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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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Original Article
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Epinephrine Auto-injector Use on YouTube: Is It Really Useful?

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Abstract

Aim: Epinephrine is the best treatment for anaphylaxis and gives the best results if given within the first few minutes of a severe allergic reaction. An auto-injector is used by the patient or her/his relatives when the reaction happens. The Internet can be useful in the education of these individuals as much as the education provided by the experts in this field. To the best of our knowledge, there is no study about epinephrine videos on YouTube. In our study, we aimed to evaluate the accuracy of YouTube videos on the use of epinephrine auto-injector and their compliance to guidelines.

Materials and Methods: In order to analyze the quality and compliance of YouTube videos on auto-injectors, the term "using epinephrine auto-injectors for anaphylaxis" was searched at YouTube in January 2015. The videos were then scored from 1 to 10 for reliability.

Results: Of the 610 videos in our study, 210 were about epinephrine auto-injectors. It was found that there was a significant relationship between reliability and uploader, upload date, video length and application model ($p<0.05$), but there was no significant relationship between reliability and the number of views ($p=0.885$).

Conclusion: In conclusion, we postulated that the social network is very efficacious in terms of medical education. In order to prevent misinformation of the community, videos should be shared by relevant authorities or physicians on social networks like YouTube.

Keywords: Auto-injector, epinephrine, YouTube

Introduction

Anaphylaxis is a systemic hypersensitivity reaction that affects many organs for various reasons. Epinephrine (adrenalin) is the first and most important step in the treatment of anaphylaxis. Most anaphylaxis-related deaths are due delayed or lack of adrenaline administration. Since most cases of anaphylaxis develop outside the hospital, patients should carry the adrenaline auto-injector with them and treat themselves (1). In terms of teaching how to use auto-injectors, websites where information can be accessed quickly and easily can be a part of education as physicians (2).

YouTube is a social network where people can easily upload and publish videos. The ease of accessibility increases the prevalence, but the possibility of misinformation in published videos may cause the spread of false information.

In this study, we analyzed the videos on YouTube by searching for "using epinephrine auto-injectors for anaphylaxis" and aimed to determine if the video contents are in accordance with the guidelines and to check their reliability.

Materials and Methods

Setting

The term "using adrenaline/epinephrine auto-injectors for anaphylaxis" was searched on https://www.youtube.com on January, 2016 and the videos were evaluated by one

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dermatologist and two emergency physicians who were trained about adrenaline auto-injectors.

Study Design and Data Collection

The exclusion criteria were as follows: a) videos about medicine, but not related to epinephrine auto-injectors, b) videos with no demonstration of application, c) videos not in the English language, c) videos including news, not training, d) advertising videos (ads about courses etc.), e) funny or non-serious videos, and f) repetitive videos. The uploaders were categorized as a) official institutions (AHA/ERC, Universities etc.), b) professionals such as medical doctors, c) news agency, d) commercial firms (course etc.) and e) unclear. In addition, number of views, upload date (year), length of videos, and application model (no application, applying to a real person, schematic application or both real person and schematic application) are questioned.

All videos were watched by two emergency physicians and one dermatologist. When there was no agreement on the score, the video was watched again together and the score was accounted mutually. The score table from one to ten was used for evaluating the reliability of videos (Table 1).

Statistical Analysis

All data from the study were evaluated by using Statistical Package for Social Sciences for Windows version 20. Quantitative factors were expressed as mean ± standard deviation and categorical factors were summarized as numbers and percentage. Frequency analysis was done. The distributions of variables were examined, and Independent Samples t-test was used for the analysis of normally distributed variables and Mann-Whitney U test was used for non-normal distributions. The differences between two groups in terms of demographic and hematological parameters were determined by backward stepwise logistic regression analysis. $P<0.05$ was considered significant in all tests.

