-2235).

Statistical Analysis

SPSS for Windows version 25.0 was used for statistical analyses. Variables were analyzed using Shapiro-Wilk test for their normality distribution where $p>0.05$ was taken as significant for normal distribution of data. Data were presented as mean ± standard deviation for continuous normally distributed variables while, continuous skew-distributed variables were presented as median (interquartile-range). Non-continuous variables were shown as numbers and frequencies. Univariate analyses were performed with χ^2 and Mann-Whitney U tests to identify variables.

Results

A record of 113 patients in total was selected for our retrospective analysis study. Almost half of them received PTZ + VAN (53/113; 46.9%). Age and gender distribution were almost equal among the groups (Table 1). Every patient who received the combination of PTZ + VAN had sepsis while only two-third of the patients who received VAN alone had sepsis. Hypertension was the most common comorbidity found in both the groups followed by Diabetes Mellitus. One-third of the patients in both the groups had their primary infective source within lung which was the major chunk of our selected patients. Patients treated with PTZ + VAN had higher exposure to other potential nephrotoxic drugs compared with VAN alone group with loop diuretic being the most common drug concomitantly taken by the overall population of our patients (35/113). Exposure to antibiotics other than PTZ and VAN was highest (34%) in our PTZ + VAN group. Median duration of antibiotic therapy was significantly higher in the PTZ + VAN group compared with VAN alone group [84 vs 36 hours, (U=1024, p=0.001)]. In the entire group of our sample population, AKI developed in 46 patients (40.6%) which was significantly higher in the VAN alone (53.3%) $\chi(1) = 8.448$, p=0.004 compared with PTZ + VAN group (26.4%). In the comparison of AKI between PTZ + VAN and VAN alone group (Table 2), it was observed that time taken for AKI development was almost equal in both the groups, but time taken for resolution was longer in VAN alone group. According to Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease staging, AKI developing in VAN alone

Table 1. Demographics and comparison between piperacillin-tazobactam + vancomycin and vancomycin groups

	PTZ + VAN (n=53)	VAN (n=60)	p
Age, years (mean +/- SD)	53.68 +/- 20.08	55.60 +/- 20.31	-
Gender			
Male (%)	31 (58.5%)	34 (56.7%)	-
Female (%)	22 (41.5%)	26 (43.3%)	-
Sepsis (%)	53 (100%)	37 (61.6%)	-
Comorbidities			
HTN (%)	20 (37.7%)	26 (43.3%)	-
DM (%)	17 (32%)	19 (31.6%)	-
CKD (%)	0 (0%)	3 (5%)	-
Source			
Lung (%)	18 (34%)	22 (36.6%)	-
Urinary Tract (%)	5 (9.4%)	6 (10%)	-
CNS (%)	3 (5.6%)	9 (15%)	-
Intra-abdominal sepsis (%)	4 (7.5%)	7 (11.6%)	-
Endocarditis (%)	0 (0%)	4 (6.6%)	-
Osteomyelitis (%)	2 (3.7%)	2 (3.3%)	-
Necrotizing fasciitis (%)	4 (7.5%)	1 (1.6%)	-
Diabetic foot (%)	3 (5.6%)	0 (0%)	-
Febrile neutropenia (%)	3 (5.6%)	0 (0%)	-
Other infection (%)	7 (13.2%)	2 (3.3%)	-
Unknown (%)	7 (13.2%)	14 (23.3%)	-
Duration of antibiotic therapy, hours (median; range)[a]	84; 24-144	36; 24-72	**0.001**
Other drugs (%)	35 (66%)	39 (65%)	-
NSAIDs (%)	11 (20.7%)	6 (10%)	-
Loop diuretic (%)	12 (22.6%)	23 (38.3%)	-
ACEI (%)	1 (1.8%)	1 (1.6%)	-
ARBS (%)	5 (9.4%)	1 (1.6%)	-
Amphotericin B (%)	1 (1.8%)	3 (5%)	-
Acyclovir (%)	2 (3.7%)	5 (8.3%)	-
Other antibiotics (%)	18 (34%)	6 (10%)	-
Total hospital stay, hours (median; range)[a]	144; 96-240	120; 84-216	0.546
Development of AKI (%)[b]	14 (26.4%)	32 (53.3%)	**0.004**

PTZ: Piperacillin-tazobactam, VAN: Vancomycin, HTN: Hypertension, DM: Diabetes Milletus, CKD: Chronic Kidney disease, CNS: Central nervous system, NSAIDs: Non-steroidal Anti-inflammatory drugs, ACEI: Angiotensin converting enzyme inhibitors, ARBS: Angiotensin II receptor blockers, AKI: Acute kidney injury, [a]: Mann-Whitney U test, [b]: chi-square test, *: Bold values indicate statistically significant difference (p<0.05), SD: Standard deviation

Table 2. Comparison between the characteristics of kidney injury in piperacillin-tazobactam + vancomycin and vancomycin groups

	PTZ + VAN (n=14)	VAN (n=32)	p
Time to development of AKI, hours (median; range)[a]	48; 24-96	48; 24-72	0.449
AKI stage[b]	-	-	0.355
Risk (%)	7 (50%)	7 (21.9%)	-
Injury (%)	4 (28.6%)	13 (40.6%)	-
Failure (%)	3 (21.4%)	9 (28.1%)	-
Loss (%)	0 (0%)	1 (3.1%)	-
ESRD (%)	0 (0%)	2 (6.2%)	-
Outcome[b]	-	-	0.055
Resolved (%)	5 (35.7%)	8 (25%)	-
Persisted (%)	3 (21.4%)	19 (59.4%)	-
Mortality (%)	6 (42.9%)	5 (15.6%)	-
Time to resolution, hours (median; range)[a]	48; 24-216 (n=5)	120; 54-180 (n=8)	0.416
Total hospital stay, hours (median; range)[a]	192; 114-288	144; 90-216	0.288

PTZ: Piperacillin-tazobactam, VAN: Vancomycin, AKI: Acute kidney injury, ESRD: End Stage Renal disease, [a]: Mann-Whitney U test, [b]: chi-square test

group was of higher stage compared with PTZ + VAN group and while AKI persisted more frequently in the VAN alone group, the mortality rate was higher in the PTZ + VAN group. However, the thing to take notice was, none of these differences between PTZ + VAN and VAN alone group was statistically significant as evident by "p-values" presented in the table. Our secondary finding showed that patients with concomitant exposure to loop diuretic had significantly higher incidence of AKI compared with patients without exposure to loop diuretic [65.7% vs 29.5% ($\chi(1) = 13.136$, $p<0.001$] AKI developing in only 29.5% of the patients who did not receive loop diuretic.

Discussion

Our study showed that the incidence of AKI was significantly higher in the VAN only group (41.3%) compared with the PTZ + VAN group (16.0%). Davies et al. (1) focused on the combination of PTZ and VAN and reinforced our findings in their study. Jensen et al. (2) meticulously evaluated the effects of PTZ on renal function which was the re-analysis of data from a 1200-patient multicenter clinical trial and showed that patients treated with PTZ exhibited delayed improvement in their SCr during antibiotic therapy, compared with patients treated with meropenem (2-4). Our study set up a match between the veterans (VAN with well-known renal toxicity) and upcoming qualifier PTZ. However, it should be highlighted that VAN-associated renal toxicity really depends on the filtration system of kidney's function.

It was considered that PTZ raised the SCr without harming the kidneys. PTZ reduces creatinine secretion via organic anion transport system which is defined as "pseudo-nephrotoxicity" and recent studies (5-9) doesn't show acute renal damage. Some studies shows that combination antibiotics might even have a nephron-protective effect (9) and further studies are needed to show the clear evidence.

Literature findings suggested that critically ill patients at the time of ED presentation were very sick and that nephrotoxicity should be kept in mind before giving antibiotics (10-12). It is hard to label combination antibiotics as nephrotoxic but it's important to deliberate when to choose the top guns to avoid further morbidity and mortality and increased financial burdens in terms of prolonged hospital stay.

Knowing the physiology, VAN causes oxidative injury while many risk factors such as preexisting renal disease, hypotension, obesity, hospitalization in critical care unit are already in play. VAN, being a favorite antibiotic for many physicians, requires rigorous pharmacy insights for its therapeutic dosing and serum level monitoring.

Study Limitations

Limitation of this study is its retrospective design and potential confounding by indicating the risk of overfitting when selecting variables for regression based on a univariate analysis and finally, the large number of predictors with respect to the numbers of observation (12). The large majority of studies supporting higher incidence of AKI in patients receiving PTZ + VAN compared with VAN alone are based on retrospective data. Nevertheless, it is said that there is no smoke without fire and considering this a potential modifiable risk factor for AKI, further research is certainly warranted. No studies in Pakistan is yet performed which have closely looked into the association of empiric antimicrobial therapies with an increased risk for AKI, which would be a much more clinically important and relevant finding. This was a retrospective single-center study and should be considered hypothesis-generating and literature review with local data set in a different set of population at best.

Conclusion

PTZ toxicity is an emerging situation with a clinical impact that is just now being increasingly recognized and appreciated. Studies stating combination of PTZ + VAN causing AKI are certainly not enough to demonstrate causation, but it is an interesting association nonetheless. Nevertheless, the study findings should encourage physicians to take the usual care in dosing PTZ and VAN with close serum VAN monitoring especially in patients receiving the combination. Antibiotics should be de-escalated as soon as feasible, such as discontinuing VAN if methicillin-resistant staphylococcus aureus is not a serious concern. Following procalcitonin levels, along with blood culture results, leukocytosis and temperature curves, can help us give physicians confidence in safely discontinuing or narrowing antibiotics.

Ethics

Ethics Committee Approval: The study was granted an exemption from the Ethical Review Committee of the Aga Khan University before initiation. (protocol no: 2019-0880-2235)

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practice: Concept: Design: Data Collection or Processing: S.S., M.A.S., M.S.K., U.J., M.S.K., Analysis or Interpretation: M.A.S., M.S.K., Literature Search: Writing: M.A.B, M.S.K.

Conflict of Interest: None declared.

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Does Neutrophil Lymphocyte Ratio Have a Clinical Value to Determine the Severity of the Patients with Acute Appendicitis?

Vehbi Özaydın[1], Sinem Doğruyol[1], Seda Nur Bağdigen[1], Burak Katipoğlu[2], Mehmet Gül[3]

[1]Department of Emergency Medicine, Medeniyet University Göztepe Training and Research Hospital, İstanbul, Turkey
[2]Department of Emergency Medicine, Ankara Training and Research Hospital, Ankara, Turkey
[3]Department of Emergency Medicine, Konya Necmettin Erbakan University Meram Faculty of Medicine, Konya, Turkey

Abstract

Aim: The aim of our study is to investigate the predictive value of the neutrophil lymphocyte ratio (NLR) assessed in the emergency department to distinguish complicated and uncomplicated patients with acute appendicitis (AA).

Materials and Methods: In our study, the files of the patients with AA who visited our emergency clinic between 01.06.2015 and 01.01.2016 and then were operated in our hospital were reviewed retrospectively. The age, gender, the imaging method performed in the emergency clinic with an AA preliminary diagnosis, the result of the radiologic report in terms of AA and histopathological examination results were recorded according to the patients' records. The patients were divided into two groups: Complicated AA (group 1) and uncomplicated AA (group 2) based on their histopathological analysis results. The laboratory parameters of the patients, which were seen within the first 30 minutes after they visited the emergency clinic, were examined.

Results: One hundred and twenty one of the 154 patients who were involved in the study were in group 1 and 33 of the patients were in group 2. A statistically significant difference was found between two groups in terms of the number of white blood cells and NLR (p=0.000). The cut-off value for NLR in the complicated AA distinction was detected as 7.3 (75.8% sensitivity, 81.8% specifity).

Conclusion: As an easy and effective analysis method, we think that NLR might be a good guide to diagnose complicated patients with AA quickly.

Keywords: Acute abdomen, complicated appendicitis, laboratory parameters

Introduction

Acute appendicitis (AA) is one of the most common causes of acute abdomen in emergency services. Although the patients usually appear to have characteristic symptoms, the number of patients with atypical complaints is not low to be underestimated (1). Despite the widespread use of imaging modalities such as ultrasound (US) and computed tomography (CT), the clinical diagnosis of AA is still challenging (2). In this process, systems that use more than one step give more satisfactory results than a single diagnostic method. These diagnostic approaches may dramatically reduce negative appendectomies, perforation numbers, and the time spent in the hospital (3).

In many parts of our country, there are centers that cannot benefit from imaging methods. In these centers, the most important diagnostic tool for AA is a careful anamnesis and a good physical examination supported by simple laboratory results. There are many studies evaluating the number of leukocytes in whole blood count in the case of AA. Differently, the neutrophil lymphocyte ratio (NLR) is a relatively new marker for studies and is associated with poor survival in many diseases (4,5). For this purpose, studies have been carried out to test if NLR can distinguish complicated and uncomplicated patients with AA (6,7).

The aim of our study is to investigate the predictive value of the NLR assessed in the emergency department to distinguish complicated and uncomplicated patients with AA. All of the patients in this

Corresponding Author: Sinem Doğruyol MD, Department of Emergency Medicine, Medeniyet University Göztepe Training and Research Hospital, İstanbul, Turkey
Phone: +90 505 847 41 24 **E-mail:** dogruyolsinem@gmajl.com **ORCID ID:** orcid.org/0000-0002-6949-7233
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study were examined with AA prediagnosis and operated after evaluating with at least one of the imaging modalities to confirm the AA diagnosis. The postoperative pathological results of the patients were evaluated retrospectively to determine whether they were complicated.

Materials and Methods

The patients with AA who visited the emergency clinic in a third-stage emergency department of a university hospital and were operated in the hospital during a 6-month period from June 1, 2015, to January 1, 2016, were reviewed retrospectively. The ethics committee's approval for the study was given by the same institution.

The files of the patients between the ages of 18-65 years who were operated by our hospital's general surgery department after visiting the emergency clinic and had complaints compatible with AA and underwent at least one imaging modality (US and/or CT) in our hospital's records during diagnostic process in the emergency clinic were reviewed. The official radiology reports of the imaging method in all these patients were available in our hospital system. The age, gender, the imaging method performed in the emergency clinic with an AA preliminary diagnosis, the result of the radiologic report in terms of AA and histopathological examination results were recorded according to the patients' records. The patients were divided into two groups: Complicated AA (group 1) and uncomplicated AA (group 2) based on their histopathological analysis results. As a result of histopathology results, the ones that had gangrenous appendicitis, perforated appendicitis, plastron appendicitis, periapical abscesses were considered as complicated AA. The white blood cell (WBC), neutrophil, and lymphocyte counts were determined by analyzing the laboratory parameters taken from the peripheral vena in the first 30 min of patients' visit to the emergency department. The NLR value was calculated by dividing the number of neutrophils by the number of lymphocytes. The reference ranges were 4000-10000/mm^3 for WBC and 1400-6500/mm^3 for lymphocytes in terms of laboratory parameters. The NLR ratios of both group 1 and group 2 were compared individually. The patients who had acute and chronic diseases which could affect laboratory parameters through inflammation markers were not included in this study.

Statistical Analysis

For statistical evaluation of the data, the statistical package software of IBM Statistics 20.0 (SPSS) was used. The suitability of continuous variables to normal distribution was assessed using the Kolmogorov-Smirnov test. The Student's t-test was used for the binary group comparisons of normally distributed data. The chi-square test was used to compare categorical variables. Percentage, frequency, mean, and standard deviation were given as descriptive statistics. The receiver operating characteristic (ROC) analysis was used to determine the diagnostic and cutoff values of NLR in complicated patients with AA. In the obtained ROC curve, the proximity of the area under the curve (AUC) value of 1 indicated a high value of the significance level of the test. The level of significance for the AUC obtained in the same test was also determined. The results were evaluated in a 95% confidence interval (CI) and at a significance level of $p<0.05$.

Results

Of the 154 patients studied, 93 (60.4%) were male and 61 (39.6%) were female. The mean age of the males was 36.39±12.69 years and the mean age of the females was 33.29±10.38. There was no significant difference in age distribution among the sexes ($p>0.005$).

There were 121 patients in group 1 and 33 patients in group 2. There was no significant difference between the two groups in terms of gender ($p>0.005$). The mean age of all patients was revealed as 34.52±11.41 years and when the mean age of the patients was examined, there was no significant difference between group 1 and group 2 ($p>0.005$). However, a significant difference was noted in the WBC count between the two groups (mean difference, 2.9; 95% CI=1.316-4.508) ($p=0.000$). A significant difference was found between the two groups in terms of NLR. The NLR values of the patients in group 2 were found to be higher compared with the values of the patients in group 2 (mean difference, 6.4; 95% CI=4.952-7.807) ($p=0.000$) (Table 1).

When the imaging method in the diagnosis process was evaluated, it was seen that 126 out of 154 cases were diagnosed with CT, 73 with CT and 45 with both US and CT. One hundred and nine cases (70.8%) were diagnosed with a single imaging method while both imaging methods were used in 45 cases (29.2%). There was no significant difference between groups in terms of selection of individual imaging methods ($p>0.005$). There was no significant difference between the groups in terms of the number of patients using both imaging methods ($p>0.005$).

Table 1. Demographic features and laboratory analyses of the groups

Variant group		Group 1 (n=121)	Group 2 (n=33)	p
Gender	Male	76 (62.8%)	17 (51.5%)	>0.005
	Female	45 (37.2%)	16 (48.5%)	-
Age		34±10.5	37±14.2	>0.005
Leukocyte		13302±3686	16215±5417	0.000
Neutrophil lymphocyte ratio		5.2±3.1	11.6±5.6	0.000

The NLR thresholds were calculated with ROC curve analysis. The AUC for NLR was calculated as 0.856 (standard error, 0.038; 95% CI=0.781-0.930) (p=0.000). For NLR, the cut-off value was found to be 7.3 (75.8% sensitivity, 81.8% selectivity) and 3.3 was determined as a threshold value which could be used for exclusion and 16.8 could be used as threshold value for diagnosis (Figure 1).

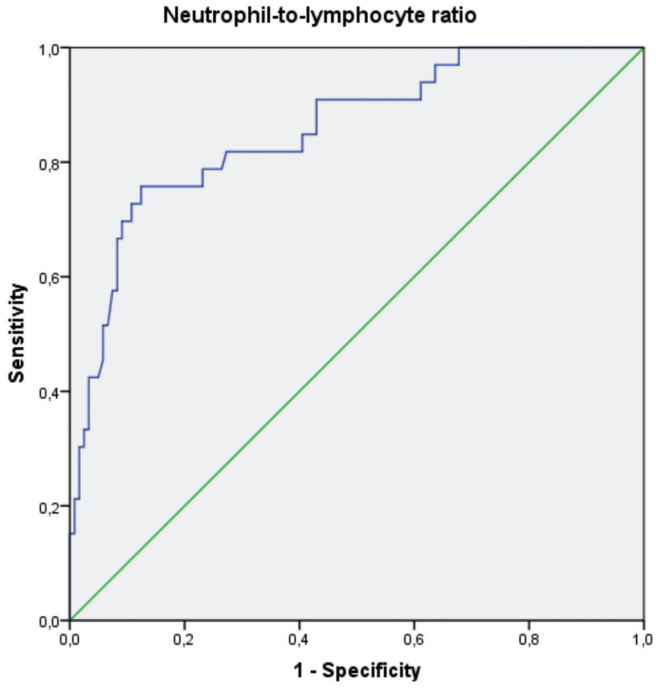

Figure 1. Receiver-operating characteristic curve for neutrophil-to-lymphocyte ratios in complicated appendicitis Area under the curve was 0.856 (standard error, 0.038; 95% CI=0.781-0.930). Ideal cutoff value was 7.3, this cutoff value yielded sensitivity of 75.8% and specificity of 81.8%

CI: Confidence interval

Discussion

The early diagnosis of AA is still a challenge. The perforation incidence in patients with AA is between 18.3% and 34% (8). As only the perforation incidence is considered to be quite high, the need for simple and useful tests becomes important for the early recognition of complicated patients.

Previous studies have shown that high WBC in total blood count is sensitive to indicate appendix inflammation (9). However, as the high WBC does not seem to be specific in AA, different tests should be considered as well. The most valuable diagnostic tool is the total blood count following anamnesis and physical examination in the rural areas where imaging methods cannot be used in the diagnosis process. Therefore, the parameter that will lead to the early diagnosis of patients with complicated AA should be selected from basic blood parameters. In the light of the studies analyzing basic blood parameters, the individual value of NLR in the evaluation of AA complications has recently become quite popular (4).

In a similar study, the cut-off value of NLR was 7.95, and it was reported to have high sensitivity and specificity to distinguish complicated patients with AA from uncomplicated patients (10). It was thought that the increase in NLR seen in complicated patients with AA occurred due to a decrease in the number of lymphocytes in severe patients which was reported in the literature a long time ago (11). In this study, a similar cut-off value was found (3,7) in terms of differentiating complicated patients with AA. Unlike in the literature, the specificity ratio at the cut-off value was higher in this study.

The WBC counts in the complicated patients with AA were significantly higher compared with the WBC count in the other patient groups. In accordance with the literature, WBC values were found to be significantly higher in complicated patients with AA (12). Thus, WBC count can be used for the early diagnosis of complicated patients with AA and is correlated with histopathological results. Although the increase in WBC count was used as a parameter in the AA diagnostic process earlier, it still remained effective to assess the severity of the cases.

From the demographic point of view, it was determined that there was a significant difference between the uncomplicated and complicated patients with AA according to gender in our country. The frequency of complicated AA was higher in women and uncomplicated AA frequency was higher in men (7). In our study, we did not find any significant difference between the patient groups in terms of gender. Similarly, no significant difference was found in terms of age distribution among the groups. As far as we can tell from the literature, there is no study evaluating the use of NLR to guide the choice of imaging method in AA. Kim et al. (13) evaluated the correlation of CT outcomes with laboratory test outcomes and explained the contribution of both tests. In our study, we evaluated the imaging modalities performed during the diagnostic process of patients with AA and did not find any significant difference between the patient groups that we categorized according to the complications. However, since this was a retrospective study, a prospective study might be useful in evaluating the guiding power of NLR to decide which imaging method would be better in the diagnostic process.

Study Limitations

The limitation of this study was that it was designed retrospectively and performed by examining the data in the patient files. A prospectively designed study contributing to scoring systems in

AA can be conducted to determine the severity of patients with AA using NLR. The NLR cutoff value determined in this study might serve as a guide due to its high specificity and sensitivity rates.

Conclusion

The early recognition of complicated patients with AA is a primary task of emergency medicine specialists and general surgery specialists. AA accounts for a large proportion of the patients diagnosed in terms of acute abdomen in emergency departments. NLR can be used as an easy and useful diagnostic tool in the rapid recognition of complicated patients with AA in rural areas where it is difficult to access imaging methods.

Ethics

Ethics Committee Approval: Retrospective study..