Table 1. The parameters used to assess the reliability of videos

Parameter	Score
A1. Does the video mention the importance of anaphylaxis?	1
A2. Does the video mention when should apply an epinephrine auto-injector?	1
A3. Does the video mention the importance of epinephrine auto-injector? (the importance of the necessity to be done)	1
A4. Does the video describe the application of epinephrine auto-injector?	1
A5. Does he/she pull the cover?	1
A6. Does he/she show the location where to apply epinephrine auto-injector in the outer-mid-thigh?	1
A7. Does he/she inject black portion into the thigh?	1
A8. Does he/she press to activate?	1
A9. Does he/she keep epinephrine auto-injector for ten seconds?	1
A10. Does he/she suggest calling emergency?	1

Results

The search yielded a total of 619 videos on 31 webpages, each webpage including 20 videos. Four hundred and ten videos were excluded according to exclusion criteria. Unrelated videos (n=141) and repetitive videos (n=79) were excluded. A total of 210 videos were included in this study (Table 2).

It was found that 63 of 210 videos were uploaded by government agencies. The uploaders of 114 videos were unclear. The mean number of views was 10704 (min-max=3-413682) and the mean video length was 2.8 seconds (min-max=0.01 to 26.23). Most of the videos (n=48) were uploaded in 2015 and only one video was uploaded in 2006. It was found that auto-injector application was shown on real people in 156 videos and the application scores were given in Table 3.

Eighty-six (41%) videos obtained a full score. The mean score of the videos was 7.6±1.6. Thus, it was identified that a video with a score of 10 was reliable. When we use this value as a statistical cut-off, it was found that there was a significant relationship between uploaders, length of video, upload date, application model and reliability ($p<0.05$). However, there was no significant relationship between the number of views and reliability ($p=0.885$).

When we divided the videos into two groups according to the uploaders (government agencies and physicians in the first group and uncertain agencies in the second group), there was a statistically significant relationship between the groups in terms of reliability and video length ($p<0.05$ and $p<0.05$). There was no statistically significant relationship between groups in terms of the number of views, upload date and application model ($p=0.129$, $p=0.635$, $p=0.064$, respectively).

Table 2. Exclusion criteria for videos

Reason for exclusion	n	%
It is medical, but not related to epinephrine auto-injector	141	22.8
There is expression, but no application	18	2.9
Language is not English	12	1.9
It is not related to education	86	13.9
Funny video	73	11
Repetitive video	79	13.6
Do not exclude	210	33.9
Total	**619**	**100**

Table 3. Upload date, uploaders, application models and application scores

Date	**n**	**%**
2006	1	0.5
2007	2	1
2008	6	2.9
2009	13	6.2
2010	10	4.8
2011	19	9
2012	22	12.9
2013	42	20
2014	42	20
2015	48	22.9
Uploader	**n**	**%**
Official institutions (like AHA/ERC or University...)	63	30
Healthcare professional(s)	17	8.1
Individual with credentials unspecified	114	54.3
News program	16	7.6
Application model	**n**	**%**
No application	33	15.7
Human	156	74.3
Manikin	2	1
Both	19	9
Score	**n**	**%**
A1 correctly applied	105	50
A2 correctly applied	118	56.2
A3 correctly applied	119	56.7
A4 correctly applied	166	79
A5 correctly applied	205	97.6
A6 correctly applied	190	90.5
A7 correctly applied	202	96.2
A8 correctly applied	200	95.2
A9 correctly applied	184	87.6
A10 correctly applied	114	54.3
Total	**210**	**100**

AHA: American Heart Association, ERC: Europen Resuscitation Council

Discussion

As a result of our study, we found that 40% of the videos on YouTube scored above average and we found that the steps related to the application were useful in terms of training because of the high rate of 90%.

The way to reduce anaphylaxis-induced mortality and morbidity depends on effective treatment on time. The increasing incidence of anaphylaxis in recent years has gained importance. For this reason, a premeasured epinephrine preparation (epipen or Auvi-Q) should be provided for emergency use in the treatment of anaphylaxis (3). YouTube and other social networks are widely used to enable people to share information in a very fast and uncontrolled way (4). Uncontrolled, widespread and rapid dissemination of data is extremely important in terms of access to information sharing. However, if there is doubt about the accuracy of the information, this means the rapid dissemination of incorrect information. In their study, Akgun et al. (5) evaluated electrocardiography videos on YouTube and found that these videos were not useful and safe. Beydilli et al. (6) examined the accuracy of the videos on YouTube about pediatric resuscitation [cardiopulmonary resuscitation, basic life support (BLS) etc.] and reported that only 232 of the 1200 videos were related to BLS and CPR, and that 15% were reliable. Similarly, Yaylacı et al. (2) investigated accuracy and reliability of 1994 YouTube videos on adult cardiopulmonary resuscitation and basic life support. They stated that 209 videos were in line with the guidelines and that videos are partially useful for training. In our study, we found that search for "epinephrine auto-injector" yielded 619 videos and that 210 of them were associated with epinephrine auto-injector. Thirty-nine point eight percent of them were rated above average and these videos were found to be beneficial for education. It was found that there was a significant relationship between the reliability of the videos and uploaders, upload date, the length of videos and application model. We believe that it is extremely important to emphasize the significant relationship between reliability and uploaders.