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: V.Ö., S.D., Design: S.D., B.K., Data Collection or Processing: S.N.B., V.Ö., Analysis or Interpretation: M.G., B.K., Literature Search: S.N.B, Writing: S.D., V.Ö.

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

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A Study of Pharmaceutical Drugs Poisoning Cases Admitted to the National Poisoning Center, Kasralainy Teaching Hospital in Cairo

Eman Abdel Monem Abdel Rasheed[1], Nashwa Elmahdy[1], Ezzeldin Shalaby[2], Huda S. Karoube[1], Sayed M. Badawy[1]

[1] National Center for Clinical and Environmental Toxicology, NECTR, Faculty of Medicine, Cairo University, Cairo, Egypt
[2] Forensic Medicine and Clinical Toxicology Department, Faculty of Medicine, Cairo University, Cairo, Egypt

Abstract

Aim: There is a necessity to identify the specific therapeutic drugs most frequently responsible for the acute medicinal poisoning to take up appropriate preventive efforts and management.

Materials and Methods: This study included all cases of medicinal poisoning exposures (7282 cases) presented to the emergency Department of The National Poisoning Center, Cairo University, during the period January 2016 to December 2016. The data were statistically analyzed to assess a correlation between gender, age, and most frequently seen agents.

Results: Therapeutic drugs (68%) were the most common cause of poisoning. It was found that 53% of medicinal poisoning patients were adults. Accidental drug agents poisoning in children younger than 4 years represented 20% of the medicinal poisoning cases. Of the patients with medicinal poisoning 74% were female and 26% were male. Detailed information on categories of drugs causing medicinal poisonings was presented. Paracetamol (9.6%), nonsteroid anti-inflammatory drugs (9.6%) and sedatives/hypnotics (10.7%) were the most common drugs causing medicinal poisoning.

Conclusion: Female gender and young age are the risk factors of medicinal poisoning. The majority of poisonings is intentional poisoning in female adults. An important concern should be raised towards availability of prescription medications within the reach of children.

Keywords: Acute medicinal poisoning, epidemiology, poisoning center

Introduction

Acute poisoning following accidental and intentional ingestion of medications or drug overdoses constitutes a high degree of mortality, morbidity and health care cost worldwide (1-5). The resources of drugs poisoning vary by region and country (6,7), which reflect the prescribing practice and the availability of drugs in the population (8).

Opioids and anti-depressants in the United Kingdom (UK) (9); sedatives-hypnotics and anti-psychotics in Japan (10); opioids, benzodiazepines, and anti-depressants in the United States (US) (11); anti-depressants and analgesics in Turkey (12); opioids and pesticides in Iran (6) and analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) followed by anti-convulsants and anti-hypertensives in Saudi Arabia (13) are the leading drugs causing to poisoning.

Drug overdoses can affect people of any age. Most of childhood poisonings are accidental, while poisoning in adolescents is mainly intentional (self-harm). Few studies have investigated the medicinal poisoning pattern in our country. There is a necessity to know the medications that contribute to poisoning cases, to take up appropriate preventive efforts and management. This study was aimed to determine the pattern of medicinal poisoning of patients who visited Kasraleiny Teaching Hospital, Cairo, for the prevention of poisoning due to pharmaceuticals.

Materials and Methods

A study was conducted in all cases of medicinal poisoning at the National Center for Clinical and Environmental Toxicology (NECTR) during the period January 2016 to December 2016. The differences between groups were investigated with statistical

Corresponding Author: Sayed M. Badawy MD, National Center for Clinical and Environmental Toxicology, NECTR Faculty of Medicine, Cairo University, Cairo, Egypt
Phone: +00201146397864 **E-mail:** sayedbadawy@hotmail.com **ORCID ID:** orcid.org/0000-0003-1825-1556

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analysis of data taken from charts which retrospectively included age, gender and agents causing poisoning.

Patients were divided into nine major groups based on the categories of pharmaceuticals: Central nervous system agents, cardiovascular system agents, respiratory system agents, analgesics, antibiotic agents, anti-diabetics, contraceptives, gastrointestinal agents and others.

Statistical Analysis

Factors that might be associated with the poison exposure were analyzed with the Pearson X^2. Yate's correction chi-square test of Med Calc software were used for a comparison between groups. Statistical p values less than 0.05 were considered significant.

The guidelines on patient consent were met. The study followed ethical principles of the Declaration of Helsinki for medical research of human subjects.

Results

The present study was conducted in 7282 patients with medicinal poisonings at the emergency department of NECTR during the period January 2016 to December 2016. Therapeutic drugs (68%) were the most common cause of poisoning (Figure 1). Substances causing poisoning were unidentified in 4% of cases. Of the patients with medicinal poisoning 74% were female and 26% were male as shown in Table 1 ($p<0.0001$). In the medicinal poisoning, adults accounted for 53% of all cases, followed by children younger than 4 years (20%), patients with ages between 13-18 years (19%) and with ages between 4-12 years (8%).

Detailed information on pharmaceutical drug categories causing medicinal poisonings is presented (Figure 2). Therapeutic drugs were categorized into analgesics (24%), central nervous system agents (21%), cardiovascular system agents (7%), respiratory system agents (6%), antibiotics (8%), contraceptives (8%), anti-diabetics (5%), gastrointestinal agents (6%) and others (15%) ($X^2=45.630$ $p<0.0001$).

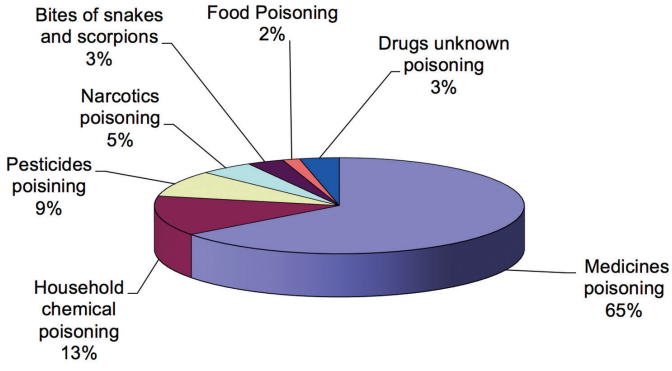

Figure 1. Distribution of poisoning types

Table 2 shows detailed information of therapeutic agents causing poisonings. Central nervous system agents were subcategorized into sedative/hypnotics (51%), anti-psychotic (20%), anti-epileptics (18%) and anti-depressants (12%) ($X^2=36.386$, $p<0.0001$). Analgesics were subcategorized into Paracetamol (40%), NSAIDs (40%) and Acetylsalicylic acid (13%) ($X^2=15.677$, $p<0.0004$). Cardiovascular system agents were subcategorized into anti-hypertension agents (49%), anti-coagulants (16%), β-blockers

Table 1. Clinical features of medicinal poisoning cases

Characteristics	n, Percentage %		Pearson X^2(df), p
Gender			
Female	5389	74%	23.040 (1), p<0.0001
Male	1893	26%	
Age group			
Children (<4 years)	2693	20%	
Children (4-12 years)	914	8%	45.630 (3), p<0.0001
Adolescents (12-18 years)	2039	19%	
Adults (>18 years)	5674	53%	
Types of poisoning			
Medicinal drugs	7282	68%	
Household agents	1487	13%	
Pesticides	993	9%	198.515 (5), p<0.0001
Abuse agents	626	5%	
Snakes and scorpions	336	3%	
Food poisoning	159	1 %	
Reasons for poison exposure	4374	39%	
Accidental	6946	61%	4.840 (1), p=0.0278
Intentional	-	-	

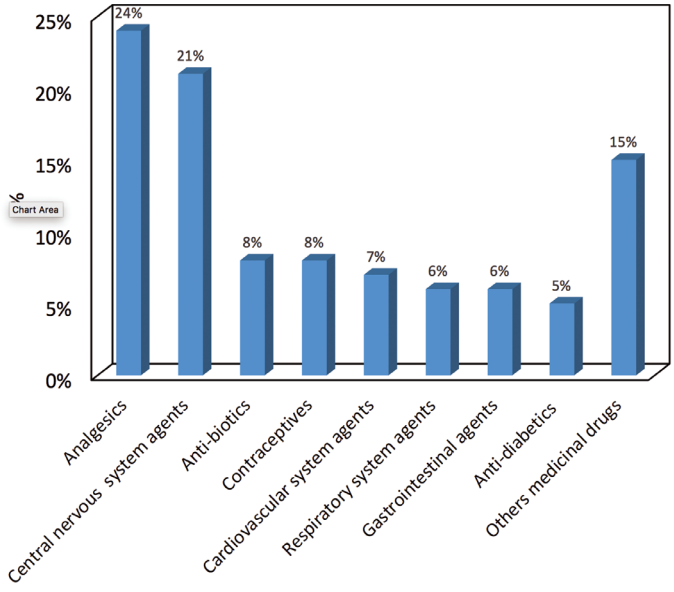

Figure 2. Distribution of medicinal poisoning

(13%), cardiotonic agent (11%), medications for hypotension (9%), and anti-hypertensive agents (49%) (X^2=56.305, p<0.0001). Respiratory system agents were subcategorized into theophylline (71%) and asthma agents (19%) (X^2=30.044, p<0.0001). Gastrointestinal agents were subcategorized into anti-parasitics (42%), anti-emetics (18%), anti-cholinergics (13%) and anti-acids (13%) (X^2=26.837, p<0.0001).

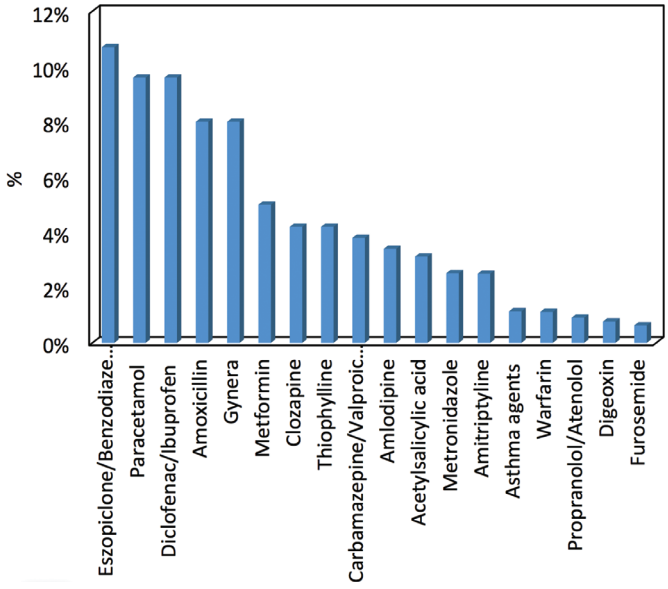

Figure 3. Most frequent agents causing poisonings

Discussion

The most common poisoning type was medicinal poisoning (68%) in our study. In agreement with other studies, medicinal drugs were the main toxic agents (14-17). Overdoses of drugs can be either accidental or intentional. Drug overdoses affect people of any age. Intentional drug overdoses are most common in female adults, whereas accidental drug overdoses are most common in very young children. Accidental drug agents poisoning in children younger than 4 years represents 20% of the medicinal poisoning cases. Drug overdoses in children are generally caused when medication is accidentally left within the child's reach. Children younger than 4 years tend to place everything they find into their mouths.

Drug overdose due to suicide attempt is more common in adolescents and adults. Patients with drug overdose suffer from mental health conditions. Many intentional poisoning patients are unwilling to give reliable history.

Of the patients with medicinal poisoning 74% were female and 26% were male (p<0.0001) which was similar to results found in other countries (14). Females are more likely to expose to emotional symptoms of stress or strain than males.

Paracetamol and NSAIDs (19.2%) were the most common pharmaceutical poisons (Figure 3). As similar, the American

Table 2. Percentage, categories, subcategories of most frequent agents causing poisonings

Most frequent agents*	%	Sub Cataegories	Cataegories
Benzodiazepine, eszopiclone	10.7	Sedatives/hypnotics	Central nervous system agents
Paracetamol	9.6	Vicodin	Analgesics
Diclofenac, ibuprofen	9.6	NSAIDs	Analgesics
Amoxicillin	8	Semisynthetic penicillins	Anti-biotics
Gynera	8	Progestin	Contraceptives
Metformin	5	Anti-type 2 diabetes	Anti-diabetics
Clozapine	4.2	Anti-psychotic	Central nervous system agents
Theophylline	4.2	Bronchodilator	Respiratory system agents
Carbamazepine, valproic acid	3.8	Anti-epileptic	Central nervous system agents
Amlodipine	3.4	Anti-hypertension agents	Cardiovascular system agents
Acetylsalicylic acid	3.12	NSAIDs	Analgesics
Metronidazole	2.52	Antiparasitic	Gastrointestinal agents
Amitriptyline	2.5	Anti-depressant	Cardiovascular system agents
Asthma agents	1.14	Asthma agents	Cardiovascular system agents
Warfarin	1.12	Anti-coagulant	Cardiovascular system agents
Propranolol/Atenolol	0.91	B-blockers	Cardiovascular system agents
Digoxin	0.77	Cardiotonic agent	Cardiovascular system agents
Furosemide	0.63	Anti-hypotension	Cardiovascular system agents

*: Others minor medicinal drugs: antihistamine, anticholinergic, antacids, etc. NSAIDs: non-steroidal anti-inflammatory drugs

Association of Poison Control Centers (AAPCC) (18) and a review of a toxicology cases (19) reported that the most common drugs causing to poisoning were analgesics, sedatives, anti-psychotics and anti-depressants. Analgesics and anti-depressants are the most common among single agent ingestions causing acute poisoning in Turkey (12). A previous study reported that paracetamol, NSAIDs and psychoactive drugs were the most common drug poisoning in the UK (20). Acetaminophen poisoning may occur either as a result of acute ingestion or following cumulative effects (21). Acetaminophen poisoning is the most common cause of drug-associated hepatitis worldwide (21) and acute liver failure requiring transplantation of liver in the UK and the US (22-24). A decrease in analgesic overdose deaths and liver transplantation cases (20) were reported in UK after legislation of analgesics pack sizes which limited the number of paracetamol tablets in packs, was promulgated.

The most common cardiovascular system drugs causing poisoning were anti-hypertensive agents (Amlodipine) (49%), anti-coagulants (Warfarin) (16%) and β-blockers (Propranolol/Atenolol) (13%) ($p<0.0001$). The most popular anti-hypertensive medication used to treat high blood pressure and Coronary Artery disease is Amlodipine. Amlodipine, sold under the brand name of "Norvasc", is a commonly prescribed long-acting calcium channel blocker. Its toxicity is the leading cause of mortality resulting from drug overdose seen in the cardiovascular medicine (25,26). Warfarin is a vitamin K antagonist which is used as an anti-coagulant for treatment of coagulopathic and thromboembolic disorders. Warfarin toxicity can be seen due to intentional adult overdose, unintentional overdose/toxicity, and pediatric ingestion by accident (27). In 2014, the AAPCC reported 1,766 single exposures to warfarin and 181 exposures to superwarfarin rodenticides. Beta-blocker drugs are a common cause of poisoning. Propranolol and Atenolol possess beta-adrenergic antagonistic properties that increase their potential toxicity with significant morbidity and mortality. Overdose of agents with membrane stabilizing activity (eg, Propranolol/Atenolol) can cause significant cardiovascular morbidity. In 2015, According to AAPCC database, 10,577 single- exposures to beta-blockers were reported. Of all the beta-blockers, propranolol accounts for the majority of cases with beta-blocker toxicity (28).

Theophylline (71%) was found to be the most common respiratory system agent causing poisoning which was followed by asthma agents (19%) ($p<0.0001$). Theophylline is primarily used as a bronchodilator for patients with asthma and Chronic Obstructive Pulmonary disease (COPD). Theophylline has a narrow therapeutic window, and even levels slightly above this therapeutic window can cause many adverse effects in the setting of acute and chronic toxicity (29). In the US, toxic exposures to theophylline have decreased significantly since its management for asthma and COPD has declined (29).

Metformin (anti-hyperglycaemic agent), is the most frequent anti-diabetic causing poisoning which accounts for 5% of the medicinal poisonings. The high rate of severe lactic acidosis caused by Metformin poisoning led to the withdrawal of it from the US (30).

Metronidazole (42%) is the most frequent gastrointestinal poisoning agent and have been reported in suicide attempts and accidental overdoses. Metronidazole is a very common worldwide anti-bacterial and anti-protozoal which is used more than 50 years (31). The mechanism of toxicity is uncertain. Metronidazole may bind to benzodiazepine receptor sites on gamma-aminobutyric acid channels of central vestibular inhibitory and cerebellar interneurons. It was found that the administration of a benzodiazepine shortened the duration of clinical signs related to metronidazole toxicity (32).

Benzodiazepines and Eszopiclone (non-benzodiazepine) sedatives/hypnotics (51%) were the most common among central nervous system agents causing poisoning, followed by anti-psychotics (20%), anti-epileptics (18%) and anti-depressants (12%) ($p<0.0001$). Sedative-hypnotic drugs become the preferred drugs for intentional overdose due to their availability and widespread use (33). The frequent prescription of psychiatric illnesses drugs has increased the incidence and the risk of accidental overdose (33). Patients suffering from epilepsy and some mental disorders, who use anti-epileptic drugs, are at increased risk of suicidal attempts. Anti-epileptic drugs (Carbamazepine/Valproic acid) constitute 3.8% of all causes with poisoning, which is similar in other countries. Annual report of the AAPCC states that anti-epileptic drugs comprise 3.2% of all causes of poisoning in adults (34). In Iran, anti-epileptic drugs poisoning accounted for 4.8% of all the pharmaceutical intoxications (35). In Turkey, 6.7% of medicinal intoxications was due to anti-epileptic drugs (36).

The incidence of cases with contraceptive overdose represented 8% of all poisoning cases. Gynera is the most common progestin which is widely used; however, significant acute toxicity has not been reported after overdose.

The incidence of cases with antibiotic overdose represented 8% of all poisoning cases. Amoxicillin is the most common antibiotic used in primary care. The amoxicillin overdoses have the potential to produce moderate and severe toxicity (37).

There are several causes of medicinal poisoning including using of wrong medicines, their easy availability at homes and suicide attempts in adults. The prevention of medicinal poisoning should merit high priority in the preventive efforts

and educational interventions to reduce the medicinal poisoning includes a change in dose of tablet, giving education, a change in the maximum daily dose, enhanced labeling and storing the drugs at homes far from the reach of children.

Study Limitations

Data taken from the charts retrospectively, were limited to therapeutic drug poisoning cases. Poisoning cases by drugs of abuse were not included in the study. The study excluded recorded calls of poisoned patients out-of-hospital who sought the advice from Emergency Medical Information Center. The percentage of intentional medicinal poisoning may not include all suicidal patients. Most self-poisoning patients were uncooperative to give reliable history.

Conclusion

The risk factors of poisoning are female gender and young age. An important concern towards drugs and abuse agents, which were available at homes within the reach of children, should be raised. The following conclusions were reached: (1) The most common type of poisoning was medicinal poisoning, (2) there was higher incidence of medicinal poisoning in females than in males, (3) the majority of poisonings was intentional poisoning in female adults, followed by accidental poisoning in children younger than 4 years (4) analgesics and central nervous system agents were the most common medicinal poisons and (5) Paracetamol, NSAID and sedatives/hypnotics were the most frequent poisoning therapeutics agents.

Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: The guidelines on patient consent were met.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: E.A.M.A.R., Design: E.A.M.A.R., S.M.B., Data Collection or Processing: E.A.M.A.R., S.M.B., Analysis or Interpretation: N.E., A.S.G., S.M.B., Literature Search: S.M.B., Writing: N.E., A.S.G., S.M.B., E.S., H.S.K.

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

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Rapid Sequence MRI Analysis of Acute Abdominal Pain

Ali Haydar Baykan[1], Şükrü Şahin[1], İbrahim İnan[2], Safiye Kafadar[1], Mustafa Göksu[3], Şükrü Mehmet Ertürk[1]

[1]Department of Radiology, Adıyaman University Faculty of Medicine, Adıyaman, Turkey
[2]Clinic of Radiology, Biruni University Hospital, İstanbul, Turkey
[3]Department of General Surgery, Adıyaman University Faculty of Medicine, Adıyaman, Turkey

Abstract

Aim: The aim of this study was to evaluate the diagnostic performance of non-contrast rapid sequences (RAMRI) visualization on cases who were clinically diagnosed as having acute abdominal pain (AAP).

Materials and Methods: Forty-six patients were chosen from 2850 patients who were admitted to the emergency service between January 2016 - January 2019 because of sudden onset abdominal pain and could not get a computerized tomography analysis. A 1.5 Tesla magnetic resonance (MR) device (GE Signa Hi-Speed, Milwaukee) was used for analysis. Coronal and axial T2-weighted single-shot fast spin-echo series were used as scan protocol. No intravenous, oral or rectal contrast material was used. The cases were identified as positive (+) or negative (-) by MRI. The cases who had symptoms related with AAP, were considered as positive (+), and the cases who did not have symptoms or had symptoms which were not related with AAP, were considered as negative (-).

Results: Of the patients, 26 (56.5%), were female and 20 (43.5%) were male. The median age was 38.65 (18-86) years. The treatment methodology was surgery for 25 cases (54%) and conservative for 21 (46%) cases. The operative group (surgically treated) included 24 MR (+) and one MR (-) cases. There was a harmony between the clinic and MRI data of all members in non-surgical group. The accuracy of the study was calculated as 95.6% (44/46). The sensitivity of RAMRI was calculated as 96% for operative group and 100% for non-operative group.

Conclusion: A successful diagnostic performance was achieved by non-contrast RAMRI in cases with AAP.

Keywords: Abdomen, magnetic resonance, pain, acute, appendicitis

Introduction

Acute abdominal pain (AAP) is one of the most common reasons of emergency service applications (1). Only a few of emergency cases can be diagnosed by physical and laboratory tests (2), because the differential diagnoses of AAP are wide and the most frequently encountered reasons are acute appendicitis (AA), biliary colic, cholecystitis, diverticulitis, ileus, gastrointestinal lumen perforation, pancreatitis and renal colic (3). Thus, radiological visualization is one of the most used methods for the diagnosis of the reasons for AAP (4). According to the conformity criteria of the American College of Radiology for the cases who have fever, delocalized stomach pain and lack of surgical background, the abdomen computerized tomography (CT) is the most suitable method (4). However, this methodology is rarely preferred for children and pregnant women because of the ionized radiation and contrast material usage which has nephrotoxic effects (5-7). Ultrasonography (US) can be preferred because it is easily accessible, cheap and safe (5). But there is a need for an operator and the stomach-intestine gas superposition prevents achieving high quality visualization, which are the disadvantages of the method (7,8). Besides, CT is more sensitive than US in delocalized AAP (4).

Magnetic resonance imaging (MRI) is not frequently used for AAP. Lack of ionized radiation and high soft tissue contrast are the advantages of MRI (5). MRI methodology is limited for intense stomach pains because of long duration for analysis and possible movement artefacts. But diagnostic images can be handled for these cases by rapid sequence abdominal MRI (RAMRI) (9). The main purpose of RAMRI analysis is to keep the patient in magnetic resonance (MR) device as short as possible and handle

Corresponding Author: Ali Haydar Baykan MD, Department of Radiology, Adıyaman University Faculty of Medicine, Adıyaman, Turkey
Phone: +90 505 351 93 07 **E-mail:** drbaykan@yahoo.com **ORCID: orcid.org/**0000-0002-9281-652X

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the diagnostic images by preventing movement artefacts. Single-shot sequences can be used for this purpose.

Single-shot fast spin-echo (SSFSE) sequence was used in this study to evaluate the performance of non-contrast RAMRI visualization on the cases who had clinic diagnosis of AAP.

Materials and Methods

The study had a retrospective design and the local ethics committee approval was obtained (2017/6-10) and it was carried out after the approval of the study. The study was in accordance of the working principles of the Helsinki Declaration.

Patients

Forty-six patients were chosen from 2850 patients for this study who were admitted to the emergency service because of sudden onset abdominal pain and could not get a CT analysis because of pregnancy, kidney dysfunction, history of contrast material reaction or did not have enough radiological data by US. The images were saved and evaluated retrospectively from University Hospital radiology archive. Patients who had low quality images, more than 72 hours of analysis duration with RAMRI and had renal colic diagnosis were excluded from the study.

MRI Protocol

For analysis, 1.5 Tesla MR device (GE Signa Hi-Speed, Milwaukee) was used. Coronal and axial T2-weighted SSFSE series were used as scan protocol (TR/TE/NEX: 634/101/1). Thickness and gap were determined as 5 mm and 0.1 mm, respectively. Additionally, axial fat-suppressed axial T2-weighted SSFSE and T2 gradient echo (GRE) were used when essential. No intravenous, oral or rectal contrast material was used. The analysis duration was shorter than 2 min. for most of the cases.

Statistical Analysis

The images were evaluated by two radiologists who had abdomen MR experience. The operation data for surgically cured patients and final clinic diagnosis for conservatively cured patients were saved. The cases were identified as positively (+) and negatively (-) by MRI. The patients who had symptoms (swelling and an inflamed appendix, enlarged ovarian torsion, pericholecystic fluid and accompanier biliary gallstone, existence of free fluid, inflamed intestinal wall) related with AAP were considered as positive (+); the patients who did not have symptoms or had symptoms (simple renal cortical cyst, liver hemangioma) not related with AAP were considered as negative (-).

SPSS 22.0 was used for statistical analysis. All data were managed, processed, and compiled in Microsoft Office Excel.

Results

Twenty-six (56.5%) of the patients were female and 20 (43.5%) of them were male. The median age was 38.65 (18-86) years. Additionally, six patients were pregnant. The treatment methodology was surgery for 25 cases (54%) and conservative for 21 (46%) patients. The operative group (surgically treated) included 24 MR (+) and one MR (-) patients. Fifteen of these patients had AA, three acute cholecystitis, one stomach perforation, two over torsion, 2 small bowel obstruction and one colon tumor. One of the patients who was reported as MR (-) was diagnosed as having AA, surgically. One of the patients who was reported as MR (+) and considered as having AA was identified as having normal appendix after surgery and pathology results. The surgical and pathologic diagnosis of other members of the operative group and MRI diagnosis of these patients were in harmony. Two of the patients were considered as having perforation, because they had periappendicular fluid and this phenomenon was proved surgically. Acute cholecystitis was evaluated in three of the patients and cholecystectomy was applied in them. Impacted cystic duct stone accompanied to one of them, cholelithiasis and choledocholithiasis accompanied to others. Perforation was considered in one of the patients because of having discontinuity at the stomach wall and free air at abdomen and this phenomenon was proved surgically (Table 1).

Three acute pancreatitis, one terminal ileitis, one colitis, one omental infarct, one pelvic inflammatory disease and one Crohn's disease were reported in the non-surgical group MR (+) which were clinically followed up and 13 cases were evaluated as non-pathologic and marked as MR (-) (Table 1). Duodenal diverticulum was diagnosed in one and gallbladder stone was detected additionally in two of the three patients who were diagnosed as having acute pancreatitis. There was a harmony between the clinic and MRI data of all members of non-surgical group. Torsion was evaluated in one of the pregnant patients because of the increase of asymmetric ovarian volume and she was detorsioned surgically. AA was diagnosed in two of the pregnant patients. No pathology was detected in the rest of the pregnant patients and the patients were discharged from hospital when the symptoms decreased. The radiological findings of some cases are shown in Figures 1 to 4.

The sensitivity of RAMRI was calculated as 96% for operative group and 100% for non-operative group.

Discussion

MRI is sensitive for the visualization of inflammatory changes at liver, biliary system, pancreas, urinary system, intestinal anses and pelvic organs (10). There are studies in literature which

Table 1. Classification of the MRI findings

	Surgery group (n=25)		Non-surgery group (n=21)	
Cases	**MR (+) (n=24)**	**MR (-) (n=1)**	**MR (+) (n=8)**	**MR (-) (n=13)**
Appendicitis	15	1	-	-
Cholecystitis	3	-	-	-
Over torsion	2	-	-	-
Intestinal obstruction	2	-	-	-
Colon tumor	1	-	-	-
Stomach perforation	1	-	-	-
Pancreatitis	-	-	3	-
Terminal ileitis	-	-	1	-
Colitis	-	-	1	-
Omental infarct	-	-	1	-
PID	-	-	1	-
Crohn	-	-	1	-

MR: Magnetic resonance, MRI: Magnetic resonance imaging, PID: Pelvic inflammatory disease

emphasize the activity of abdominal MRI on AA (11,12), acute diverticulitis (13), acute pancreatitis (14) and acute cholecystitis (15). Nevertheless, there is a lack of literature about the MRI application in AAP. Besides, there is no study on the cost analysis (2). MRI is generally applied to the pregnant patients in whom the US is not an option. However, CT is the first option for AAP and MRI is generally considered as an alternative. It has been considered as a good alternative, especially for the pregnants and children, to prevent patients from ionized radiation (16).

AA is still the most common reason for AAP and the ratio of AA in patients with AAP is between 11-23% (17). The ratio of AA in this study was 32% (15 of 45 patients) which was higher than the literature. CT analysis was not applied to the patients and this might be a reason for the high ratio. In one case, reactive fluid increase and mild enlargement were detected by RAMRI at appendix lumen radius and periappendicular area, respectively and reported as AA. But after the surgery it was concluded that there was no AA and the appendix symptoms improved. One of the other patients was reported as MR (-) by RAMRI but surgical evidences showed that the diagnosis was AA. In both patients, the duration between the RAMRI analysis and surgery was more than 24 hours. There are still blur parts in visualization data for AA which is an inflammatory disease. New studies should be organized with higher number of patients.

The images should be handled quickly, and they should be diagnostic in patients with AAP. The sequences like SSFSE, which have short analysis duration, can be used for this purpose. The analysis duration is shorter than 2 min. in most of the cases.

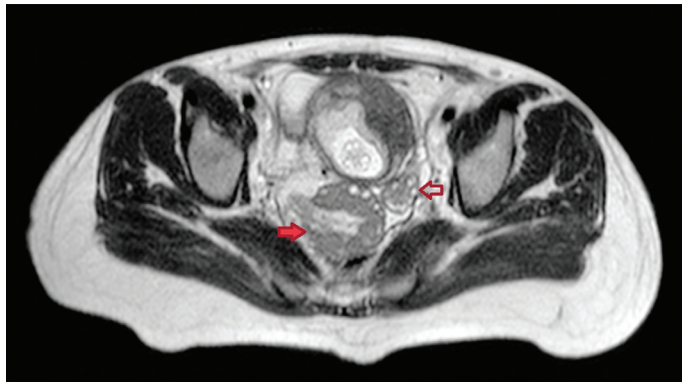

Figure 1. Increased right ovary dimensions (filled red arrow), peripherally displaced follicles and normal left ovary dimensions (empty red arrow). Right ovarian torsion

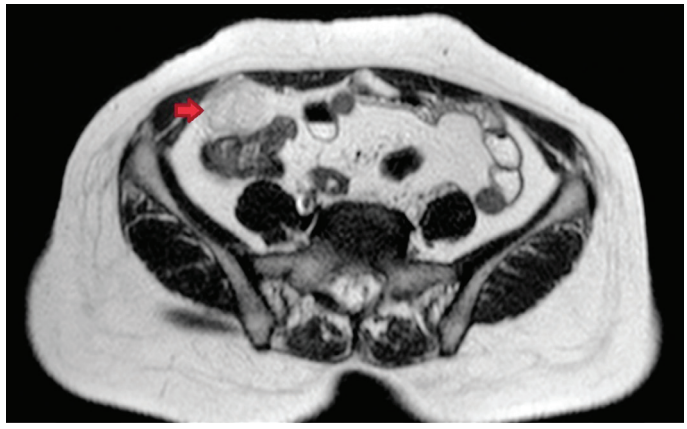

Figure 2. Inflammation at mass like fatty tissue which is at the neighborhood of anterior cecum in a patient with omental infarct

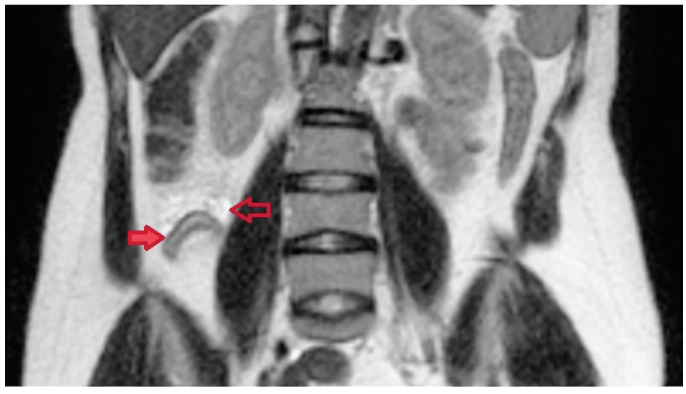

Figure 3. Dilated appendix (filled arrow) and periappendicular fluid (empty arrow) in a patient with acute appendicitis

Soft tissue resolution is considerably high and the inflammatory changes, like edema and fluid, can be diagnosed easily. It was reported that the detection sensitivity of air at GRE and inflammatory changes at T2A sequences were increased (10). These two sequences were applied in the current study when they were necessary. It was concluded that the RAMRI was significant and hopeful because the radiological analysis duration was shorter and it provided enough information.

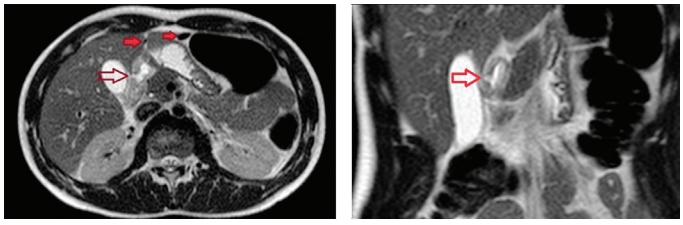

Figure 4. Free air (filled arrow) and perforation area (empty arrow) in a patient with stomach perforation

There are some disadvantages of the method; the patients who have claustrophobia and hearth battery are not allowed for MRI (17). Despite short analysis duration, diagnostic images may not be handled because of pain. The radiologist may not be familiar to the images of acute abdomen. This disadvantage can be eliminated by reputation of MRI on AA.

It was proved that rapid sequence MR was highly sensitive for the diagnosis of the AA pathology. Retrospective design of study, low patient number, absence of patients under 18 years and short follow up duration for the conservatively watched patients were the limitations of the study.

Conclusion

Rapid sequence MR is an important diagnostic tool for patients with AA when US can not provide enough data and CT is not possible. has important properties; it has high resolution for soft tissue, does not include radiation and does not need contrast material. Radiologists may not be familiar to AAP pathologies in RAMRI, because it is not a routine methodology. Frequently application of rapid sequence MRI in patients with AAP may improve the experience of radiologists.

Ethics

Ethics Committee Approval: The local ethics committee approval was obtained (2017/6-10) and it was carried out after the approval of the study. The study was in accordance of the working principles of the Helsinki Declaration.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Author Contributions

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

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Necessity of Emergency Chest X-ray in a Patient with Multiple Trauma with Injury Severity Score >15

Alireza Ala[1], Samad Shams-Vahdati[2], Golnaz Majidi[1], Respina Jalilian[3]

[1]Department of Emergency Medicine, Tabriz University Faculty of Medicine, Tabriz, Iran
[2]Department of Emergency Medicine, Tabriz University Faculty of Medicine, Road Traffic Injury Research Center, Tabriz, Iran
[3]Department of Emergency Medicine, Tabriz University Faculty of Medicine, Tabriz, Iran

Abstract

Aim: It was aimed to evaluate necessity of performing chest X-ray (CXR) in patients with multiple traumas and injury severity score (ISS) >15 in this study.

Materials and Methods: In this cross-sectional study conducted on trauma patients, the clinical and radiographic findings of all the patients were collected and the relationships between these variables were analyzed based on advanced trauma life support guidelines.

Results: A total of 170 patients was included in the study. Of them, 114 (67.1%) were male. The mean age of males was 33.86±17.36 years and it was 37.75±18.33 years in females (p=0.181). Twenty six patients had symptoms; seven patients had dyspnea and 19 had chest pain. Clinical examination was abnormal in 28 patients. Emphysema was detected in one patient, ecchymosis in one patient and local tenderness in 26 patients. CXR was performed in all patients and it was normal in 161 patients (94.7%). It detected rib fracture in six patients (3.5%), pulmonary contusion in two patients (1.2%) and hemothorax in one patient (0.6%).

Conclusion: Investigation of the necessity of emergency CXR in patients with multiple trauma with ISS >15 showed that there was no need to perform CXR in stable patients lacking signs and symptoms and instead we suggest physical exam to detect any problem.

Keywords: Chest X-ray, multiple trauma patients, injury severity score, chest injury

Introduction

Management of patients with multiple trauma is a real challenge for every physician (1). Assessment of traumatic patients is composed of two phases according to advanced trauma life support (ATLS) instructions: 1- Initial quick assessment to detect life threatening injuries, 2- Complete detailed assessment to locate injured body parts (2,3). Finding symptoms in traumatic patients is a time-consuming process. Moreover, it is much harder to rule out asymptomatic injuries than finding positive symptoms (3). Due to difficulty in management of patients with trauma and importance of this topic, trauma is a major hazard in every society, which affects health, economic and social indicators (4).

Injuries due to trauma, abdominal and chest injuries in particular, have increased steadily following an increase in road accidents, along growing urbanization and industrialization related problems.

Thoracic trauma is the most important type of emergency traumas, which can cause complications. Accurate follow up of patients, repeated examinations and regular paraclinical tests are helpful in the prevention of serious complications in these patients. Regular and control thoracic radiographies are performed in many centers with interval of 6-8 hours to follow up complications in stable patients. There are different ideas about follow up procedure and interval between actions. Some believe that even 3 hours is adequate for monitoring in patients with asymptomatic penetrating trauma (4).

Corresponding Author: Respina Jalilian MD, Tabriz University Faculty of Medicine, Department of Emergency Medicine, Tabriz, Iran
Phone: +98 93 72857020 **E-mail:** respina.jalilian@gmail.com **ORCID ID:** orcid.org/0000-0002-5334-251X

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Some traumatic patients need quick administrations and emergency surgeries while some of the cases can discharge from hospital without comprehensive investigation following initial assessments. A high percentage of these patients cannot be classified into the aforementioned two groups because their condition calls for more precise assessments. Proper use of diagnostic instruments in hospitals is a method to reduce costs imposed to patients and hospitals (3).

Blunt or penetrating chest trauma can cause death in 25% of cases and surgery is required in 10-15% of patients with chest trauma. Death due to chest trauma comprises half of all deaths due to trauma and usually occurs immediately after the chest injury (5).

Most patients with chest injury can be treated conservatively with close observation and tube thoracostomy. Blunt trauma, head injury and abdominal injury independently and adversely affect mortality after chest trauma. Investigation of causes and patterns in stab injuries assists to effective prevention (6,7).

Thoracic computed tomography (CT) is highly sensitive in detecting thoracic injuries of blunt chest trauma and is preferred to routine chest X-ray (CXR) to visualize lung contusions, pneumothorax, and hemothorax (8).

Different imaging studies exist to diagnose thoracic trauma injuries such as CXR, CT-scan and ultrasonography although these methods may not be efficient. Numerous studies revealed that CT-scan was more effective in diagnosis of injuries such as pneumothoraces, hemothoraces, and lung contusions (9,10). CT-scan is also more effective for these patients compared with CXR in terms of diagnostic error (11).

According to ATLS, it is necessary to obtain chest radiographic images in patients with multiple traumas and injury severity score (ISS) levels of higher than 15 or in patients at levels 3 or 4 in triages. Since most of the radiographic images in these patients are normal, the present study is based on the assessment of costs imposed on health care system and more importantly, of unnecessary X-rays imposed on patients' bodies. In addition, normal radiographic images obtained from these patients are assessed and compared with results of clinical examinations.

This study investigates normal chest radiography and unnecessary costs as well as relationship between results of chest radiography and clinical examination of patients with multiple traumas.

Materials and Methods

This is a prospective descriptive-analytic study that is performed in the emergency department of Tabriz University of Medical Sciences in traumatic patients to determine necessity of imaging in patients with multiple traumas and ISS >15. Assessments are performed according to ATLS. ISS is an emergency assessment with CT and other modalities beside first presentation vital sign.

This study included 170 patients with multiple trauma referred to emergency department between March 2015 and March 2016 during the four intermediate days of each month. Ethical committee of Tabriz University of Medical Sciences approved this study before patients' enrollment.

CXR was performed in every patient according to ATLS and the person performing serial examinations was blind to the results. Residents of emergency medicine in emergency room performed serial examination and monitored vital signs of patients. The person performing chest radiography was blind to the results of serial examinations. Serial examinations were performed every half an hour to 3 hours in the primary survey. Results were recorded as well.

Exclusion criteria included the following:

1. Patients below 18 years and over 65 years

2. Patients with ISS <15

3. Patients with the emergency severity index (ESI) 1, 2 and 5 (Patients with ESI 3 and 4 were enrolled in the study).

Statistical Analysis

Data obtained from patients were analyzed using the SPSS ver. 15 software. We used t-test method or Mann-Whitney U test method for independent groups to compare quantitative data after determining data distribution and chi-square test method or Fisher's exact test to compare qualitative data. A p value less than 0.05 was considered statistically significant.

Moral Considerations

Since there was no intervention during examining process and only routine information about patients was obtained, this study caused no moral problem. All of the moral criteria concerning use of patients' files were observed and file contents would stay completely confidential and inaccessible.

Results

In this study, we evaluated 170 patients with multiple traumas. The results are as follows:

Among all patients, 114 (67.1%) were male and 56 (32.9%) were female. Mean age of patients was 35.15±17.73 years ranging from 1 to 95 years. Mean age of male and female patients was

33.86±17.36 and 37.75±18.33 years, respectively (p=0.181). One hundred and fifty eight patients (92.9%) were in ESI III triage level and 12 (7.1%) were in ESI-IV triage level. Table 1 shows trauma causes by gender. There was no significant relationship between physical exam and triage level (p=0.189), between physical exam and trauma (p=0.64), between chief complaint and triage level (p=0.457), between chief complaint and gender (p=0.053) and also between gender and physical examination (p=0.306).

Twenty six patients had respiratory problems manifested as dyspnea in seven patients and chest pain in 19 patients. Physical examination of 28 patients detected positive clinical findings including skin emphysema in one patient, ecchymosis in another patient and local tenderness in 26 patients.

CXR was performed in all patients, 168 patients had one CXR (98.8%) and it was repeated in two patients (1.2%). CXR was normal in 161 patients (97.7%), while six patients had rib fracture (3.5%), one patient had hemothorax (0.6 %) and two patients had lung contusion (1.2%) all of whom had symptoms or positive findings in physical exam.

Table 2 shows CXR findings by trauma causes. There was no significant relationship between physical examination and CXR (p=0.647), between chief complaint and CXR (p=0.176) and also between CXR and trauma (p=0.844).

Discussion

Trauma is one of the most common causes of death in patients aged 1-44 years and the third common cause of death for all ages. The main cause of thoracic injuries is car accidents (12,13).

In this study, we decided to eliminate radiation dose on the patients, reduce additional costs imposed to health care system and maximize the efficiency of clinical evaluation.

Diagnostic value of imaging in patients with chest trauma is proven. But this procedure is not useful in patients with blunt trauma as a method of screening because it is time consuming.

Rib fractures occur in 2/3 of thoracic injuries during accidents (14,15). Multiple fractures of the ribs are observed in 5% of the people, which may cause intra-thoracic injuries (16-18). The results of our study were consistent with the results of the above mentioned studies. Six patients had rib fractures (3.5%) in our study, which was the most common findings in CXR.

CXR is recommended as a primary test for all patients with thoracic blunt trauma (19-21). It is inexpensive, convenient and non-invasive (22). CXR is applicable in diagnosing fractures, hemothorax, pneumothorax, pulmonary injuries and aorta injuries, however it has less efficacy in small lesions (21). Initial evaluation is performed by portable CXR in patients with higher risks such as unstable hemodynamics, severe tenderness, hypoxia, seat belt sign on the abdomen and symptoms of fractures in several ribs. Posteroanterior CXR is beneficial in normal states (23-25). Serial imaging is utilized in those with probability of rib's fracture with no findings in their radiography. This is more important in the elderly (26-28). In some cases of penetrating trauma, initial CT scanning is replaced with serial CXR. Performing serial CXR and the interval between them are still a controversy (19). CT scan gives more information about thoracic lesions (29-32), but it is not appropriate for all patients. Thoracic CT scan is used in patients with positive findings in CXR or positive symptoms like thoracic pain or dyspnea (26-28).

Serial examination every 6 hours can be replaced with control X-ray that reduces number of radiographies from 5 to 2 in the first 24 hours after trauma. Results of this study was similar with some researches. In them, serial X-rays were not required and

Table 1. Trauma causes by gender

	Gender		Total
	Male	Female	
Car accident	24	16	40
Pedestrian accident	9	15	24
Falling	15	11	26
Rollover	28	9	37
Bike accident	38	5	43

Table 2. Chest X-ray findings based on trauma causes

	CXR				Total
	Normal	Rib fracture	Hemothorax	Lung contusion	
Car accident	38	2	0	0	40
Pedestrian accident	20	2	0	2	24
Falling	24	2	0	0	26
Rollover	37	0	0	0	37
Bike accident	42	0	1	0	43

CXR: Chest X-ray

in some cases with penetrating trauma, primarily CT scan was adequate (19). Seamon et al. (20) suggested that even 3 hours of follow-up was adequate in penetrating traumas without chest pain. In another study it was shown that there is no significant difference after 3 hours of X-ray and 6 hours in non-penetrating thoracic trauma (33).