We could not find any studies in the literature on epinephrine auto-injectors on YouTube or similar social networks. Therefore, we believe that this study is important because it is the first study in the literature. Two studies were found on epinephrine auto-injectors, but they were not related to education. In a trial conducted with students at the primary school and secondary schools, 20.6% of participants correctly applied epinephrine auto-injector including all 4 steps of the procedure (grey cap removal, place the injector on the middle of the outer thigh, push down to activate and hear the click sound, wait for at least 10 seconds). In a study conducted with medical students, it was determined that 2% of participants applied the 6 steps of the procedure correctly (introduction of epinephrine auto-injector, remove the gray cap, place the injector on the middle of the outer thigh, push down to activate, hear the click sound, wait for at least 5 seconds) (7,8). Our study found that the steps of application were correctly described in the videos, but the importance of anaphylaxis and recommended steps for contacting emergency services were less accurate. It was observed that most of our videos were uploaded in 2015 and approximately one third of them were uploaded by relevant institutions or healthcare professionals and physicians. Güneş et al. (9) examined YouTube videos on varicose veins in their study and found that the number of views of videos uploaded by related institutions was higher than that uploaded by healthcare personnel who uploaded 32.7% of the videos. However, in our study, no significant relationship was found between the number of views and uploaders.

Conclusion

In conclusion, we think that social networks such as YouTube are especially useful for medical education. However, in order to avoid misinforming the society, we believe that official institutions or physicians should share videos on YouTube and other social networks or the uploader should be presented in more detail in the video.

Ethics

Ethics Committee Approval: N/A.

Informed Consent: N/A.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: E.T.A., Design: E.T.A., Data Collection or Processing: E.T.A., Ö.D.A., E.A., Analysis or Interpretation: E.T.A., Ö.D.A., E.A., Literature Search: E.T.A., Ö.D.A., E.A., Writing: E.T.A.

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References

1. Ridolo E, Montagni M, Bonzano L, Savi E, Peveri S, Costantino MT, et al. How far from correct is the use of adrenaline auto-injectors? A survey in Italian patients. Intern Emerg Med. 2015;10:937-41.
2. Yaylacı S, Serinken M, Eken C, Karcioglu O, Yılmaz A, Elicabuk H, et al. Are You Tube videos accurate and reliable on basic life support and cardiopulmonary resuscitation? Emerg Med Australas. 2014;26:474-7.
3. Duncan I, Yarwood-Ross L, Haigh C. YouTube as a source of clinical skills education. Nurse Educ Today. 2013;33:1576-80.
4. Murugiah K, Vallakati A, Rajput K, Sood A, Challa NR. You Tube as a source of information on cardiopulmonary resuscitation. Resuscitation. 2011;82:332-4.
5. Akgun T, Karabay CY, Kocabay G. Kalayci A, Oduncu V, Guler A, et al. Learning electrokardiogram on YouTube: how useful is it? J Electrocardiol. 2014;47:113-7.
6. Beydilli H, Serinken M, Eken C, Elicabuk H, Dal O, Acar E, et al. The Validity of YouTube Videos on Pediatric BLS and CPR. Telemed J E Health. 2016;22:165-9.
7. Nguyen Luu NU, Cicutto L, Soller L, Joseph L, Waserman S, St-Pierre Y, et al. Management of anaphylaxis in schools: Evaluation of an epinephrine auto-injector (EpiPen®) use by school personnel and comparison of two approaches of soliciting participation. Allergy Asthma Clin Immunol. 2012;8:4.
8. Mehr S, Robinson M, Tang M. Doctor - How do I use my EpiPen? Pediatr Allergy Immunol. 2007;18:448-52.
9. Güneş T, Serinken M, Alur İ, Beydilli H, Karcioglu O, Eken C. YouTube as a source of information on varicose veins. Phlebology. 2016;31:501-5.

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Investigation of the Clinical Course and Outcomes of Bonsai Use

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Abstract

Aim: We aimed to contribute to the contemporary literature by investigating the clinical course and outcomes of bonsai, a synthetic cannabinoid with progressively increasing use.

Materials and Methods: Our study retrospectively reviewed the medical records of 149 patients with symptoms related to bonsai use. The parameters included age, gender, blood pressure, heart rate, respiratory rate, body temperature, Glasgow coma scale, route and duration of bonsai use, time used, symptoms, follow-up period in the emergency department, regular ward and intensive care unit, need for mechanical ventilation, biochemistry panel, abstinence, intoxication, mortality, and morbidity.

Results: The most common symptoms were agitation (49.7%) and anxiety (28.9%). Intoxication was correlated with creatinine and creatine kinase-myocardial band ($p<0.05$). Patients who were intoxicated had more agitation, impaired consciousness, and speech disturbances ($p<0.05$). The mean emergency department follow-up period was 8 hours. The follow-up period was 4 days in the intensive care unit and 2 days in the regular ward. The overall mortality rate was 2%.

Conclusion: Bonsai use is characterized by ischemic symptoms and can therefore be fatal.

Keywords: Bonsai, synthetic cannabinoids, emergency department

Introduction

Narcotic substance use and addiction is a major public health problem worldwide. Novel or atypical narcotic substances have been developed in the last decade. Among these, cheaper and easily accessible ones have become increasingly popular (1).

Tetrahydrocannabinol is a synthetic cannabinoid and its derivatives were first manufactured in Europe in 2004 under the name Bonsai (2). Having the central effects of marijuana, these substances have been introduced as "harmless", "legal marijuana", and as "a designed drug" (2). Being readily accessible and cheap, as well as lacking the narcotic substance status, these substances have gained a rapidly increasing popularity, particularly among adolescents and young adults (3,4).

Today, synthetic cannabinoids have 11 groups, containing 130 subgroups (5). Although synthetic cannabinoids exert sympathetic effects such as palpitation, sweating, agitation and restlessness, the diversity of synthetic cannabinoid combinations and manufacturing techniques complicate clinical predictions about their effects (6,7). Recently, it has been reported that they cause severe conditions such as myocardial infarction, pulmonary embolism, ischemic stroke, seizure, acute renal failure and death (8-10). Cases of intoxication have also been reported recently due their widespread use (11).

In this study, we aimed to contribute to the contemporary literature by investigating the clinical course and outcomes of Bonsai use, a synthetic cannabinoid with increasing popularity.

*This study was presented as an oral presentation on November 10-13, 2016 at the 15th 5th Eurasian Congress on Emergency Medicine Congress (EACEM 2016).

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Materials and Methods

Our study was retrospectively performed on patients who presented to the emergency department of our hospital with complaints related to isolated Bonsai use between January 1, 2013 and December 31, 2015 in Ankara, Turkey.

Study Population and Data Collection

The medical records of patiens were accessed via hospital automation system and patient follow-up cards. Patient data were recorded in specific forms prepared for each patient and were then transferred to a computer.

A total of 170 patients, who presented to our hospital's emergency department with disturbing symptoms after Bonzai intake, were enrolled. JWH-18 and JWH-73 metabolites in urine samples were searched using the Rapid K2 Test Card [An immunochromatographic assay for the rapid visual detection of synthetic cannabis (K2) in human urine]. Twenty-one patients with no noticeable metabolite were excluded. Among patients with noticeable urinary metabolites, other narcotic drugs were screened in urine using a toxicology panel. Ethanol level was measured from blood samples obtained from all patients. We excluded patients with following conditions: under the age of 18, history of using any additional substance, lacking complete medical data, receiving medical treatment for any other disorder and limited access to medical records. The recorded data included age, gender, vital parameters [systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate, respiratory rate, and saturation], Glasgow coma scale (GCS), route and duration of Bonsai use, time used, symptoms, follow-up period (emergency department, regular ward, and intensive care unit), need for mechanical ventilation, biochemical parameters (glucose, urea, creatinine, potassium, aspartate transaminase (AST), alanine aminotransferase (ALT), creatine kinase (CK), and creatine kinase-myocardial band (CK-MB), abstinence, intoxication (Table 1), and mortality.