Because of concerns about using unnecessary X-Rays in patients with blunt trauma and about excessive radiation dose on body, a study was performed. Although the role of CXR in detecting significant intra-thoracic injuries was very low, it was believed that it was standard part of trauma work up (34). Another study sought to evaluate performing CXR in patients with blunt trauma and found that these patients did not need CXR routinely if they were stable and if they had no symptoms (35). Forouzanfar et al. (36) concluded in a recent study in patients with multiple blunt trauma that the diagnostic yield of CXR was not high enough and that it could be ignored in stable patients who were conscious, under 60 years old, had no decrease in pulmonary sounds, no dyspnea, no thoracic skin abrasion, and no crepitation. According to some studies, physical examination had high sensitivity for the diagnosis of chest lesions in patients with GCS >14 (37-39).

We should also mention that in a research done in 2003, it was shown that clinical examination alone was not adequate for the accurate detection of chest lesions in 90% of cases, especially in patients with blunt trauma (40). In another study that was carried out in 2010 in Virginia, It was shown that 10% of patients had hidden lesions without any evidence in the examination (41). In a study published in 2003, it was determined that physical examination had 99% sensitivity and 44% specificity in the diagnosis of thoracic lesions and due to the low specificity, it was better to do X-ray alongside the clinical examination (42).

This data in support of our data showed that in patients with blunt trauma there was no need of performing CXR if they were stable and had no sings and symptoms. Instead, we can perform a complete physical examination.

Conclusion

We found that CXR was not used in diagnostic process of patients with thoracic blunt trauma who were stable and had no finding in physical exam and no symptoms. In this study, from a total of 170 patients with blunt multiple trauma, 161 patients (97.7%) had a normal CXR and only 9 patients (2.3%) had a positive finding in CXR. All these patients had symptoms like dyspnea or chest pain or positive finding in physical exam like skin emphysema, ecchymosis and local tenderness. According to ATLS it is necessary to obtain chest radiographic images in patients with multiple traumas and ISS higher than 15 or patients at levels 3 or 4 in triages and CXR is performed as a routine process of trauma patients management. Actually, there is no need to impose this excessive radiation dose to patient and it is better to reduce costs in health care system. We suggest performing physical exam instead of CXR in patients with blunt chest trauma with ISS >15 without any discomfort in the chest.

Ethics

Ethics Committee Approval: Ethical committee of Tabriz University of Medical Sciences approved this study before patients' enrollment.

Informed Consent: Informed consent was taken.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.A., S.S.V., G.M., R.J., Design: A.A., S.S.V., G.M., R.J., Data Collection or Processing: A.A., S.S.V., G.M., R.J., Analysis or Interpretation: A.A., S.S.V., G.M., R.J., Literature Search: A.A., S.S.V., G.M., R.J., Writing: A.A., S.S.V., G.M., R.J.

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

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Surgical Treatment Results in Pediatric Supracondylar Humerus Fractures

Erdinç Acar[1], Recep Memik[2]

[1]Department of Orthopedics and Traumatology, Konya Necmettin Erbakan University Meram Faculty of Medicine, Hand and Upper Extremity Surgery Division, Konya, Turkey
[2]Department of Orthopedics and Traumatology, Konya Necmettin Erbakan University Meram Faculty of Medicine, Konya, Turkey

Abstract

Aim: This study aims to evaluate the outcomes of cross fixation with Kirschner wire (K-wire) following closed reduction of displaced supracondylar humerus fractures in children.

Materials and Methods: Between December 2012 and June 2015, a total of 32 patients with suprachondral humerus fractures were retrospectively analyzed. Data including demographic data, causes and types of fracture, associated injuries, postoperative complications, radiological parameters, and cosmetic and functional outcomes were recorded.

Results: Of the patients, 24 (75%) were male and eight (25%) were female with a mean age of 6.5 years (range: 2 to 12 years). The mean follow-up was 19 months (range: 13 to 26 months). None of the patients developed iatrogenic vascular or nerve injuries. No postoperative complications were observed during follow-up. The functional result according to the Flynn criteria was excellent in 93.4% and good in 6.6% patients, while cosmetic results were excellent in 93.4%, good in 5.2%, and fair in 1.4%.

Conclusion: Percutaneous fixation with K-wire following closed reduction of displaced supracondylar humerus is a reliable method which can be applied with high success rates in pediatric cases.

Keywords: Child, flynn criteria, humerus supracondylar fracture, closed reduction, kirschner wire

Introduction

Supracondylar humerus fractures are the second most common fractures in the childhood, while they occupy the first place with 60% including the elbow circumference fractures (1). The incidence of supracondylar fracture was reported to be 1.8 in 1000 (1,2).

Supracondylar fractures are divided into two types as extensor and flexor. Extension type fractures are more frequent and particularly visible after palm falls, when the elbow is hyperextended (3). With many classifications being defined, the Wilkins-modified Gartland classification system is the most commonly used system for the classification of extension type supracondylar humerus fractures (3). There are three types in this class: type 1 covers non-displaced humerus fractures; posterior cortex is intact and angulation at varying degrees is present in type 2; and cortical integrity is completely lost in type 3 (3).

Most supracondylar humerus fractures occur in 5 to 7-year-old children (4). Although many techniques in treatment such as traction, casting after closed reduction, open reduction and internal fixation are used, the most commonly used one is closed reduction and percutaneous Kirschner wire (K-wire) technique (4,5). In this study, we aimed to evaluate the clinical results of displaced supracondylar humerus fractures treated by percutaneous K-wire following closed reduction.

Corresponding Author: Erdinç Acar MD, Department of Orthopedics and Traumatology, Konya Necmettin Erbakan University Meram Faculty of Medicine, Hand and Upper Extremity Surgery Division, Konya, Turkey
Phone: +90 530 065 00 77 **E-mail:** erdal240@gmail.com **ORCID ID:** orcid.org/0000-0002-2154-0108

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Materials and Methods

A written informed consent was obtained from each patient. The study was approved by the Necmettin Erbakan University Faculty of Medicine Ethics Committee and was conducted in accordance with the principles of the Declaration of Helsinki (protocol no: 2017/950).

In this study, 32 patients who were surgically treated by medial and lateral cross-sectional K-wire between December 2012 and June 2015 due to Gartland type 3 humeral supracondylar fractures were retrospectively analyzed. A detailed medical history was obtained from each patient and their relatives. In addition, local and systemic examinations of the patients were also performed. No additional injury and neurovascular deficit were present in any of the patients. Patients who were scheduled for surgical treatment by evaluating their two sided radiographs of both elbows were included in the study (Figure 1). The patients underwent operation within the first 12 hours, unless there was an obstruction to emergency surgery. All patients under general anesthesia were operated by a single surgeon. For closed reduction, medial or lateral displacement of the distal segment relative to the humerus shaft was corrected after longitudinal traction was applied to the forearm under the guidance of scopy. Then, while the elbow was at 120 degrees of flexion and the forearm was in pronation, the thumb was pressed against the olecranon to provide its reduction. After the reduction was controlled by assessment of front and rear views under the fluoroscopy, the fixation was performed by cross K-wire. Firstly, K-wire at lateral position was sent, then the ulnar nerve was secured under the thumb and medial K-wire was sent, when the medial epicondyle was palpated. Afterwards, fixation of the fracture was seen under the fluoroscopy control (Figure 2). Postoperative long arm was splinted. Postoperative X-ray imaging was performed (Figure 3). A dressing was suggested to the patient and their relatives every three days. On day 7, all patients were scheduled for the first follow-up visit. There was no loss of reduction with the radiographs taken (Figure 4). According to the X-ray results in the third week (Figure 5), the splints were removed and the elbow movements were started. At four weeks, the K-wires of all patients were removed in the outpatient setting (Figure 6). According to the literature data, a rehabilitation program was administered to the patient by the parents at home, and the range of motion was examined at six weeks and three months after the operation. After the third month, those who returned to normal range of motion were scheduled for follow-up at 6, 12, and 18 months postoperatively (Figure 7).

In our study, radiological parameters, cosmetic and functional results were evaluated. On the functional evaluation; the flexion, extension, internal and external rotation grades of both arms were examined. The difference between the intact elbow and the operated elbow was assessed by measuring and collecting flexion and extension values. The difference between the good elbow and the operated elbow according to the amount of motion angle was functionally excellent at 0-5 degrees, good at 6-10 degrees, fair at 11-15 degrees, and poor at 15 degrees when the Flynn criteria were applied (Table 1).

For the cosmetic evaluation, the carrying angle from both arms was measured by using a goniometer with McRae method. The difference was regarded as the loss of the carrying angle. The carrying angle loss was assessed by cosmetic criteria based on Flynn's evaluation criteria and the angle ranges used for functional evaluation were performed.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) Statistics for Windows, Version 17.0 (SPSS Inc., Chicago, IL, USA). Descriptive data are primarily presented as means. The chi-square test was used to compare the qualitative data of the patients. Statistical significance was defined at the 5% ($p<0.05$) level.

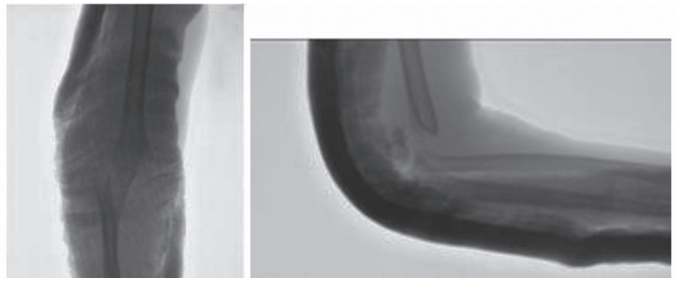

Figure 1. Preoperative supracondylar fracture X-rays (AP and lateral)

AP: Anterior and posterior

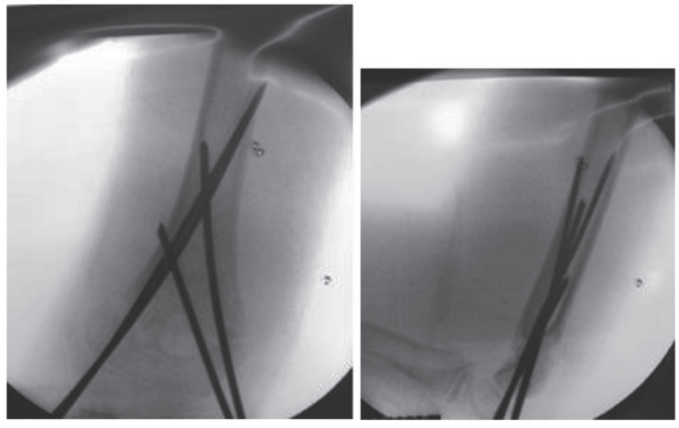

Figure 2. Intraoperative view (AP and lateral)

AP: Anterior and posterior

Results

Of the patients, 24 (75%) were male and eight (25%) were female. The mean age was 6.5 years (range: 2 to 12 years). The mean time to discharge was 1.5 days (range: 1 to 3 days). No postoperative neurovascular deficits were observed.

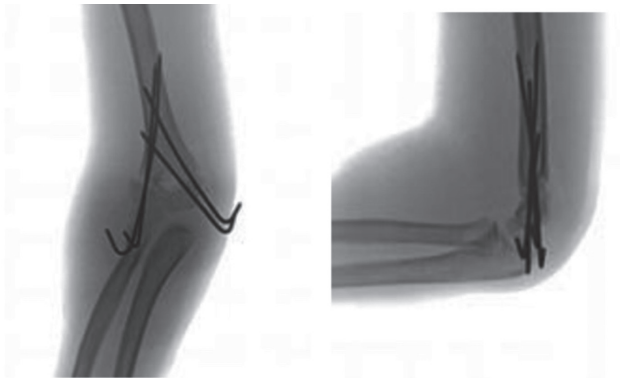

Figure 3. Postoperative X-rays (AP and lateral)
AP: Anterior and posterior

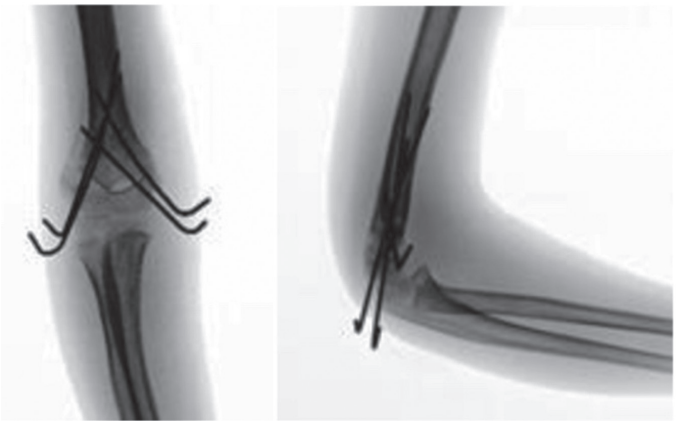

Figure 4. Postoperative first week X-rays (AP and lateral)
AP: Anterior and posterior

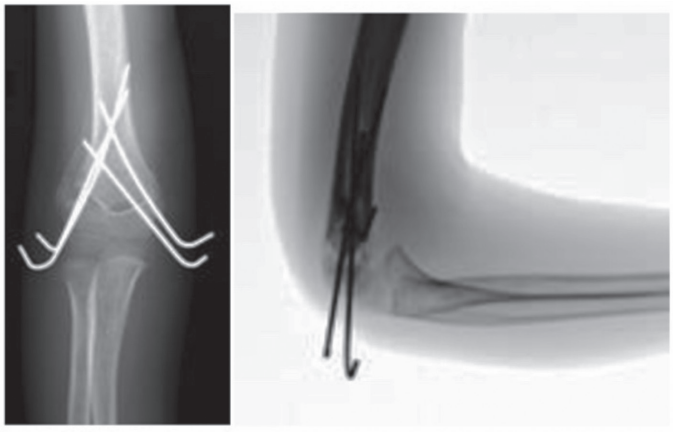

Figure 5. Postoperative third week X-rays (AP and lateral)
AP: Anterior and posterior

The mean time to removal of the K-wire during follow-up was 4 weeks. The mean follow-up was 19 months (range: 13 to 26 months). Twelve patients had a simple domestic fall, whereas the fracture developed after the fall in 20 of them while playing outside the home. The functional result according to the Flynn criteria was excellent in 93.4% and good in 6.6% patients, while cosmetic results were excellent in 93.4%, good in 5.2%, and fair in 1.4%. Bone union was not considered as a problem on radiological evaluation. None of the patients developed any complication during follow-up.

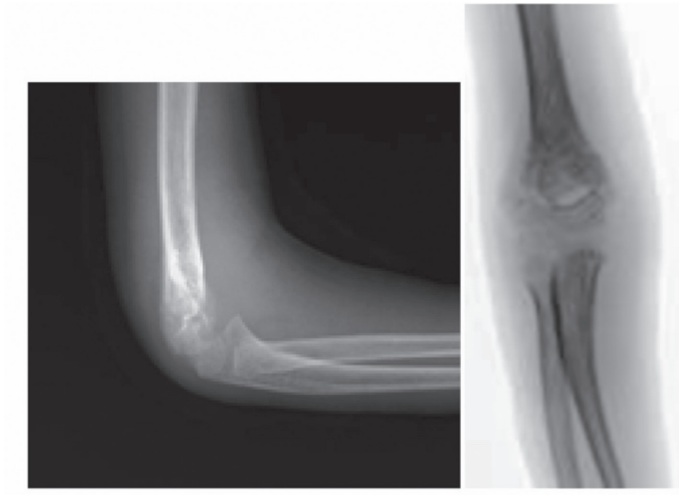

Figure 6. Postoperative forth week X-rays (AP and lateral)
AP: Anterior and posterior

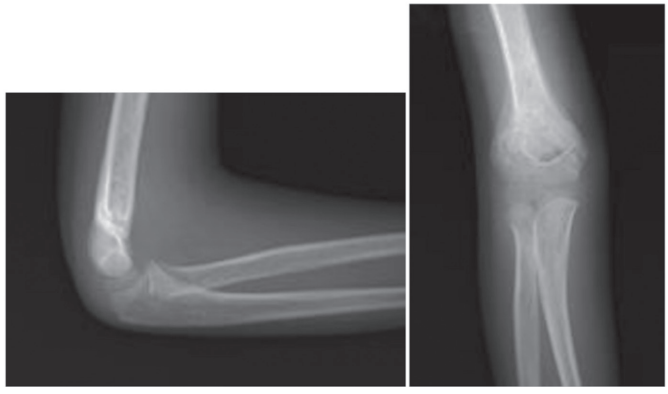

Figure 7. Postoperative eighteenth month X-rays (AP and lateral)
AP: Anterior and posterior

Table 1. Flynn Criteria

	Change in carrying angle of cosmetic factor (degree)	Movement loss of functional factor (degree)
Excellent	0-5	0-5
Good	6-10	6-10
Fair	11-15	11-15
Poor	>15	>15

Discussion

The most common cause of injury in children is falling. Children protect themselves by falling on the hand while the upper extremity is in extension position. This reflex mechanism causes injury to the upper extremity. The distal radius is affected most frequently whereas the elbow is affected as second most. Injury rate is seen to be frequent in elbow injuries in the first two periods if age groups are classified as 3-6 years (preschooler), 7-11 years (schooler), and 12-14 years (teenager) (1,2). In children, supracondylar humerus fractures account for 60% of the elbow fractures. In general, supracondylar humerus fractures are two times more common in males than females (1,6). In this study, supracondylar fractures all occurred as a result of falling. In addition, these types of fractures were seen three times more in males and the mean age of fractures was 6.5 years.

The main goal of treatment in supracondylar humerus fractures in children is the full acquisition of elbow movements as well as protection of the patient from any possible neurovascular complications, while obtaining an elbow with cosmetically normal appearance. Review of the literature reveals that there are many publications related to the method of closed reduction and percutaneous wiring. Ekşioğlu et al. (7) compared closed reduction and percutaneous K-wire methods with open reduction and internal fixation. In the aforementioned study, it was emphasized that although closed reduction and percutaneous K-wire technique had less traumatic characteristics due to the fracture line not opening, the open reduction and internal fixation method in closed non-reducible cases is a treatment method that can achieve as successful results as closed reduction and percutaneous wiring with the advantages of allowing the fractured line to be seen with full anatomical reduction and reducing the risk of iatrogenic vessel and nerve injury. In the study performed, 80.84% of patients with closed reduction and percutaneous fixation reported excellent and good results in cosmetic evaluation while 80.95% of them had excellent and good results in functional evaluation. Open reduction was not required, as all fractures in our study were treated with closed reduction. As a result, in accordance with the literature, patients had excellent and good cosmetic and functional results.

Iatrogenic ulnar nerve injury can be observed when K-wire is placed from medial side during performing closed reduction and percutaneous K-wire (8), Lyons et al. (9) detected that 19 ulnar nerve lesions occurred postoperatively and reported that 17 of them recovered in a study in which retrospectively evaluated 375 cases treated with closed reduction and percutaneous K-wire were included. Moreover, ulnar nerve lesions resolved spontaneously after surgery; however, if these lesions persisted after 4 months and there were EMG findings, they suggested that exploration could be performed. No ulnar nerve lesions were observed in the present study.

Biomechanical studies have demonstrated the requirement for cross K-wire use to obtain maxillary stabilization in pediatric supracondylar humerus fractures. Eralp et al. (10) compared the results of fixation with a third wire and a conventional cross-fixation in addition to cross K-wire fixation. As a result of that study, they reported that they achieved more stable fixation with three wire configurations. Likewise, it was determined in biomechanical studies that stable fixation was obtained from cross K-wire fixation, whereas performing additional K-wire from lateral side increased the stability (5,11-13). As seen in the current study, not only the application of cross K-wire, but also more stable fixation with additional K-wire from lateral side were performed. It is also possible that the fixation can be further stabilized by applying two K-wires medially and laterally. Furthermore, Zionts et al. (14) reported that the most durable composition of K-wire was two crossed K-wires performed medially and laterally. In the present study, cross K-wire was applied in all fixations, suggesting that stabilization was sufficient.

Study Limitations

The implications of this study are limited due to its retrospective design and the relatively small number of patients. In addition, Gartland type 2 fractures and T type fractures were excluded from the study.

Conclusion

Closed reduction and percutaneous K-wire, which is a well-known treatment method, is accepted as the most current and reliable method. Satisfactory results according to the Flynn criteria were obtained with medial-lateral cross K-wire placement following closed reduction suggesting that it was safe and acceptable to apply the K-wires transversely following closed reduction with preservation of the ulnar nerve in pediatric displaced supracondylar humerus fractures.

Ethics

Ethics Committee Approval: The study was approved by the Necmettin Erbakan University Faculty of Medicine Ethics Committee and was conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent: A written informed consent was obtained from each patient.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practice: E.A., R.M., Concept: E.A., R.M., Design: E.A., R.M., Data Collection or Processing: E.A., R.M., Analysis or Interpretation: E.A., R.M., Literature Search: E.A., R.M., Writing: E.A., R.M.

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

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The Ameliorative Effects of Ethyl Pyruvate and Dimethyl Sulfoxide on Ischemic Tissue Injury in Experimental Carbon Monoxide Intoxication

Sinan Paslı[1], Melih İmamoğlu[2], Mustafa Çiçek[3], Metin Yadigaroğlu[4], Aynur Şahin[5], Yunus Karaca[5], Esin Yuluğ[6], Özgür Tatlı[5]

[1]Clinic of Emergency Medicine, Gümüşhane State Hospital, Gümüşhane, Turkey
[2]Clinic of Emergency Medicine, Rize State Hospital, Rize, Turkey
[3]Clinic of Emergency Medicine, Bayburt State Hospital, Bayburt, Turkey
[4]Clinic of Emergency Medicine, Fatih State Hospital, Trabzon, Turkey
[5]Department of Emergency Medicine, Karadeniz Technical University Faculty of Medicine, Trabzon, Turkey
[6]Department of Histology and Embryology, Karadeniz Technical University Faculty of Medicine, Trabzon, Turkey

Abstract

Aim: The purpose of this study was to investigate the protective effects of ethyl pyruvate (EP) and dimethyl sulfoxide (DMSO) on ischemic tissue in brain and cardiac and hepatic tissues in experimentally induced carbon monoxide (CO) intoxication.

Material and Methods: Thirty-five mature female Sprague Dawley rats were randomized into five groups of seven animals each. Group 1 received no CO or treatment. Rats in groups 2, 3, 4 and 5 were made to inhale a high-concentration 5000 ppm CO gas mixture for 60 min at 4 L/min. CO levels were then measured from 1 mL tail vein blood. Group 2 received no therapeutic agent, group 3 received 6 mg/kg intraperitoneal (ip) DMSO, group 4 received 50 mg/kg ip EP, group 5 received 50 mg/kg EP and 6 mg/kg DMSO ip. All rats were sacrificed by decapitation. Brain, cardiac and hepatic tissues were removed and histopathological scores were compared.