Table 1. Diagnostic criteria for cannabis-induced intoxication

A.	Recent cannabis use
B.	Clinically significant behavioral or psychological alterations that occur during or shortly after cannabis use
C.	The occurrence of two or more of the criteria below within 2 hours of cannabis use (conjunctival redness, increased appetite, dry mouth, tachycardia)
D.	Admission signs and symptoms either incompatible with any other medical condition or unexplained by the intake of any other substance or any other mental disorder

Statistical Analysis

The study data were analyzed using the Statistical Package for Social Sciences 18.0 for Windows package program (SPSS Inc., Chicago, IL, USA). Kolmogorov-Smirnov test was used to test the normality of the distribution of continuous and discrete numerical variables. Descriptive statistics included median, interquartile range (IQR), and minimum-maximum values for nonparametric continuous and discrete numerical variables, and number and percentage (%) for categorical variables. The nonparametric variables were analyzed using Mann-Whitney U test and the categorical variables using chi-square and Fisher's exact chi-square test. Unless stated otherwise, a p-value less than 0.05 was considered statistically significant for all comparisons.

Results

This study included a total of 149 patients (121 male and 28 female) with a median age of 25 years [IQR: 6.5]. According to the follow-up data and treatment results, 123 (82.5%) patients had symptoms related to Bonsai use and 26 (17.5%) to Bonsai Abstinence syndrome. The development of Bonsai intoxication was not correlated with age and gender (Table 2). The most common route of Bonsai use was smoking, and the majority of patients had a history of repetitive Bonsai use. No significant correlation was found between the route and duration of Bonsai use and intoxication ($p<0.05$) (Table 2).

Intoxication was not correlated with SBP, DBP, pulse rate, respiratory rate, body temperature, saturation, and GCS ($p>0.05$) (Table 2). It was also not correlated with glucose, AST, ALT, BUN, potassium, and CK levels ($p>0.05$), whereas creatinine and CK-MB levels were significantly increased in patients who were intoxicated ($p<0.05$) (Table 3).

Patients admitted to the intensive care unit had higher heart rate, respiratory rate, glucose, AST, ALT, urea, creatinine, and CK-MB levels, but a lower GCS ($p<0.05$). The patients who died had higher heart rate, respiratory rate, and glucose levels, but GCS was lower ($p<0.05$) (Table 3).

Ninety-two percent of patients were discharged from the emergency department, 7.4% were admitted to the intensive care unit and 0.6% were admitted to a regular ward (Table 3). Six (4.0%) patients needed mechanical ventilation. The follow-up period was eight hours [IQR: 4] in ED, four days [IQR: 3] in intensive care unit and two days in regular ward. The intoxicated patients had significantly longer ED follow-up periods ($p<0.05$) (Table 3). The overall mortality rate was 2% (Table 3). All patients who were admitted, who needed mechanical ventilation and who died were intoxicated (Table 4).

Table 2. The correlation of demographic data with Bonsai intoxication

		Total (n=149)	Intoxication			Intensive care			Death		
		Yes (n=123)	No (n=26)	p	Yes (n=11)	No (n=138)	p	Yes (n=3)	No (n=146)	p	
Age, median [IQR]		25 [6.5]	25 [7]	23.5 [5.75]	0.082[T]	25 [9]	25 [6.25]	0.686[T]	21 [-]	25 [6.25]	0.645[T]
Gender	Male, n (%)	121 (81.2)	98 (79.7)	23 (88.5)	0.411*	10 (90.9)	111 (80.4)	0.690*	3 (100)	118 (80.8)	>0.999*
	Female, n (%)	28 (18.8)	25 (20.3)	3 (11.5)		1 (9.1)	27 (19.6)		0	28 (19.2)	
Route of use	Cigarette, n (%)	141 (94.6)	116 (94.3)	25 (96.2)	>0.999**x	11 (100)	130 (94.2)	>0.999**	3 (100)	138 (94.5)	>0.999**
	Hookah, n (%)	6 (4.0)	6 (4.9)	0		0	6 (4.4)		0	6 (4.1)	
	Oral, n (%)	2 (1.3)	1 (0.8)	1 (3.8)		0	2 (1.4)		0	2 (1.4)	
Frequency of use	First time, n (%)	14 (9.4)	10 (8.1)	4 (15.4)	0.269**	0	14 (10.1)	0.600**	0	14 (9.6)	>0.999**
	Repetitive n (%)	135 (90.6)	113 (91.9)	22 (84.6)		11 (100)	124 (89.9)		3 (100)	132 (90.4)	
Duration of use, median [IQR]		6 [4]	6 [4]	3 [4]	0.063[T]	8 [4]	4 [2]	<0.001[T]	8 [6]	4.5 [3]	0.059[T]
Symptoms and signs	Agitation	74 (49.7)	69 (56.1)	5 (19.2)	0.001*	1 (9.1)	73 (52.9)	0.009*	0	74 (50.7)	0.245*
	Anxiety	43 (28.9)	38 (30.9)	5 (19.2)	0.233*	1 (9.1)	42 (30.4)	0.178*	0	43 (29.5)	0.557*
	Impaired consciousness	27 (18.1)	27 (22.0)	0	0.004**	7 (63.6)	20 (14.5)	0.001**	3 (100)	24 (16.4)	0.05**
	Speech disturbance	27 (18.1)	27 (22.0)	0	0.004**	2 (18.2)	25 (18.1)	>0.999**	0	27 (18.5)	>0.999**
	Dyspnea	27 (18.1)	25 (20.3)	2 (7.7)	0.166**	2 (18.2)	25 (18.1)	>0.999**	1 (33.3)	26 (17.8)	0.454**
	Hallucination	26 (17.4)	24 (19.5)	2 (7.7)	0.253**	0	26.8 (18.8)	0.213**	0	26 (17.8)	>0.999**
	Nausea vomiting	20 (13.4)	17 (13.8)	3 (11.5)	>0.999**	2 (18.2)	18 (13)	0.643**	0	20 (13.7)	>0.999**
	Paranoia	13 (8.7)	12 (9.8)	1 (3.8)	0.467**	0	13 (9.4)	0.599**	0	13 (8.9)	>0.999**
	Craving	13 (8.7)	1 (0.8)	12 (46.2)	<0.001**	0	13 (9.4)	>0.999**	0	13 (8.9)	>0.999**
	Palpitations	13 (8.7)	13 (10.6)	0	0.126**	1 (9.1)	12 (8.7)	>0.999**	0	13 (8.9)	>0.999**
	Restlessness	9 (6)	0	9 (34.6)	<0.001**	0	9 (6.5)	>0.999**	0	9 (6.2)	>0.999**
	Syncope	7 (4.7)	7 (5.7)	0	0.606**	2 (18.2)	5 (3.6)	0.085**	1 (33.3)	6 (4.1)	0.135**
	Sweating	5 (3.4)	0	5 (19.2)	<0.001**	0	5 (3.6)	>0.999**	0	5 (3.4)	>0.999**
	Dizziness	4 (2.7)	2 (1.6)	2 (7.7)	0.141**	0	4 (2.9)	>0.999**	0	4 (2.7)	>0.999**
	Headache	4 (2.7)	0	4 (15.4)	0.001**	0	4 (2.9)	>0.999**	0	4 (2.7)	>0.999**
	Diffuse pain	4 (2.7)	4 (3.3)	0	0.999**	3 (27.3)	1 (0.7)	0.001**	0	4 (2.9)	>0.999**
	Nervousness	2 (1.3)	2 (1.6)	0	0.999**	0	2 (1.4)	>0.999**	0	2 (1.4)	>0.999**
	Dry mouth	2 (1.3)	1 (0.8)	1 (3.8)	0.320**	0	2(1.4)	>0.999**	0	2 (1.4)	>0.999**
	Abdominal pain	1 (0.7)	1 (0.8)	0	0.999**	0	1 (0.7)	>0.999**	0	1 (0.7)	>0.999**
	Fatigue	1 (0.7)	1 (0.8)	0	0.999**	0	1 (0.7)	>0.999**	0	1 (0.7)	>0.999**