Results: Comparison of group 2 with group 3 and group 2 with group 5 revealed that DMSO alone and EP + DMSO exhibited a reducing effect on degree of cerebral neuronal alteration, degenerative neuron rates, and total cardiac injury score (p=0.005, p=0.002, p=0.004 and p=0.002, p=0.001, p=0.004 respectively). There was no histopathological difference between group 2 and group 4 suggesting EP alone had no therapeutic effect on histopathological injury.

Conclusion: Based on our study findings, EP administered alone exhibited no protective effects on the organ injuries investigated, while DMSO exhibited reducing effects on degree of neuron alteration, rates of degenerative neurons, and total cardiac injury scores. An ameliorating effect on cardiac and hepatic injury was more prominent with combined treatment.

Keywords: Carbon monoxide, dimethyl sulfoxide, ethyl pyruvate, experimental, intoxication

Introduction

Carbon monoxide (CO) is a colorless, odorless, tasteless, non-irritating gas which normally presents at a level of 0.001% in the atmosphere. It emerges when carbon-based compounds used as fuels for cooking and heating are incompletely consumed, or during fires (1). CO is one of the most important global agents in injury- and intoxication-related mortality (2). Children and the elderly are more rapidly affected. Other factors increasing disposition are exercise, stress, and anemia. High atmospheric concentrations and long-term exposure are other important factors. Due to their high oxygen requirements, brain, heart, and liver are the most susceptible organs to the hypoxic effects of CO exposure (3). Studies have determined that the cardiac effect is associated with

Corresponding Author: Sinan Paslı MD, Clinic of Emergency Medicine, Gümüşhane State Hospital, Gümüşhane, Turkey
Phone: +90 541 553 50 73 **E-mail:** drsinanpasli@gmail.com **ORCID ID:** orcid.org/0000-0003-0052-2258
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formation of carboxyhemoglobin (COHb) which causes hypoxia, and that CO-related oxidative stress leads to neurological injury (4). The synthesis of reactive oxygen products increases secondary to tissue hypoxia in CO intoxication. The numbers of studies of the place and importance of antioxidant therapies as an alternative to oxygen therapy are therefore increasing rapidly. Several studies agree that antioxidant therapy can be a novel therapeutic option in the treatment of CO intoxication (5). Dimethyl sulfoxide (DMSO) is a strong penetration enhancer, cell fusogen and cryoprotectant. It is a widely used molecule in cell biology (6). It is mainly intended for use in many gastrointestinal diseases, thanks to its anti-inflammatory and reactive oxygen species cleaning activities (7). DMSO crosses the blood-brain barrier and has been effective in treating traumatic brain edema (8,9). It has also been used in the treatment of musculoskeletal disorders (10), rheumatologic diseases (11), dermatological diseases and as a topical analgesic (12). In addition, it has been recommended for the treatment of Alzheimer's disease (13). Ethyl pyruvate (EP) is a stable and simple lipophilic ester originating from the endogenous metabolite pyruvate. It has been shown to provide protection against inflammation and reduce organ dysfunction in some models of clinical disease, such as burns, sepsis, and acute pancreatitis (14,15). Shen et al. (16) has shown that ethyl pyruvate improves hypoxic-ischemic brain injury through the anti-inflammatory and anti-cell death mechanism. The effect of ethyl pyruvate on ischemia reperfusion injury has also been demonstrated by scientists. Hu et al. (17) have shown that ethyl pyruvate reduces myocardial ischemia reperfusion injury by inhibiting HMGB1 protein expression in rats. In addition, Tsung et al. (18) has shown that ethyl pyruvate protects against hepatic ischemia / reperfusion (I/R) injury by reducing hepatic necrosis and apoptosis. The purpose of this study was to investigate the protective effects of ethyl pyruvate and DMSO at the histopathological level in experimentally-induced CO intoxication in rats.

Materials and Methods

Study Design

This randomized, controlled, non-blinded, interventional animal study was performed following receipt of approval from Karadeniz Technical University Animal Care and Ethics Committee (approval no: 2016/23). A 5000 ppm experimental CO intoxication protocol was applied when establishing the experimental model (19). Intraperitoneal (ip) administration of 6 mg/kg DMSO and 50 mg/kg EP was planned in the light of previous studies.

Animal Subjects

Thirty-five mature female Sprague Dawley rats (10-week old, weighing 250±25 g) were used in this study. Until the day of the study, rats were housed in steel cages at 22 ºC room temperature with access to water and standard rat chow. The CO gas to be used in the experimental protocol was ordered from HABAŞ Sınai ve Tarım Gazlar Endüstrisi A.Ş. (İzmit, Turkey) such as to contain 5000 pp CO concentrations. A special mechanism consisting of a two-chamber aquarium tank 100x40x50 cm in size, with holes capable of receiving gas from one end and permitting gas to escape from the other was employed for the experiment.

Study Protocol

The 35 rats were randomly assigned into five groups of seven animals each.

Group 1 (Sham group, n=7): After being placed into the glass container, these rats inhaled room air for 60 min, after which CO levels were measured from 1 mL blood gas from the tail veins.

Group 2 (Control group, n=7): After being placed into the glass container, these rats inhaled high-concentration 5000 ppm CO gas mixture at 4 L/min for 60 min, after which CO levels were measured in 1 mL blood gas from the tail veins.

Group 3 (DMSO group, n=7): After being placed into the experimental glass container, these rats inhaled high-concentration 5000 ppm CO gas mixture at 4 L/min for 60 min, after which CO levels were measured in 1 mL blood gas from the tail veins. Immediately after removal from the glass jar, 6 mg/kg DMSO was administered ip.

Group 4 (EP group, n=7): After being placed into the experimental glass container, these rats inhaled high-concentration 5000 ppm CO gas mixture at 4 L/min for 60 min, after which CO levels were measured in 1 mL blood gas from the tail veins. Immediately after removal from the glass jar, 50 mg/kg EP was administered ip.

Group 5 (DMSO plus EP group, n=7): After being placed into the experimental glass container, these rats inhaled high-concentration 5000 ppm CO gas mixture at 4 L/min for 60 min, after which CO levels were measured in 1 mL blood gas from the tail veins. Immediately after removal from the glass jar, 50 mg/kg EP and 6 mg/kg DMSO were administered ip.

Histopathological Examination

All rats were sacrificed by decapitation 24 h after removal from the glass tank. Brain, cardiac, and hepatic tissues were removed. Each tissue was divided into two parts down the midline, ensuring that each part contained all layers. These tissue specimens were fixed in 10% neutral formalin for 48 h. Specimens were dehydrated by being passed through increasingly greater alcohol concentrations, made transparent in xylene, and embedded in paraffin blocks for histopathological examination. Sections 5 µm in thickness were taken from the paraffin block using a

fully automatic microtome (Leica RM 2255, Tokyo, Japan) and stained with hematoxylin-eosin (H&E) for detailed evaluation. Cerebral tissue specimens were also stained with cresyl violet for more detailed examination. Preparates were evaluated by an experienced histologist (E.Y.) blinded to the study groups using a light microscope (Olympus BX-51; Olympus Optical Co., Tokyo, Japan). Preparates were scored semi-quantitatively for all organs (0=none, 1=mild, 2=moderate, 3=severe). Tissues' histopathological damage scores are shown in Table 1 (20,21,22,23). Neuronal alterations in cerebral tissue were scored histologically (20).

Total cardiac and hepatic injury scores were obtained by adding the histopathological parameter scores for cardiac and hepatic tissues, and statistical comparisons were performed on the basis of these scores.

COHb Measurement

COHb levels were determined using an automatic blood gas measurement device (Rapidlab 1265, Bayer Health Care LLC, Pittsburgh, PA, USA).

Statistical Analysis

Statistical analyses were performed on SPSS 23.0 (IBM SPSS, Armonk, NY, USA) software. Results were expressed as median and 25-75% quartiles. Kruskal-Wallis analysis of variance was used for group comparisons (Mann-Whitney U test with post hoc Bonferroni correction). P values <0.05 were considered statistically significant.

Table 1. Histopathological classification of tissue damage in brain, cardiac, and hepatic tissues
Brain
Neuronal changes (20)
1- Group with mildly shrunken neurons with / without cytoplasmic vacuolization,
2-Moderately shrunken neurons (eosinophilic cytoplasm) and increased nuclear basophilia or vacuoles with cytoplasm and vesicular nucleus,
3-Severely shrunken neurons (eosinophilic cytoplasm), piknotic nucleus Cells with shrinkage in the cell body, loss of Nissl substance and eosinophilia, and cells with a shrunken nucleus were regarded as degenerative **(21)**
Cardiac (22)
Myocardial cell degeneration
0-No degeneration in myocytes,
1-Some degenerated myocytes,
2-Approximately 50% myocyte degeneration,
3-More than 50% myocyte degeneration (Myocytes with multifocal vacular degeneration and piknotic nuclei were regarded as degenerative.)
Edema, vascular congestion, increased spaces between muscle fibers
0-None
1-Mild
2-Moderate
3-Severe
Hepatic
Hepatic injury (23)
0-None or minimal
1-Mild injury wth cytoplasmc vacuolization and focal nuclear piknosis,
2-Diffuse nuclear piknosis of variable severity, and loss of cell margins,
3-Severe necrosis with neutrophil infiltration and hemorrhage
Hepatocyte degeneration, vascular congestion, and sinusoidal dilatation (23)
0-None
1-Mild
2-Moderate
3-Severe

Results

Mean COHb concentrations for all groups are shown in Table 2. Although all groups were exposed to CO for the same time and at the same concentrations, CO levels differed significantly among the groups. Analysis revealed no significant differences between group 2, 3, and 4 CO levels among the CO-exposed groups. However, differences were determined between group 5 CO levels and those of groups 2 and 4 (p=0.033 and 0.019, respectively).

Histopathological Evaluation

The study groups' histopathological results and median injury values are shown in Table 2. Kruskal-Wallis analysis performed to compare the five groups revealed significant differences between them in terms of injury parameters (p=0.000). Bonferroni correction was applied to determine which groups representing the source of the variation (Table 3).

Brain tissue evaluation investigated shrinkage in the cell body, loss of Nissl substance and eosinophilia in cytoplasm, and degenerative neurons with a dark, shrunken nucleus. Diffuse pyramidal neurons with a normal architecture were observed in the cerebral cortex in group 1 (Figure 1). Diffuse degenerative neurons were observed in all layers of the cortex in group 2 (Figure 2). Diffuse pyramidal neurons with normal architecture were observed in addition to degenerative neurons in group 3 (Figure 3). Occasional pyramidal neurons with normal architecture in addition to diffuse degenerative neurons in all layers were observed in group 4 (Figure 4). Diffuse pyramidal neurons with normal morphology in addition to degenerative neurons were observed in group 5 (Figure 5). Cardiac tissue evaluation revealed a normal myocardial cell structure in group 1 (Figure 6). Degeneration in cardiac muscle cells and vascular congestion and edema between muscle fibers were observed in group 2 (Figure 7). Cardiac muscle cells in group 3 exhibited a close to normal morphology, and occasional vascular

Table 2. Mean carbon monoxide levels among the groups

COHb	Group 1	Group 2	Group 3	Group 4	Group 5
Median	0.350	36.4	29.05	35.850	18.600
Minimum	0.3	25.2	22.7	24	11
Maximum	4.4	47.8	39.9	52.6	33.8
25-75%	0.3-3.4	29.9-42.8	23.3-38.1	28.9-51.9	14.6-28.3

CO: Carbon monoxide, COHb: Carboxyhemoglobin

Table 3. Histopathological examination results

Histopathological Parameter	Group 1 (Sham) Median %95 CI	Group 2 (CO) Median 95% CI	Group 3 (DMSO) Median %95 CI	Group 4 (EP) Median 95% CI	Group 5 (EP + DMSO) Median 95% CI	p values
Neuron alterations (Grade)	1.500 0.581-2.419	3.000 2.263-3.166	1.000 0.454-2.046	3.000 2.125-3.209	2.000 1.125-2.209	0.005 P^{1-2}=0.002 P^{1-4}=0.004 P^{2-3}=0.005
Degenerative brain cell rates	11.500 6.834-17.666	65.000 59.246-70.468	25.500 18.069-30.931	55.000 50.519-61.815	27.500 22.074-31.593	0.005 $p^{1-2.3.4.5}$=0.002 $p^{2-3.5}$=0.002 p^{3-4}=0.002 p^{4-5}=0.002
Total cardiac injury score	2.000 0.163-3.837	6.000 5.077-6.066	4.000 3.454-5.046	5.000 4.249-6.417	2.500 1.399-3.601	0.005 $P^{1-2.3.4}$=0.001 P^{2-3}=0.004 P^{2-5}=0.001 P^{4-5}=0.002
Total hepatic injury score	2.000 0.701-3.299	7.000 5.503-8211	5.000 3.909-7.091	5.500 4.802-6.865	3.500 2.810-4.524	0.005 $P^{1-2.3.4}$=0.001 P^{1-5}=0.003 $P^{2-5=}$0.004 P^{4-5}=0.002

CO: Carbon monoxide, EP: Ethyl pyruvate, DMSO: Dimethyl sulfoxide, CI: Confidence interval, DMSO: Dimethyl sulfoxide

DMSO exhibited a greater capacity to reduce neuronal alteration grades, the degenerative neuron rates, and cardiac total injury score in Group 3, compared to Group 2 (CO) (p=0.005, p=0.002, and p=0.004, respectively). Comparison between Group 5 (EP + DMSO) and Group 2 revealed that EP + DMSO reduced the degenerative neuron rate, total cardiac injury score, and total hepatic injury score (p=0.002, p=0.001, and p=0.004, respectively). No significant difference was determined between Group 3 and Group 5 in terms of treatment results

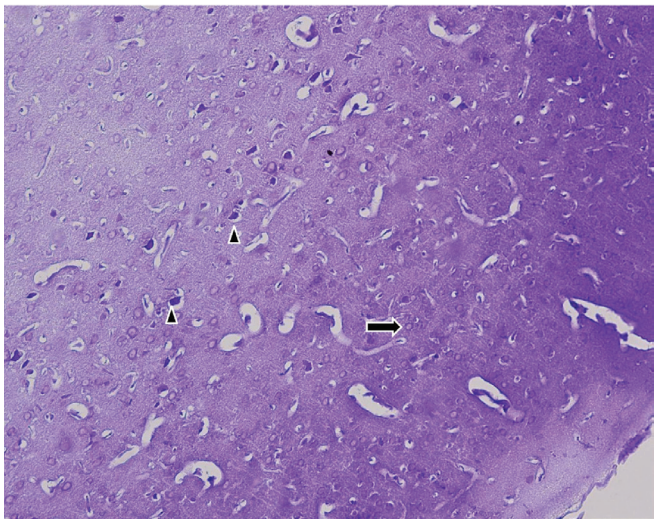

Figure 1. (Group 1) Cerebral cortex microphotographs (cresyl violet X 200). Normal pyramidal neurons (↑), degenerative pyramidal neurons (Δ)

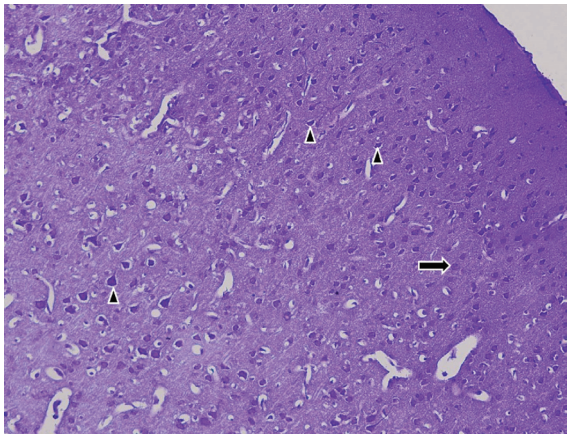

Figure 2. (Group 2) Cerebral cortex microphotographs (cresyl violet X 200). Normal pyramidal neurons (↑), degenerative pyramidal neurons (Δ)

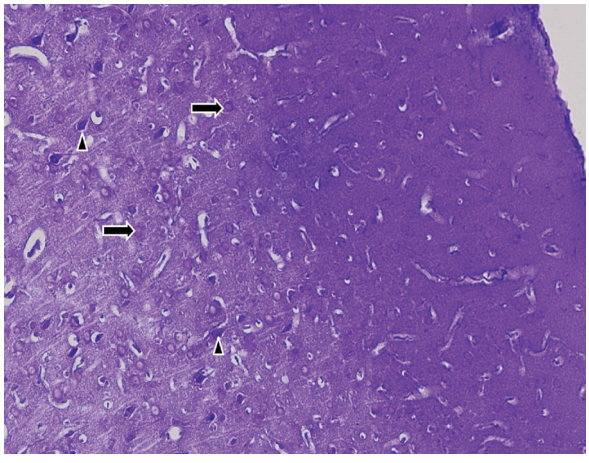

Figure 3. (Group 3) Cerebral cortex microphotographs (cresyl violet X 200). Normal pyramidal neurons (↑), degenerative pyramidal neurons (Δ)

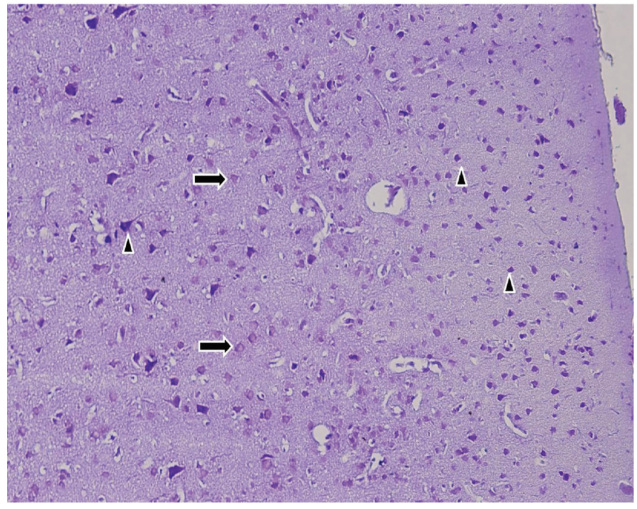

Figure 4. (Group-4) Cerebral cortex microphotographs (cresyl violet X 200). Normal pyramidal neurons (↑), degenerative pyramidal neurons (Δ)

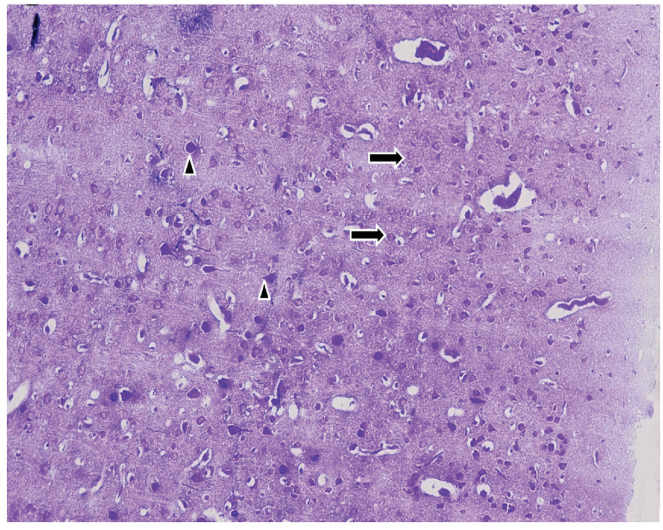

Figure 5. (Group-5) Cerebral cortex microphotographs (cresyl violet X 200). Normal pyramidal neurons (↑), degenerative pyramidal neurons (Δ)

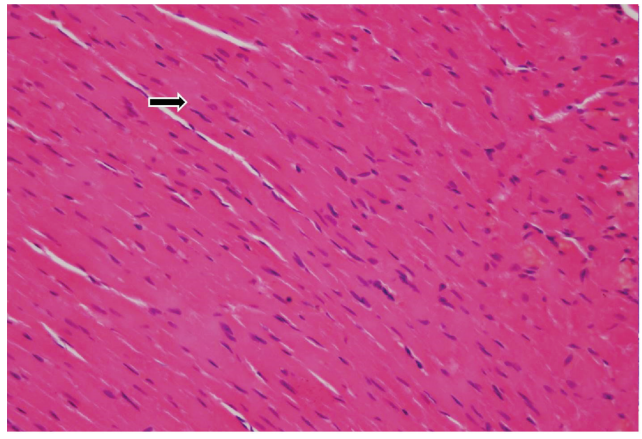

Figure 6. (Group-1) Myocardial tissue microphotograhs (H&E X 200). Myocardial cells (↑)

congestion and edema between muscle fibers were observed (Figure 8). Occasional degeneration in muscle fibers, and diffuse vascular congestion and edema were observed in group 4 (Figure 9). Cardiac muscle cells in group 5 exhibited a close to normal morphology, although occasional edema was observed between muscle fibers (Figure 10). Evaluation of hepatic tissues revealed a normal architecture in group 1. Normal morphology

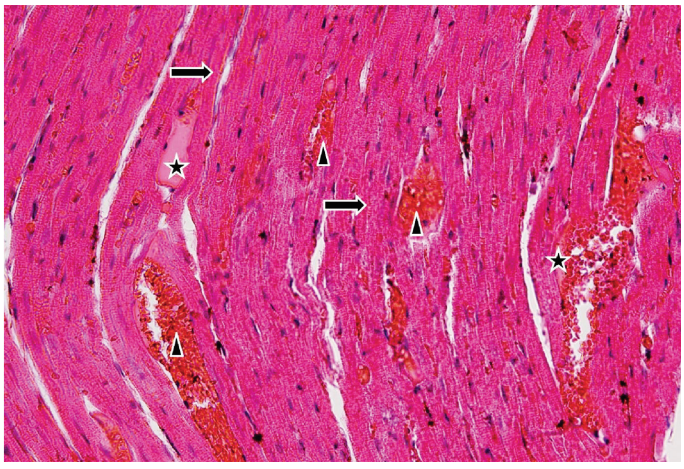

Figure 7. (Group-2) Myocardial tissue microphotograhs (H&E X 200). Myocardial cells (↑), vascular congestion (Δ), edema (star)

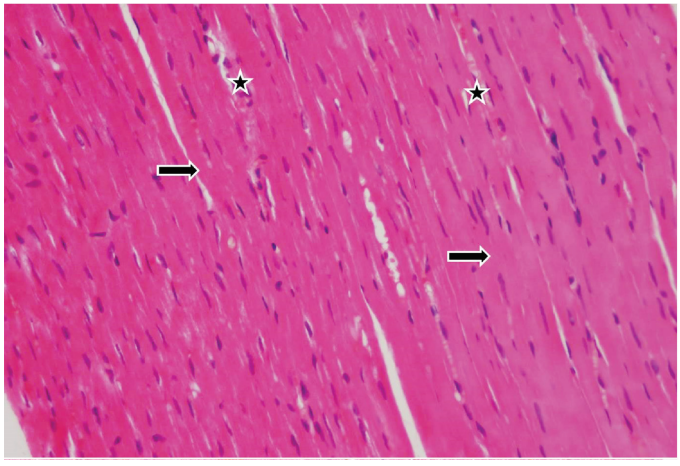

Figure 8. (Group-3) Myocardial tissue microphotograhs (H&E X 200). Myocardial cells (↑), edema (star)

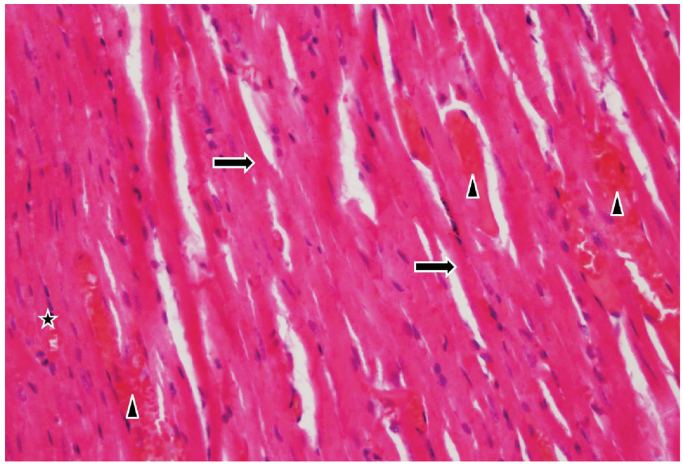

Figure 9. (Group-4) Myocardial tissue microphotograhs (H&E X 200). Myocardial cells (↑), vascular congestion (Δ), edema (star)

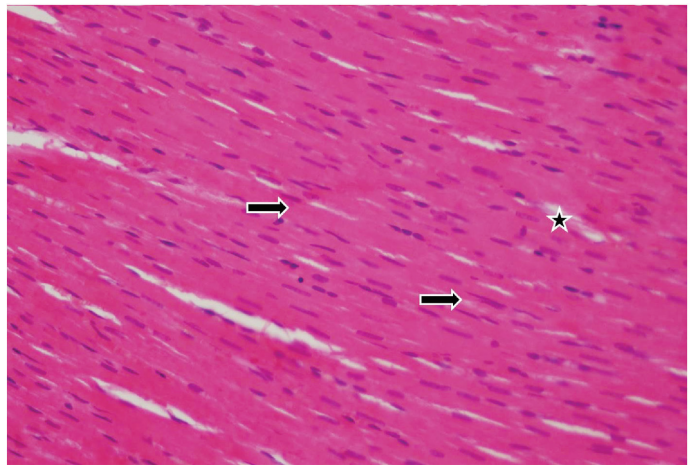

Figure 10. (Group-5) Myocardial tissue microphotograhs (H&E X 200). Myocardial cells (↑), edema (star)

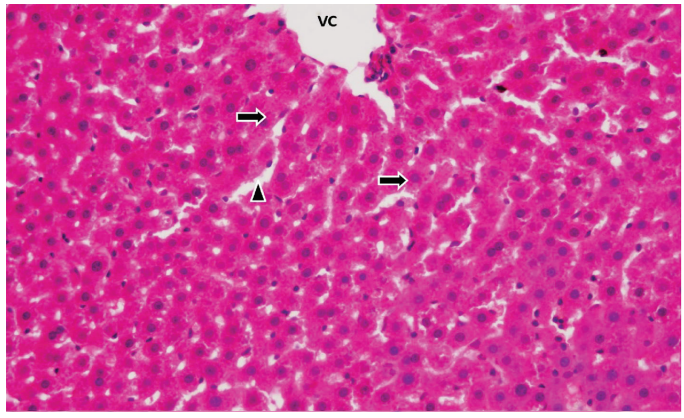

Figure 11. (Group-1) Liver tissue microphotograhs (H&E X 200). Hepatocytes (↑), sinusoidal dilatation (Δ)

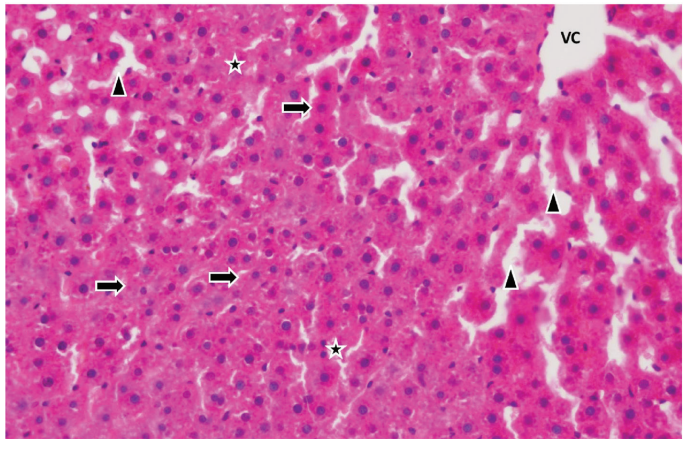

Figure 12. (Group-2) Liver tissue microphotograhs (H&E X 200). Hepatocytes (↑), sinusoidal dilatation (Δ), hepatocytes with pyknotic nuclei (star)

was observed in hepatocytes and sinusoidal spaces (Figure 11). Diffuse hepatocytes with pyknotic nuclei and cell margin losses were observed in group 2. Diffuse expansion of sinusoidal spaces were also determined (Figure 12). Occasional hepatocytes with pyknotic nuclei and cell margin losses were observed in group 3. Occasional sinusoidal dilatation was observed in areas close to the vena centralis (Figure 13). Diffuse sinusoidal dilatation and degenerative hepatocytes with pyknotic nuclei were observed in group 4 (Figure 14). In group 5, diffuse hepatocytes with normal morphology were observed in addition to occasional hepatocytes with pyknotic nuclei (Figure 15).

Discussion

This study investigated the protective effects of EP and DMSO against injury caused in important target organs including liver, brain and heart by potentially life-threatening CO intoxication, which is frequently encountered worldwide. Our findings indicated that EP had no protective effect against histopathological damage occurring in brain, cardiac, and hepatic tissues. However, our findings also suggested that DMSO might exhibit protective effects against damage occurring in brain and cardiac tissue, but not against hepatic injury. However, this needs to be confirmed by further studies.

CO intoxication is a frequent health problem in worldwide. Approximately 40.000 people present to emergency departments in the USA every year due to CO intoxication, and 5000-6000 individuals die due to exposure to the gas. CO is held responsible for more than half of all fatal intoxications worldwide (24). The most common sources of CO are engine exhaust gases, gas-powered engines, smoke caused by fires, and paints containing methylene chloride (1).

The pathophysiology of CO intoxication is complex. In addition to the cellular damage caused by CO itself, the hypoxia and ischemia produced by the CO-hemoglobin complex also play an important role in the process (25). Endogenously produced CO results in 1% COHb. Low endogenous CO levels are physiological, but excessive exogenous CO intake causes the principal problem (26). The main target of CO is hemoglobin (Hb). The affinity of Hb for CO is 210 times greater than that for oxygen. CO binding to Hemoglobin (Hb) replaces the oxygen in Hb, giving rise to COHb. Since the oxygen binding regions on the COHb molecule have a high affinity for oxygen, the oxygen binded to these is not presented to tissues. This increased affinity is known as the Haldane effect. As a result of the Haldane effect, a left shift occurs on the oxyhemoglobin curve, and it becomes difficult for oxygen to separate from Hb at the tissue level (27). Tissue hypoxia develops since oxygen cannot be transported to tissues. Following recent studies, it is now thought that different mechanisms are also involved in CO toxicity. One such is the damage occurring in the central nervous system with reoxygenation following hypoxia caused by CO. Measuring COHb levels is today considered an important

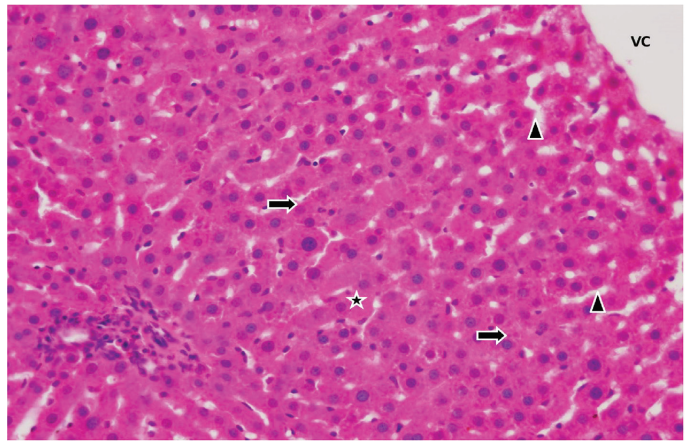

Figure 13. (Group-3) Liver tissue microphotograhs (H&E X 200). Hepatocytes (↑), sinusoidal dilatation (Δ), hepatocytes with pyknotic nuclei (star)

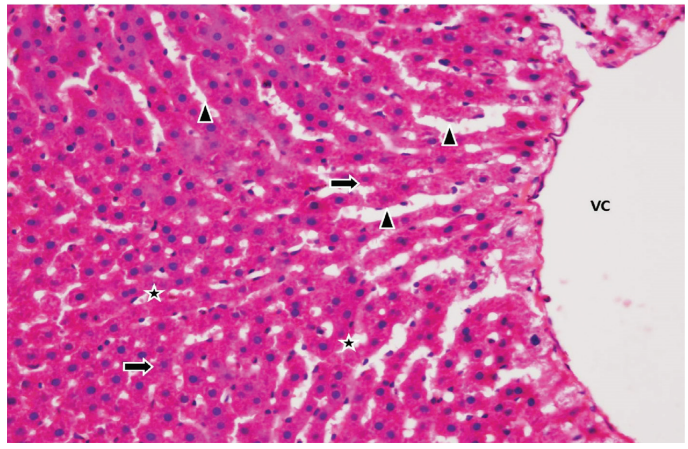

Figure 14. (Group-4) Liver tissue microphotograhs (H&E X 200). Hepatocytes (↑), sinusoidal dilatation (Δ), hepatocytes with pyknotic nuclei (star)

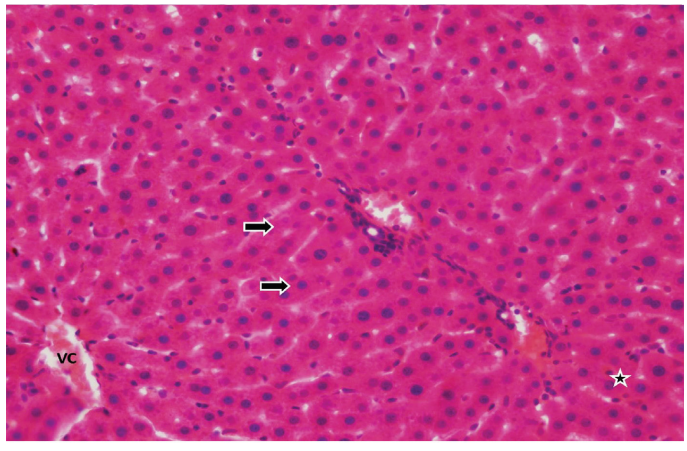

Figure 15. (Group-5) Liver tissue microphotograhs (H&E X 200). Hepatocytes (↑), hepatocytes with pyknotic nuclei (star)

diagnostic technique. However, there is only a weak correlation between blood or tissue COHb levels and organ damage. Generally, COHb levels exceeding 60% result in mortality, while lower levels can result in clinical findings ranging from mild symptoms to coma, and it is not always possible to determine this by means of COHb levels (28). The therapeutic options in treatment planning for patients with CO intoxication are not numerous. Reactive oxygen product synthesis increases in CO intoxication secondary to tissue hypoxia. There is therefore a growing number of studies investigating the role and importance of antioxidant therapies as an alternative to oxygen therapy. In their experimental study, Wang et al. (29) showed that hydrogen-rich saline solution reduced lipid peroxidation in cerebral tissue, and might therefore have a positive effect on neurological sequelae. Another study determined that N-acetylcysteine (NAC) and melatonin reduced CO-induced brain and lung damage (30).

DMSO is an anti-inflammatory drug with a free oxygen radical (FOR) binding capacity (31). In clinical terms, it is used in the symptomatic treatment of interstitial cystitis (32). In experimental sepsis models, the inhibitory effects of DMSO on nuclear factor kappa receptors have been shown to regulate cellular gene expression in inflammation. It has been shown to exhibit a protective effect at the histological level with its powerful antioxidant activity in corrosive burns in experimental rat models (33,34).

EP is a promising antioxidant and anti-inflammatory agent with known neuroprotective efficacy. Pyruvate, the end product of glycolysis and an initial substrate of the tricarboxylic acid cycle, is the anionic form of 2-oxo-proprionic acid. It has been reported to be capable of scavenging FORs and hydroxyl radicals. EP is the ethyl ester of pyruvate and has been reported to be a more powerful antioxidant than pyruvate (35).

To our knowledge, this is the first study investigating the protective effects of DMSO and EP on CO intoxication. DMSO is generally used in in vivo experiments as a solvent to dissolve chemicals. Because of this feature, it was used in the control group of many studies. In an experimental traumatic brain injury study, Di Giorgio et al. (36) wanted to evaluate the neuroprotective effect of curcumin and compare its effect with a known antioxidant α-tocopherol. DMSO was used as a solvent for curcumin in the treatment groups in this study. In the study there was both DMSO group and normal saline group for control. Surprisingly, Di Giorgio et al. (36) found that α-tocopherol, DMSO and all curcumin groups reduced the number of degenerating neurons compared to normal saline group and there was no significant difference between α-tocopherol, DMSO and curcumin groups. They concluded that, DMSO was an effective neuroprotective agent in experimental traumatic brain injury (36). Similarly, in our study, we determined that DMSO had a therapeutic effect on ischemic injury.

There are several studies showing antioxidant and anti-inflammatory effects of EP. Suha et al. (37) investigated the protective effects of NAC and EP in an experimental electric burn model and found that EP had protective effects on heart and brain (37). But in our study, we observed EP alone did not have a therapeutic effect on CO intoxication. This may be due to the dose of EP administered. Administration of EP at different doses may have a protective effect. Further studies are needed to demonstrate this.

Our findings revealed a significant difference in all parameters between group 1 (SHAM) and group 4 (EP) ($p=0.004$), while no statistically significant difference was observed between group 2 (CO) and group 4. This suggested that EP alone had no therapeutic effect against histopathological injury. DMSO exhibited a greater capacity to reduce neuronal alteration grades, the degenerative neuron rates, and cardiac total injury score in group 3, the DMSO group, compared to group 2 ($p=0.005$, $p=0.002$, and $p=0.004$, respectively). Comparison between group 5 and group 2 revealed that EP + DMSO reduced the degenerative neuron rate, total cardiac injury score, and total hepatic injury score ($p=0.002$, $p=0.001$, and $p=0.004$, respectively). However, this treatment had no ameliorating effect on neuronal alteration grade. No significant difference was determined between group 3 and group 5 in terms of treatment results. In other words, DMSO administered alone was as effective as DMSO + EP. Comparison between group 1 and group 5 revealed no difference in terms of injury occurring in cardiac tissue, suggesting that the protective effect of EP + DMSO was more prominent against damage occurring in the heart.

Study Limitations

Due to ethical committee requirements, this study was performed with a limited number of rats. It therefore needs to be supported by further studies involving larger sample numbers. Although this was a controlled study, it may not have mimicked typical cases of CO intoxication seen in clinical practice. In addition, this study examined only histopathological damage resulting from high-dose CO exposure over 60 min and the therapeutic effect of antioxidants against that injury. Higher-dose intoxication concentrations were not investigated. The therapeutic agents EP and DMSO were administered at doses of 50 mg/kg, and 6 mg/kg, respectively, and the effectiveness of other doses could not be measured. In addition, although all animals inhaled CO in the same apparatus and for the same time, the same blood COHb level may not have been obtained in all rats.

Conclusion

Our findings showed that EP alone exhibited no protective effect on the organ injuries investigated, while DMSO exhibited a reducing effect on neuronal alteration grade, degenerative neuron rates, and total cardiac damage score. The ameliorating effect of combined treatment was more prominent in cardiac and hepatic injury.

Ethics

Ethics Committee Approval: Karadeniz Technical University Animal Care and Ethics Committee (approval no: 2016/23).

Informed Consent: Informed consent was not obtained due to the fact that the study is animal testing.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.P., M.İ., Ö.T., Concept: S.P., M.İ., Ö.T., Design: S.P., M.İ., Ö.T., Data Collection or Processing: M.Ç., M.Y., Analysis or Interpretation: M.Ç., M.Y., E.Y., Literature Search: S.P., M.İ., A.Ş., Y.K., Writing: S.P., M.İ., Ö.T.

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

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Measurement of Optic Nerve Sheath Diameter to Detect Increased Intracranial Pressure in Hypertensive Patients

Cesareddin Dikmetaş[1], Mehmet Ergin[2], Çiğdem Savaş Duman[3], Mustafa Gülpembe[4], Tarık Acar[5], Kenan Yavuz[6], Başar Cander[1], Sadık Girişgin[7], Sedat Koçak[7]

[1]Clinic of Emergency Medicine, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul Health Sciences University, İstanbul, Turkey
[2]Department of Emergency Medicine, Yıldırım Beyazıt University Faculty of Medicine, Ankara, Turkey
[3]Konya Provincial Health Directorate, Konya, Turkey
[4]Clinic of Emergency Medicine, Konya Training and Research Hospital, Konya, Turkey
[5]Clinic of Emergency Medicine, Beyhekim State Hospital, Konya, Turkey
[6]Clinic of Emergency Medicine, Rize State Hospital, Rize, Turkey
[7]Department of Emegergency Medicine, Necmettin Erbakan University Faculty of Medicine, Konya, Turkey

Abstract

Aim: Our aim was to measure optic nerve sheath diameter (ONSDM) by ultrasonography and to detect whether ONSDM reflected intracranial pressure in hypertensive patients.

Materials and Methods: This observational study was performed prospectively in 149 individuals, 77 (51.7%) of whom were female, including 54 hypertensive-symptomatic patients, 45 hypertensive-asymptomatic patients, and 50 healthy volunteers referred to Emergency Medicine Service of Necmettin Erbakan University, Faculty of Medicine. Blood pressure was measured on the right and left upper extremities by the same sphygmomanometer following at least five minutes of rest. ONSDM was recorded. All measurements of hypertensive-symptomatic patients were repeated at 30th minute following antihypertensive therapy.

Results: Moderate-to-well statistically significant correlations were determined between initial mean systolic blood pressure and ONSDM (rho=0.629, p=0.001) as well as between initial mean diastolic blood pressure and ONSDM (rho=0.561, p=0.001) in all study groups. Statistically significant differences were determined between the mean pre- and post-treatment systolic and diastolic blood pressures as well as the mean pre- and post-treatment ONSDM values of 40 patients who received antihypertensive therapy (p=0.000, p=0.000, p=0.000, respectively).

Conclusion: Ultrasonographic ONSDM reflected increased intracranial pressure in hypertensive patients. The reduction of intracranial pressure was also detected by the same method following antihypertensive treatment. Ultrasonographic ONSDM along with clinical findings and blood pressure measurements may be used for evaluation of response to treatment and deciding on further imaging.

Keywords: Hypertension, intracranial pressure, optic nerve sheath diameter, ultrasonography

Introduction

Hypertension is a health problem for preventive medicine with a gradually increasing importance. Prevalence of hypertension increases with age. Hypertension is detected more than half of people between 60 and 69 years of age and in 3/4 of people at the age of 70 years or older (1). Approximately one billion people are predicted to be hypertensive worldwide, and almost seven million people die due to hypertension every year (2). The rate of annual hospitalization related to hypertensive emergencies is 1-2 per million, and this rate appears to be more frequent in developing countries (3). Zampaglione et al. (4) ranked the most common referral complaints of patients with hypertensive emergencies as chest pain (27%), dyspnea (22%) and neurological disorders (2%).

Corresponding Author: Cesareddin Dikmetaş, Clinic of Emergency Medicine, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul Health Sciences University, İstanbul, Turkey
Phone: +90 505 556 73 62 **E-mail:** drcesareddindikmetas@gmail.com **ORCID ID:** orcid.org/0000-0002-3203-2029

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Hypertension may cause an increase in intracranial pressure (ICP). Such an increase is generally detected at a blood pressure over 180/120 mmHg (5). The sensitivity of fundoscopic examination performed for pupil edema in physical examination and used to detect acute ICP increase varies between 20% and 30% and depends on the attainment of the clinician (6,7). Papilledema may appear several hours after ICP increase (6). The measurement of optic nerve sheath diameter (ONSDM) by ultrasonography (US) is a non-invasive and useful method for the measurement of increased ICP (8).

In the present study, ONSDM by ultrasound was performed to detect ICP increase in hypertensive patients who were referred to ER to investigate whether the optic nerve sheath diameter (ONSD) increased in the presence of hypertension and whether ONSD was altered following antihypertensive treatment.

Materials and Methods

Male and female patients over 18 years of age who were referred to the Emergency Room of Emergency Medicine, Department of Necmettin Erbakan University Faculty of Medicine between May, 1st, 2012 and January, 1st, 2013 due to high blood pressure (systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg) were enrolled in the study. Informed consent was obtained from all patients participating in the study.

Hypertension-induced symptoms were determined as headache, double vision, blurry vision, dyspnea, chest pain, dizziness, dullness, nausea, abdominal pain, pain or weakness on extremities, nasal bleeding and confusion in the present study. Patients included in the study were investigated for these symptoms, and they were divided into two groups as "hypertensive-symptomatic" and "hypertensive-asymptomatic".

Healthy volunteers (normotensive and asymptomatic) without any complaints whose blood pressures were below specified limits and whose consents for participation were obtained constituted the control group.

Young patients, patients with incarceration, those who did not give consent, patients who were unstable and required urgent medical therapy, and symptomatic patients with normal blood pressure were excluded from the study.

Blood pressures of the patients and the volunteers enrolled into the study were measured from the right and left upper extremities following at least 5 minutes of rest by using a sphygmomanometer with an appropriately sized sleeve which was calibrated every year, and the results were recorded on the study form. The blood pressure measurements of the patients in the hypertensive-symptomatic group were repeated at the 30th minute following antihypertensive therapy, and the results were also recorded on the study form. The arithmetic means of recorded systolic and diastolic blood pressures measured from both extremities were calculated for statistical analysis.

ONSDM was performed on axial and sagittal planes from both eyes by a Philips Envisorc brand ultrasound device (serial number: US60608496) using a 7.5 MHz linear probe. Researchers carrying out the study were selected from physicians who were certificated by basic US courses. US imaging was performed in the supine position. Eyelids of the patients were irrigated with water while the eyes were closed. The gel was applied to the US probe. A protective sheath was placed onto the probe to prevent any possible allergic reaction against the gel. The image was saved when the optic nerve sheath image was captured. The distance of 0.3 cm posterior to the globe was marked, and the distance between both hypoechoic areas surrounding the optic nerve sheath at this plane was measured. Such measurements were applied to both eyes on the sagittal and axial planes. The measurement results were recorded in the study form.

Blood pressure measurements of the patients in the symptomatic hypertensive group were repeated at the 30th minute following antihypertensive therapy. The average of four measurements was calculated to be used for statistical analysis.

The study included a total of 149 participants, including 54 patients in the hypertensive-symptomatic group, 45 patients in the hypertensive-asymptomatic group, and 50 individuals in normotensive- asymptomatic (control) group.

Statistical Analysis

SPSS™ 16.0 version program was used for statistical analysis of the data obtained. The chi-square test was utilized for categorical data. Normality analysis was performed for numeric data. The Wilcoxon sign test was utilized for dependent groups, whereas the Kruskal-Wallis test was used for more than two independent groups, which did not fit a normal distribution. When needed, the Mann-Whitney U test was performed for two independent groups which did not fit a normal distribution. Pearson's and Spearman's correlation analysis were applied to numeric data. For all tests, p values below 0.05 were considered as statistically significant.

Results

One hundred and forty-nine participants, including 77 (51.7%) females and 72 (48.3%) males were enrolled in the study. The control group consisted of 50 healthy volunteers, including 26 (52%) males and 24 (48%) females. The hypertensive-asymptomatic group consisted of 45 patients, including 27 (60%)

females and 18 (40%) males. The hypertensive-symptomatic group consisted of 54 patients, including 28 (51.9%) males and 26 (48.1%) females (Table 1). There were no statistically significant differences among the study groups regarding gender (p=0.409).

The average age was 27.76±5.77 years in the control group, whereas it was 65.11±15.96 years in the hypertensive-asymptomatic group and 64.98±13.06 years in the hypertensive-symptomatic group (Table 2). A statistically significant difference was determined between the control group and hypertensive-asymptomatic group as well as the control group and hypertensive-symptomatic group (p=0.000, p=0.000, respectively) regarding age. However, there was no statistically significant difference regarding age between the hypertensive-asymptomatic group and hypertensive-symptomatic group (p=0.816). This result was referred to the fact that the control group consisted of normotensive and asymptomatic healthy volunteers.

The mean of initial systolic blood pressure measurements in ER was found as 111.70±9.77 mmHg in the control group, 165.66±18.19 mmHg in the hypertensive-asymptomatic group, and 177.12±22.58 mmHg in the hypertensive-symptomatic group (Table 3). In the comparison of the study groups regarding the mean initial systolic blood pressure, statistically significant differences were determined between the control group and the hypertensive-asymptomatic group as well as the control group and hypertensive-symptomatic group (p=0.000, p=0.000, respectively). Furthermore, a statistically significant difference was found to be present between the hypertensive-asymptomatic group and hypertensive-symptomatic group regarding the initially measured mean systolic blood pressure (p=0.009) (Table 3).

The mean initial diastolic blood pressure in ER was 76.35±7.71 mmHg in the control group, 93.66±10.73 mmHg in the hypertensive-asymptomatic group and 100.32±11.79 mmHg in the hypertensive-symptomatic group (Table 3). In the comparison of the study groups regarding the mean initial diastolic blood pressure, statistically significant differences were determined between the control group and hypertensive-asymptomatic group as well as the control group and hypertensive-symptomatic group (p=0.000, p=0.000, respectively). Furthermore, a statistically significant difference was found to be present between the hypertensive-asymptomatic and hypertensive-symptomatic groups (p=0.005).

The mean of initial ONSDM in ER was 0.442±0.0386 cm in the control group, 0.523±0.0570 cm in the hypertensive-asymptomatic group, and 0.527±0.0652 cm in the hypertensive-symptomatic group (Table 4). In the comparison of the study groups regarding the initial ONSDM in ER, statistically significant differences were determined to be present between the control group and the hypertensive-asymptomatic group as well as the control group and the hypertensive-symptomatic group (p=0.000, p=0.000, respectively). However, no statistically significant difference was detected between the hypertensive-asymptomatic and hypertensive-symptomatic groups regarding ONSDM (p=0.254).

A statistically significant moderate-to-well correlation was detected between the initial mean systolic blood pressure measured during admission to ER and ONSDM in all study groups (rho=0.629, p=0.046). A moderate-to-well correlation

Table 1. Distribution of the study groups according to the gender

Study Group	Gender		Total
	Male n (%)	Female n (%)	n (%)
Normotensive-asymptomatic	26 (52%)	24 (48%)	50 (100%)
Hypertensive-asymptomatic	18 (40%)	27 (60%)	45 (100%)
Hypertensive-symptomatic	28 (52%)	26 (48%)	54 (100%)
Total	72 (48%)	77 (52%)	149 (100%)

Table 2. Mean, median, minimum, and maximum values of the study groups regarding age

Study group	Age (years)	
	Mean ± SD	Median (min-max)
Normotensive-asymptomatic	27.76±5.77	26 (19-49)
Hypertensive-asymptomatic	65.11±15.96	68 (18-97)
Hypertensive-symptomatic	64.98±13.06	68 (19-85)

SD: Standard deviation, min: Minimum, max: Maximum

Table 3. The mean, median, minimum, maximum values of systolic blood pressure and diastolic blood pressure of the study groups initially measured in the emergency room

Study group	Initial mean systolic blood pressure (mmHg)		Initial mean diastolic blood pressure (mmHg)	
	Mean ± SD	Median (min-max)	Mean ± SD	Median (min-max)
Normotensive-asymptomatic	111.70±9.77	110 (90-130)	76.35±7.71	80 (60-90)
Hypertensive-asymptomatic	165.66±18.19	160 (145-220)	93.66±10.73	90 (80-130)
Hypertensive-symptomatic	177.12±22.58	175 (145-240)	100.32±11.79	100 (75-125)

SD: Standard deviation, min: Minimum, max: Maximum

was detected between the initial mean diastolic blood pressure measured during admission to ER and ONSDM in all study groups, and such correlation was also statistically significant (rho=0.561, p=0.000).

A statistically significant correlation was detected between the initial mean systolic blood pressure and ONSDM in both hypertensive groups (hypertensive-asymptomatic and hypertensive-symptomatic) (rho=0.382, p=0.000). Moreover, a statistically significant correlation was detected between the initial mean diastolic blood pressure and ONSDM (rho=0.280, p=0.005).

A statistically significant difference was detected between the pre- and post-treatment mean systolic blood pressures of 40 patients in the hypertensive-symptomatic group who received antihypertensive treatment in ER (p=0.000). Similarly, a statistically significant difference was detected between the pre- and post-treatment mean diastolic blood pressures in the same group (p=0.000).

The mean of ONSDM in the hypertensive-symptomatic group who received antihypertensive treatment in the ER was 0.528±0.072 cm before the treatment, and 0.461±0.058 cm after the treatment (Table 5). A statistically significant difference was determined between the pre- and post-treatment ONSDM values (p=0.000).

Nineteen patients in the hypertensive-symptomatic group were detected to have at least one of head/brain computed tomography (CT), head/brain MR, head/brain CT angiography and/or head/brain MR angiography imaging tests. The evaluation of these tests by the Radiology Department, revealed no acute pathology in five patients. Various pathologies were detected in 14 patients as follows: four patients with intraparenchymal bleeding, 1 patient with subarachnoid bleeding, 1 patient with subdural bleeding, three patients with acute/subacute infarction, three patients with chronic infarction, one patient with meningioma, and one patient with encephalitis. Since encephalitis, meningioma, and chronic infarction were not acute complications of hypertension, they were excluded from the subgroup analysis. Therefore, nine patients with acute pathology were compared with the other five patients regarding ONSDM. The average value of ONSDM was 0.480±0.044 cm in the group with no acute pathology and 0.571±0.057 cm in the group with an acute pathology (Table 6). A statistically significant difference was found to be present between the two groups regarding ONSDM (p=0.009).

Table 4. The mean, median, minimum, maximum values of ONSDM of the study groups initially determined in the Emergency Room

Study group	Initial ONSDM (cm)	
	Mean ± SD	Median (min-max)
Normotensive-asymptomatic	0.442±0.0386	0.435 (0.371-0.533)
Hypertensive-asymptomatic	0.523±0.0570	0.523 (0.389-0.619)
Hypertensive-symptomatic	0.527±0.0652	0.527 (0.388-0.706)

ONSDM: Optic nerve sheath diameter measurement, SD: Standard deviation, min: Minimum, max: Maximum

Table 5. Mean, median, minimum, maximum values of ONSDM before and after the treatment of the hypertensive-symptomatic patients

Study group	ONSDM (cm)	
	Mean ± SD	Median (min-max)
Before treatment	0.528±0.072	0.532 (0.388-0.706)
After treatment	0.461±0.058	0.449 (0.361-0.586)

ONSDM: Optic nerve sheath diameter measurement, SD: Standard deviation, min: Minimum, max: Maximum

Table 6. Mean, median, minimum and maximum values of ONSDM of the hypertensive-symptomatic patients with/without pathology detected by advanced imaging tests

Study group	ONSDM (cm)	
	Mean ± SD	Median (min-max)
No pathology (n=5)	0.480±0.044	0.487 (0.418-0.532)
Pathology (n=9)	0.571±0.057	0.573 (0.514-0.706)

ONSDM: Optic nerve sheath diameter measurement, SD: Standard deviation, min: Minimum, max: Maximum

Discussion

Although ICP measurement by invasive intracranial devices is a gold standard, the measurement is not always possible because the procedure is invasive, requires being specialized in neurosurgery, and has some contraindications such as coagulopathy or thrombocytopenia (9). Non-invasive techniques such as MRI or CT may be preferred; however, they are both expensive and time-consuming (10). Furthermore, CT scanning cannot be performed in unstable patients. Neuroimaging should be performed in a patient with a suspicion of ICP increase to exclude a space-occupying lesion, which requires surgical decompression (11). Moreover, findings supporting the diagnosis of increased ICP include signification of the subarachnoid field around the optic nerve, papilledema (posterior sclera flattening), vertical curvature of the optic nerve, prominent prelaminar part of the optic nerve, partially empty sella turcica, flow reduction in dural venous sinus, and sinus compression (12,13). Transcranial doppler US, which requires experience, might be insufficient (14).

The optic nerve is a part of the central nervous system during development and surrounded by subarachnoid cerebrospinal

fluid and dura mater; therefore, ONSDM is affected by cerebrospinal fluid changes (15). There are many studies addressing the relation between ONSDM and ICP in the literature. Kimberly et al. (16) analyzed the correlation between ONSDM and direct invasive ICP measurement in their study conducted in 15 individuals (11 individuals with spontaneous intracerebral hemorrhage; 4 individuals with traumatic injury) by optic US. They determined the presence of a significant correlation between ICP and ONSDM. When ONSDM was measured to be larger than 0.5 cm, the sensitivity and specificity were 88% and 93%, respectively, regarding the detection of ICP increase (16).

Blaivas et al. (17) conducted their study in 35 individuals and detected increased ICP findings in CT scan of 14 patients. Mean ONSDM of the patients with increased ICP and without pathology by CT was measured 6.27 mm and 4.42 mm, respectively. They reported that they found no statistically significant difference between the two groups. The sensitivity and specificity for detection of ICP increase by ONSDM by US were found to be 95% and 100%, respectively (17).

Roque et al. (8) measured ONSD by US to detect the increase of ICP in hypertensive patients. In their study, patients with a systolic blood pressure of ≥140 mmHg and/or diastolic blood pressure of ≥90 mmHg were included in the hypertensive group. The patients in the hypertensive group were divided into two subgroups. A patient was placed in the hypertensive-symptomatic group if he/she had one or more complaints such as headache, double vision, chest pain, shortness of breath, drowsiness, dizziness, nausea/vomiting, abdominal pain, and pain/weakness on the extremities and in the hypertensive-asymptomatic group if no complaint was present. Patients with a systolic blood pressure of <140 mmHg and/or diastolic blood pressure of <90 mmHg who did not have any complaints were included in the normotensive-asymptomatic group (8). In line with the present study, Roque et al. (8) detected a correlation between the mean systolic blood pressure and ONSDM when they analyzed all groups. Moreover, a weak correlation was found between the mean diastolic blood pressure and ONSDM when compared with the correlation between systolic blood pressure and ONSDM (8). We detected a moderate-to-well and significant correlation in our study. Similarly, in the study of Roque et al. (8), a correlation was detected between systolic blood pressure and ONSDM in the hypertensive group. Roque et al. (8) also found a correlation between the mean diastolic blood pressure and ONSDM. We detected a significant correlation in the present study. Furthermore, Roque et al. (8) accepted ONSDM ≥0.5 cm as abnormal and detected the best systolic and diastolic blood pressure threshold providing that level as 166/82 mmHg. In the same study, no statistically significant difference was detected in ONSDM before and after antihypertensive treatment. However, in the present study, a statistically significant difference was detected in the hypertensive-symptomatic group before and after antihypertensive treatment.

Girisgin et al. (18) enrolled 54 individuals, including 26 healthy volunteers in their study. CT scan reports of the patient group revealed brain injury, intracerebral hemorrhage, cerebral infarction, and hypoxic brain. Mean ONSDM was found as 4.6 mm in healthy volunteers and 6.4 mm in the patient group. A statistically significant difference was detected between the two groups (18). A significant difference was detected between the patients with and without acute intracranial pathology by CT within the hypertensive symptomatic group of the present study.

Amini et al. (19) measured ONSDM on 50 patients who were hemodynamically stable and had lumbar puncture because of various causes. ICP measurement was performed by lumbar puncture in that study. ICP was detected to be normal in 36 patients and increased in 14 patients. Mean ONSDM in the patients with increased ICP was found 6.66±0.58 mm and mean ONSDM in the patients with a normal ICP was detected 4.60±0.41 mm. A statistically significant difference was detected between the two groups ($p<0.001$). A statistically significant correlation was detected between the ONSDM value and ICP ($rho=0.88$, $p<0.05$). When ONSDM was over 5.5 mm, the sensitivity and specificity regarding ICP over 20 cm H2O were 100% and 100%, respectively (19).

Bäuerle et al. (20) searched the relation between ONSDM and ICP on 25 patients diagnosed with IIH. The control group included 25 healthy volunteers who did not have lumbar puncture before. In the aforementioned that study, ICP was measured by lumbar puncture and 30 to 50 mL cerebrospinal fluid was discharged as a treatment. After the discharge procedure, ONSDM was performed again. Mean ONSDM in the patients with IHH and in the control group was found 6.4±0.6 mm and 5.4±0.5 mm; and there was statistically significant difference between groups ($p<0.001$). Moreover, the best threshold of ONSDM to detect ICP increase was found to be 5.8 mm; sensitivity and specificity were 90% and 84%, respectively. ONSDM decreased on both eyes in the patients with IHH after lumbar puncture (right ONSDM 5.8±0.7 mm, $p<0.004$; left ONSDM 5.9±0.7 mm ($p<0.043$) (20). The results of the present study and of the studies conducted by Amini et al. (19) have led us to think that the efficacy of treatments for reduction of ICP can be monitored by ultrasonographic ONSDM.

Study Limitations

In the present study, the control group was created from normotensive-asymptomatic healthy volunteers. The average ages of the control and hypertensive study groups were different.

Importance should be given to age factor regarding the selection of healthy volunteers in more extensive studies planned in the future.

Researchers did not affect clinical follow-up and progress of the patients enrolled in the observational study, which was performed prospectively. Therefore, the number of advanced imaging studies in the symptomatic hypertensive group was 19. Within the scope of further studies, advanced imaging may be performed in all patients included in the symptomatic hypertensive group on the condition to obtain approval of the ethics committee and consent of the patient.

Complaints expressed by the patients were considered for the differentiation of hypertensive-asymptomatic and hypertensive-symptomatic groups in the present study. Therefore, groups were determined according to the subjective criteria. We believe that this might have contributed to the outcome that the increase of ONSDM is independent of the symptoms. We suggest a review of the relation between symptoms of hypertension and ONSDM in further studies.

Conclusion

Since ultrasonographic examination does not involve radiation, and it is an applicable, repeatable, and cost-efficient method. Use of US increases in ERs gradually. Measurement of ONSD by US may provide information about ICP increase and may be used for diagnosis and follow-up of patients with suspicion of ICP increase, including hypertensive emergencies. Emergency medicine physicians should learn how to use US in this field along with other fields of use.

Ethics

Ethics Committee Approval: This prospective clinical study was approved by the Local Ethics Committee at Necmettin Erbakan University Meram Medicine Faculty (date: 13/04/2012 - no: 2012/76) and conducted at Faculty of Medicine Hospital Emergency Department.

Informed Consent: Informed consent was obtained from all patients participating in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: C.D., M.E., Ç.S.D., M.G., T.A., K.Y., B.C., S.G., S.K., Design: C.D., M.E., Ç.S.D., M.G., T.A., K.Y., B.C., S.G., S.K., Data Collection or Processing: C.D., M.E., Ç.S.D., M.G., T.A., K.Y., B.C., S.G., S.K., Analysis or Interpretation: C.D., M.E., Ç.S.D., M.G., T.A., K.Y., B.C., S.G., S.K., Literature Search: C.D., M.E., Ç.S.D., M.G., T.A., K.Y., B.C., S.G., S.K., Writing: C.D., M.E., Ç.S.D., M.G., T.A., K.Y., B.C., S.G., S.K.

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The Effects of Repeated Basic Life Support Training on Teachers' Knowledge and Skill Levels: A Quasi-experimental Study

Kenan Gümüş[1], Seval Keloğlan[1], Nurhan Doğan[1], Aslı Yılmaz[2], Gamze Fışkın[2], Merve Yurttaş[3]

[1]Department of Nursing, Amasya University Faculty of Health Sciences, Amasya, Turkey
[2] Department of Midwifery, Amasya University Faculty of Health Sciences, Amasya, Turkey
[3]Department of Nutrition and Dietetics, Amasya University Faculty of Health Sciences, Amasya, Turkey

Abstract

Aim: The purpose of this study is to research the effect of repeated theoretical and practical up to date basic life support (BLS) training that provides teachers the opportunity to improve knowledge and skill levels.

Materials and Methods: This research was a pre-test, post-test, quasi-experimental study. The scope of the study included 65 teachers who participated in theoretical and practical up to date BLS training thirty days apart. A survey form including 19 questions was administered to determine pre-test and post-test theoretical knowledge about BLS. Skill level in BLS was assessed via BLS simulator model in terms of the followings; correct hand positioning, correct head positioning, sufficient depth and frequency of chest compressions.

Results: A significant difference was found between pre-test level of knowledge before BLS training and post-test after the second training session ($p<0.05$). The levels of competence for correct hand positioning (38.2% vs 61.8%; $p=0.001$), correct head positioning (27.6% vs 72.4%; $p=0.006$) and adequate compression frequency (35.0% vs 65.0%; $p=0.005$) increased and excessive compression rate (40.0% vs 60.0%; $p=0.005$) rose when pre-test and post-test levels were compared.

Conclusion: Promoting teachers' up to date BLS knowledge and skills with continuous training is beneficial. Repeated BLS training showed that the ability of the participants to develop adequate compression frequency with correct hand and head positioning was increased.

Keywords: Basic life support, cardiopulmonary resuscitation training, cardiopulmonary resuscitation simulation

Introduction

Cardiac arrest (CA) known as the cessation of circulation, is an emergency situation with high mortality rate. Basic life support (BLS) is defined as an intervention for obstructed airway due to a foreign body, CA or stroke; initiating basic steps to restore circulation and respiration (1). In the majority of cases, the first person to act in CA is a victim's closest person, usually a nonmedical person. Approximately 70% to 75% of cases of CA are witnessed by nonmedical people (2). In the case of CA, BLS performed by a trainedcivil first aider can decrease mortality to a large extent (3). In recent years, trainings and seminars have been organized for individuals who are health providers to increase awareness of BLS. Upon the recommendation of American Heart Association (AHA), BLS training was included in school curriculums to train teachers and students in developed countries (4). In addition, school accidents are a significant cause of death in children over five years old (5), therefore, acquiring BLS skills are important for individuals who are not health care professionals. Teachers in school environment are likely to witness a cardiac case more frequently. Thus, BLS training for teachers can decrease morbidity and mortality rates due to early intervention (1,3,4,6,7). The purpose of this study is to investigate the effect of repeated training on teachers' knowledge and skill level (correct hand and head position giving, provide adequate depth of compression and frequency)

Corresponding Author: Kenan Gümüş MD, Department of Nursing, Amasya University Faculty of Health Sciences, Amasya, Turkey
Phone: +90 537 220 34 54 **E-mail:** kenan.gumus@amasya.edu.tr **ORCID ID:** orcid.org/0000-0002-3582-6609

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Materials and Methods

Study design

The study was designed as a pre-test, post-test and quasi-experimental test. The study was conducted with 65 teachers who worked in schools in Amasya city center, voluntarily participated and were chosen by basic random sampling. The consent form was signed by all participants who approved to participate in the study. Data were collected using a survey form to assess level of knowledge of BLS and a BLS simulator model. The study was conducted between May and December 2017. The Scientific Research and Publication Ethics Committee of Amasya University gave consent (no: 15386878-044) and an institutional approval was obtained. The study included the teachers who approved to participate, did not work in a school providing health education and were not professional BLS providers.

Questionnaire form

A multiple-choice questionnaire based on 2015 AHA guidelines and relevant literature was used to determine teacher's demographical characteristics and knowledge level of BLS procedures (3,8-12). The questionnaire included 26 questions. Seven questions pertained to teachers' demographical characteristics (age, gender, level of education, years of work experience etc.) and 19 questions assessed BLS practical knowledge (consciousness assessment, chest compression location and frequency, checking airway patency, hand positioning, external defibrillator use etc.). The questionnaire was given to 20 individuals to test the clarity of the form before use in the study. Subsequently, the questionnaire was finalized after making necessary corrections. Each interview took approximately 15 minutes. The same questionnaire form was used for pre-test and post-test.

BLS Simulator Model

The "CPR Lilly Pro", a half-body BLS simulator model, was used to determine the teachers' level of BLS skills before and after training. The BLS model had the following features; correct hand positioning, correct head and chin positioning, compression depth and frequency. The BLS simulator model testing each skill was successful at least 80% of the time. Data obtained from the model were transferred to a tablet via bluetooth and recorded.

Training and Practice

The research was conducted in two phases. Theoretical and practical BLS training was provided after administering the pre-test questionnaire in the first phase. The training was set up for 10 hours (4 hours theoretical and 6 hours practical). Audio and visual presentations were used in the theoretical training session. Three presentations including fundamental cardiopulmonary anatomy and physiology, the importance of intact cardiopulmonary circulation for survival, state of consciousness, assessment of levels of consciousness and BLS practices structured according to the AHA 2015 guidelines. After theoretical training, a six-hour practice session on the BLS simulator model was conducted until the teacher acquired competency in necessary BLS skills. Following this session, BLS skills were tested on the BLS simulator model with the teachers for 2 minutes and the data were recorded.

To assess the efficacy of repeated training, the same participants were trained with the same training materials on the same BLS simulator model thirty days later. The same questionnaire form was administered as a post-test. After the second phase, BLS training on the BLS simulator model was done for two minutes with the teachers and the data were recorded. Pre-test and post-test answers were recorded. Trainers did not intervene in the meanwhile during the testing on the BLS simulator models. Competencies were all conducted in the same laboratory. Trainers and teachers entered the laboratory solo to prevent interactions with each other.

Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) 20 (IBM Corporation, New York). Kolmogorov-Smirnov and Shapiro-Wilk tests were used for normality. Data were analyzed using numbers, percentage, mean and chi-square (x2). Frequencies and percentages were used to describe categorical parameters. The participants' answers to pre-test and post-test questions were evaluated using the chi-square test. A p-value less than 0.05 is statistically significant.

Results

Teachers' distribution according to their descriptive characteristics is shown in Table 1. The mean age was 40.30±8.59 years and min-max was 26-52 years. Undergraduate teachers made up 86.9% of the participants. Of the teachers 99.2% thought that BLS was required to be known while 87.7% had not received BLS training before (Table 1).

Findings Before and After Training

Of the teachers 43.1% were reluctant to practice BLS before training and 75.4% knew the practice phases wrong. After the training, the teachers' hesitation rate for practicing BLS decreased to 26.2% ($p=0.043$) and their rate of correct responses to practice phases increased to 78.5% ($p<0.001$). Teachers who knew loss of consciousness symptoms increased from 33.8% to 56.9% ($p<0.007$) and the rate who knew BLS training phases increased from 9.2% to 60.0% ($p<0.001$). All the teachers had known the correct emergency phone number before training. Of the teachers,

Table 1. Distribution of teachers according to their descriptive characteristics			
Descriptive Characteristics	**Category**	**n**	**%**
Gender	Female	62	47.7
	Male	68	52.3
Age	26-34	39	30.0
	35-43	51	39.2
	44 years and older	40	30.8
Mean age (year)	40.30±8.59		
Duration of employment	1-10	45	36.4
	11-20	40	30.8
	21 years and older	45	34.6
Mean employment duration (years)	16.35±9.77		
Educational level	Undergraduate	113	86.9
	Postgraduate	17	13.1
Is is necesary for teachers to know BLS?	Yes	129	99.2
	No	1	0.8
Previous first-aid training	Yes	16	12.3
	No	114	87.7
Teachers included in the assessment	Before training (Pre-test)	65	50.0
	After training (Post-test)	65	50.0
Total		130	100
BLS: Basic life support, n: Number			

76.9% did not know the necessary assessment duration before starting the BLS training while this rate decreased to 29.2% after training (p<0.001). The minimal increase in the correct answer to the question "which tissue/organ is not affected negatively in a person whose respiration stops?" was not statistically significant (p=0.069). Of the teachers, 49.2% gave a correct answer to the length of time that organ damage occured in individuals following CA. This rate increased to 89.2% after training (p<0.001). Of the teachers, 96.9% gave an incorrect answer to length of respiration in BLS before training, while 86.2% gave the correct answer after training (p<0.001). Teachers who responded correctly that chest compressions should not be more than 5-6 cm for effective BLS was 40.0%, however after the training, every teacher answered this question correctly (p<0.001). Of the teachers, 13% correctly knew that the number of chest compressions to be performed in one minute during BLS, while this number increased to 95.4% after training (p<0.001). Of the teachers 61.5% and 58.5% did not know the rate of artificial respiration to chest compression in BLS performed on children and adults, respectively, however after training, 92.3% and 100% of teachers responded correctly (p<0.001 and p<0.001, respectively). The rate of those who knew the correct chest compression site was 16.9%, and the number increased to 72.3% after training (p<0.001). Of the teachers, 81.5% knew the method used in respiratory assessment before training, however, and all knew the correct method after the training (p<0.001). Of the teachers 69.2% and 98.5% answered correctly the necessary procedure to ensure a patent airway before and after training, respectively (p<0.001). Of the teachers, 69.2% did not know the correct BLS procedure when they faced with a situation in which no response was taken from the patient, patient did not breath and the heart did not beat, however 90.8% of the teachers learned the correct procedure for this situation (p<0.001). The percentage of participants who knew that only chest compression should be applied to someone who did not have opportunity to make artificial respiration was 46.2% before training and 100% after training (p<0.001). Of the teachers 47.2% knew BLS termination criteria before training and this rate increased to 98.5% after training (p<0.001). Only 18.5% of the teachers stated that they knew about external defibrillators and its function, while 95.4% learnt that this device could be used by civil servant first-aid practitioners, could administer shock when necessary and should be provided in crowded places after training (p<0.001). Table 2 shows detailed information of the responses given by teachers before and after BLS training.

BLS Simulator Model Findings

According to the findings obtained from the BLS simulator model before and after the training, the level of competence for correct hand positioning (38.2% vs 61.8%; p=0.001), correct head positioning (27.6% vs 72.4%; p=0.006), adequate compression frequency (35.0% vs 55.4%; p=0.100) and the rate of excessive compression application (40.0% vs 60.0%; p=0.005) significantly increased when pre-test and post-test results were compared. The increase providing the recommended compression depth (44.6% vs 55.4%; p=0.100) was insignificant (Figure 1).

Discussion

This study analyzed the change in level of knowledge and skills of teachers who were provided with repeated theoretical and practical BLS training. Schools are places where people live together, and possible life-threatening accidents may occur. Training of teachers with BLS is important in such places. Mortality and morbidity rates can decrease when correct intervention is given by trained specialists appropriately when BLS is necessary. However, uncertainty exists about performing BLS when necessary. A study found some teachers hesitant about practicing BLS when necessary. The fear of hurting the victim due to insufficient skills was found to be a significant reason for hesitating (13,14). Repeated trainings were found to dramatically decrease teachers' uncertainty (43.1 vs 26.2%), however the uncertainty was not completely removed. A study by Mpotos et al. (15), conducted in a wide sampling, showed

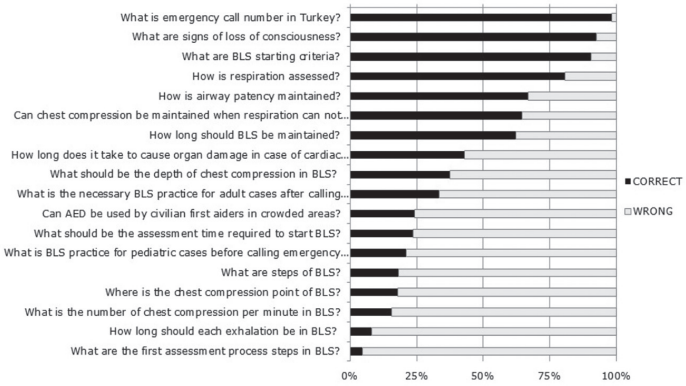

Figure 1. BLS Simulator Model Findings
BLS: Basic life support

a positive relationship between teacher's BLS training and BLS applicability. The same study showed that uncertainty in BLS administration decreased in teachers who received training. Therefore, it is thought that current and repeated theoretical and practical training can be effective in terms of decreasing teacher's hesitancy in performing BLS. Another reason for teachers' uncertainty with BLS is the perception that it is only administered by health care professionals. This misperception can be overcome through trainings provided to all civil servants, first-aid providers and teachers.

Previous studies showed that teachers had low to moderate knowledge levels of BLS (6,16). However, other studies found

Table 2. Distribution of teachers' answers regarding basic life support knowledge before and after training

Questions	Before training (Pre-test)*		After training (Post-test)**		p
	Correct (n%)	Wrong (n%)	Correct (n%)	Wrong (n%)	
I hesitate to administer BLS	28 43.1%	37 56.9%	17 26.2%	48 73.8%	p=0.043
What are BLS applications phases?	16 24.6%	49 75.4%	51 78.5%	14 21.5%	<0.001
What are the findings showing that patient is experiencing unconsciousness?	22 33.8%	43 66.2%	37 56.9%	28 43.1%	<0.001
Which one is the correct BLS practice in patients experiencing unconsciousness?	6 9.2%	59 90.8%	39 60.0%	26 40.0%	<0.001
What is the emergency phone number in Turkey?	65 100.0%	0 0.0%	65 100%	0 0.0%	p=0.0154
How much time (seconds) does it take to do the necesary assessment to pass on BLS practice?	15 23.1%	50 76.9%	46 70.8%	19 29.2%	<0.001
What is the first tissue/organ that will be affected when an individual stops breathing?	53 81.5%	12 18.5%	60 92.3%	5 7.7%	p=0.069
After the heart stops, how long time after (seconds) does the organ damage start to occur if it is not intervened?	32 49.2%	33 50.8%	58 89.2%	7 10.8%	<0.001
How long should each artificial respiration (seconds) take in BLS?	2 3.1%	63 96.9%	56 86.2%	9 13.8%	<0.001
How many cm should the chest be compressed for an effective BLS heart massage?	26 40.0%	39 60.0%	65 100.0%	0 0.0%	<0.001
What is the rate of heart massage per minute that should be administered for BLS?	9 13.8%	56 86.2%	62 95.4%	3 4.6%	<0.001
What should be the breathing-compression rate for pediatric BLS?	25 38.5%	40 61.5%	60 92.3%	5 7.7%	<0.001
What should be the breathing-compression rate for adult BLS?	27 41.5%	38 58.5%	65 100.0%	0 0.0%	<0.001
Where is the exact point of cardiac compressions?	11 16.9%	54 83.1%	47 72.3%	18 27.7%	<0.001
What is the method used for respiration assessment?	53 81.5%	12 18.5%	65 100.0%	0 0.0%	<0.001
What is the necessary procedure to provide airway patency?	45 69.2%	20 30.8%	64 98.5%	1 1.5%	<0.001
What should be BLS practice for someone who does not respond, does not breath and whom you are not sure about heartbeat?	20 30.8%	45 69.2%	59 90.8%	6 9.2%	<0.001
Can heart massage only be done in BLS if there is no chance of doing artificial aspiration?	30 46.2%	35 53.8%	65 100.0%	0 0.0%	<0.001
Is it necessary to continue BLS until a person gets tired, ambulance arrives, somebody else arrives or patient regains consciousness?	30 47.2%	35 53.8%	64 98.5%	1 1.5%	<0.001
Can automatic external shock device, (required to be in public places), does not necessitate specialty in use and saves people's lives be used by civil first-aid provides?	12 18.5%	53 81.5%	62 95.4%	3 4.6%	<0.001

BLS: Basic life support, cm: centimeter, n: Number
n*=65, n**=65

that trainings could boost their BLS knowledge level (17,18). This study found that repeated trainings given under current guidelines significantly increased teachers' practical knowledge. However, the currentness of the provided and repeated training is effective to create this quality and its duration. A study found that teachers' knowledge level increased from 39.79% to 71.73% with a BLS training after four hours (19). Although teachers' knowledge level increased with the training, the important consideration was to provide frequent updated knowledge. To this end, repetitiveness of the training plays a key role. Six months following BLS training, teachers experienced loss of knowledge (20,21). Therefore, teachers' level of preparedness can be retained when current BLS training is given regularly and repetitively by public institutions.

It is more objective to assess practical skills in BLS training with BLS simulator model as this assessment protects teachers' level of knowledge and their skills (22,23). This study found that teachers who received training with a BLS simulator model had a significant increase in correct hand positioning, correct head and chin positioning and creating sufficient compression frequencies. The first condition of efficient and sufficient chest compression is to use correct hand position. Even if other skills are appropriate, improper hand position on the chest results in ineffective BLS and survival rate decreases. This study found significant improvement (38.2 vs 61.8%) in terms of correct hand positioning used by teachers following training. A study by Pichel López et al. (24) found that teachers who received BLS training had improvement in correct hand positioning compared to pre-training, similar to our study. This improvement provided by training teachers was also seen in correct head positioning. Management of airway patency and sufficient respiratory support are considered as important components of BLS application. However, providing airway patency is a controversial issue in previous studies. New recommendations put forward aggressive chest compression. It was reported that stopping compression and slowing it down would lead to fast and continuous deterioration of coronary perfusion pressure (25). This situation was considered by researchers during training. Teachers were notified that if respiration and/or airway support was not provided, BLS practice had to be applied only with chest compression. It was found in the post-test that teachers highly adopted this (46.2 vs 100%) practice.

At the end of the study, it was found that teachers' skill for providing appropriate compression depth significantly increased. In addition, a significant increase was found in the rate of teachers who applied excessive compressions. Sufficient chest compression is an important component of BLS and there is a direct relationship between chest compression and survival of patients with CA outside the hospital (26,27). Previous studies found that even in short procedures that took 5 minutes, compression depth and frequency criteria determined by AHA were not met (28). Teachers' insufficient experience and physical effort may have affected the result of this study in this way. Ineffective chest compressions cause the practitioner to tire quickly. In addition, trainers determine that chest compressions and frequency must meet the guidelines for an effective BLS practice. Therefore, if teachers focus on the frequency during compressions they can understand if they administer insufficient compression depth and frequency. The focus of appropriate technique in BLS training should be compression rate and depth to improve the quality of BLS. It was determined that creating correct compression depth and rate in BLS were the most difficult skills to acquire (6,15). The least acquired skills in this study were giving appropriate compression depth and preventing excessive compressions.

As a result, BLS training must be given grounded on practical, repetitive and current knowledge. Providing education in this way will enable efficient BLS administration in case of CA at schools and in cultivation of teachers as civil servant first-aid providers.

Study Limitations

The limitations of the study were as follows: a small sample size, short intervals between the assessments, provision of the questions and trainings by the same people and practical assessments being limited to two minutes.

Conclusion

BLS is considered a necessary skill to develop. However, the significant point is to train teachers with current and sufficient theoretical and practical training. This study showed that teachers with low levels of BLS knowledge and skills could perform BLS at a higher level and with increased readiness. Consequently, BLS training must be given grounded on practical, repetitive and current knowledge. Providing education in this way will enable efficient BLS administration in case of CA at schools and in cultivation of teachers as civil servant first-aid providers. State institutions and universities should work in cooperation with health care professionals and update their information frequently.

Ethics

Ethics Committee Approval: The Scientific Research and Publication Ethics Committee of Amasya University gave consent (No. 15386878-044) and an institutional approval was obtained.

Informed Consent: The consent form was signed by all participants who approved to participate in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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Case Report
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Acute Urinary Retention: Should We Call It a Manifestation of Appendicitis?

Sadaf Sheikh, Umair Javed, Muhammad Akbar Baig

Department of Emergency Medicine, Aga Khan University Hospital, Karachi, Pakistan

Abstract

Acute urinary retention is a fairly common presentation in the elderly but it is a rare manifestation of acute appendicitis in a healthy young individual. We presented a 32-year-old male with decreased urine output with mild tenderness at the suprapubic region later on shifted to right iliac fossa. Computed tomography of abdomen showed acute appendicitis. Emergency physicians should recognize the uncommon presentation of acute appendicitis and should be aware of this common complaint as a rare presentation. This case also highlights the importance of repeated abdominal examinations to seek diagnostic clarity.

Keywords: Appendicitis, acute urinary retention, repeat abdominal examination

Introduction

The classical presentation of acute appendicitis is well known: periumbilical pain radiating to right iliac fossa with nausea, vomiting and anorexia. Yet, this presentation is not always there to indicate the diagnosis. Less is been published regarding atypical presentation of acute appendicitis and one needs to think of alternative diagnosis in the setting of acute urinary retention (AUR).

Case Report

A previously healthy 32-year-old gentleman, presented to emergency room with complain of inability to pass urine for the past 8 hours associated with low abdominal pain. Lower abdominal pain was non-radiating, dull in character with no clear aggravation and relieving factor. There was no associated nausea and vomiting. He reported normal appetite and no history of fever. He had no prior urological history and denies any history of urethral discharge. Sexual history was unremarkable. Past surgical and medical history was unremarkable. Moreover, there was no prior history of kidney stones or urethral stricture. Bowel habits were normal and patient denied any addiction.

On arrival patient was afebrile, had heart rate of 76 bpm, blood pressure of 126/72 mmHg, respiratory rate of 18/min and oxygen saturation on pulse oximeter of 99% at room air. General physical examination was unremarkable except for dry mucosa and skin. Abdominal examination revealed soft abdomen with mild tenderness in lower abdomen. Bladder was palpable midway between symphysis pubis and umbilicus. Normal gut sounds were found on auscultation. There was no rebound tenderness or costo-vertebral tenderness. Rest of the systemic examination was unremarkable. Genitourinary examination was also unremarkable.

Foley catheterization was done without any complication. Post void residual of 400 mL was obtained. (Table 1).

Urinalysis reported negative leucocyte esterase, nitrites and leukocytes with hemoglobin 1+ and ketone 1+ on dipstick testing.

Corresponding Author: Sadaf Sheikh MD, Department of Emergency Medicine, Aga Khan University Hospital, Karachi, Pakistan
E-mail: sheikh.sadaf@gmail.com **ORCID ID:** orcid.org/0000-0001-7457-0012

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Reassessment performed after 2 hours revealed that lower abdominal pain did not settle. Abdominal examination after 2 hours revealed lower abdominal tenderness more marked in right iliac fossa. Rovsing sign, obturator sign and psoas sign were negative. Rebound tenderness was positive. Alvarado score was 5 points (1 for rebound tenderness, 1 for right iliac fossa tenderness, 2 for elevated leukocyte count and 1 for leukocyte left shift).

Focus assessment computed tomography reported dilated appendix of 10.5 mm with multiple high density foci within its lumen representing appendicoliths. Mild free fluid and peri-appendiceal inflammatory changes were present (Figure 1, 2).

Table 1. Initial laboratory investigations were as follows	
Hemoglobin	15.9
Hematocrit	46.1
Mean corpuscular volume	82.5
White blood cells	14.1
Neutrophils	88.1
Lymphocytes	5.2
Platelets	265
Blood urea nitrogen	9
Creatinine	1
Sodium	135
Potassium	3.3
Chloride	96
Bicarbonate	28.8
Urine cultures	-

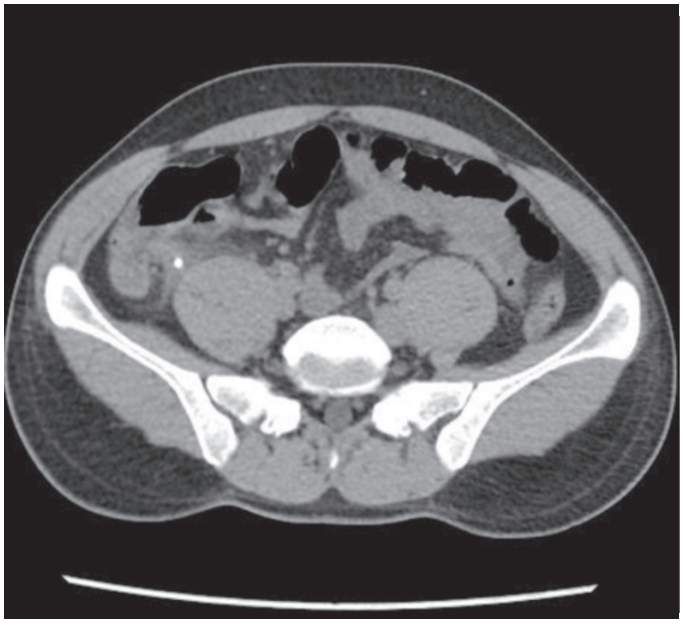

Figure 1. Image showing appendicolith

Discussion

Acute appendicitis is the high volume diagnosis in the emergency room. As emergency physicians, we don't always consider the mimicking conditions of

acute appendicitis, moreover it has a complex and atypical range of presentation leading to missed diagnosis (1).

It is common to operate an ureteric stone with a pre-operative diagnosis of appendicitis but on the contrary, mistakes could happen in the case of urological manifestations of acute appendicitis.

This case report focused on the variability in manifestation of acute appendicitis notably AUR and hematuria. This variability is likely originating from the location of appendix leading to diagnostic dilemmas. Appendicitis manifesting as AUR is rare. Urological manifestations of acute appendicitis which may otherwise point to the pathology of genito-urinary system, could be dysuria, urinary frequency, AUR, rectal pain or testicular pain (2).

Dysuria is the result of irritation of urinary bladder in case of peri-appendiceal inflammation. In case of pelvic appendix, it's not common to have abdominal rigidity misleading the examiner to think about bladder pathology. Patients complain that they get full bladder but have no complaints about passing urine (2). It is mainly when appendix is behind cecum, in the iliac fossa or deep in the pelvis.

Retention of urine is due to the irritation of bladder sphincter which is uncommon. Difficulty in urination is the common complaint in this situation (2).

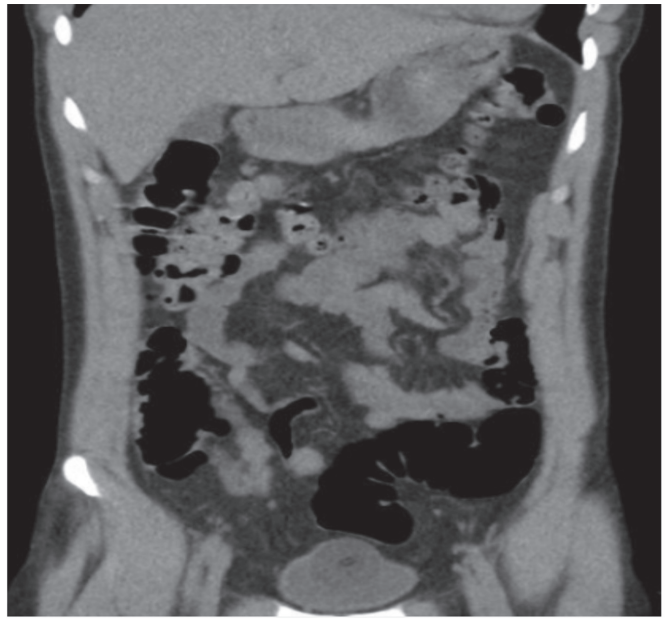

Figure 2. Image showing peri-appendiceal inflammation

Differential diagnosis is relatively easier when urine is well examined. While differentiating it from pyelitis, acute appendicitis is associated with normal urine analysis with rigidity of abdominal muscles and fever. Tenderness at right erector-costal angle does present in the acute appendicitis due to irritation of tenth dorsal spinal nerve which innervates the appendix (2). Literature showed such rare presentation in acute appendicitis with gross hematuria, acute prostatitis and acute pyelonephritis (3,4). Such unusual manifestations should be sought in the differential diagnosis of AUR.

Ethics

Informed Consent: Informed consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.S, U.J., M.A.B., Design: S.S, U.J., M.A.B., Data Collection or Processing: S.S, U.J., M.A.B., Analysis or Interpretation: S.S, U.J., M.A.B., Literature Search: S.S, U.J., M.A.B., Writing: S.S, U.J., M.A.B.

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