[T]Mann-Whitney U test, *Chi-square test, **Fisher's Exact test, IQR: Interquartile range

Table 3. The correlation of vital and biochemical parameters with Bonsai intoxication

		Intoxication			Intensive care			Death		
	Total n (%)	Yes (n=123) median [IQR]	No (n=26) median [IQR]	p*	Yes (n=11) median [IQR]	No (n=138) median [IQR]	p	Yes (n=3) median [IQR]	No (n=146) median [IQR]	p
SBP (mmHg)	110 (20)	110 [30]	110 [12.5]	0.484	140 [52.5]	110 [20]	0.105	90 [-]	110 [20]	0.259
DBP (mmHg)	70 (10)	80 [10]	70 [2.5]	0.091	80 [30]	70 [10]	0.122	60 [-]	70 [10]	0.336
Pulse rate (beats/min)	81 (21)	81 [23]	81.5 [13.5]	0.863	116.5 [29]	81 [16.5]	0.003	126 [-]	81 [19]	0.015
Respiratory rate (respirations/min)	18 (4)	19 [4]	18 [5]	0.289	23 [9.3]	18 [3.8]	0.002	30 [-]	18 [4]	0.015
Body temperature (°C)	36.7 (0.9)	36.7 [0.9]	36.5 [1.0]	0.865	36.7 [0.6]	36.7 [0.9]	0.496	36.7 [-]	36.7 [1]	0.707
Saturation	94 (6)	93 [6]	96 [6.3]	0.358	91 [10.75]	94 [6]	0.168	80 [-]	94 [6]	0.240
GCS	15 (0)	15 [0]	15	0.080	8 [9.5]	15 [0]	<0.001	4 [-]	15 [0]	<0.001
Glucose (mg/dL)	116 (56)	118 [69]	103.5 [34]	0.087	176.5 [151.8]	113 [51.3]	0.041	203	113 [52]	0.031
AST (U/L)	24 (16.8)	25 [26]	22.5 [7]	0.107	282 [653]	24 [13.3]	<0.001	55 [-]	24 [16]	0.433
ALT (U/L)	21 (24.5)	21 [29.5]	19 [15.5]	0.135	193 [540]	19.5 [16.3]	<0.001	49 [-]	21 [23]	0.081
BUN (mg/dL)	27 (13.5)	27 [14.7]	27.5 [7.3]	0.970	34.5 [31.3]	27 [13]	0.015	33 [-]	27 [14]	0.525
Creatinine (mg/dL)	0.96 (0.34)	0.97 [0.31]	0.78 [0.43]	0.017	1.5 [1.5]	1 [0.3]	0.006	1.3 [-]	1 [0.3]	0.181
Potassium (mEq/L)	4 (0.6)	4 [0.6]	4 [0.6]	0.454	4 [0.8]	4 [0.6]	0.432	4.3 [-]	4 [0.6]	0.705
CK (U/L)	161.5 (381)	167 [420.7]	132 [26.5]	0.098	729 [2149]	159 [335.8]	0.280	222 [-]	160 [8.8]	0.563
CK-MB (ng/mL)	18 (24.8)	20 [27.5]	15 [12.8]	0.011	181.5 [223.8]	18 [20]	<0.001	63 [-]	18 [23.5]	0.081

*Mann-Whitney U test, IQR: Interquartile range, ALT: Alanine aminotransferase, AST: Aspartate transaminase, GCS: Glasgow coma scale, CK: Creatine kinase, CK-MB: Creatine kinase-myocardial band

Table 4. The correlations of admission status, need for mechanical ventilation, and follow-up durations with intoxication

	Total (n=149)	Intoxication		
		Yes (n=123)	No (n=26)	p
Discharged from ED	137 (92)	111 (90.2)	26 (100)	0.127
Intensive care unit admission	11 (7.4)	11 (9.0)	0	
Regular ward admission	1 (0.6)	1 (0.8)	0	
Need for mechanical ventilation, n (%)	6 (4.0)	6 (4.0)	0	0.591
Follow-up period in the ED (hours)	8 (4)	6 (4)	2.5 (1.3)	<0.001
Follow-up period in the intensive care unit	4 (3)	4 (3)	-	N/A
Follow-up period in the regular ward (days)	2	2	-	N/A
Mortality n (%)	3 (2.0)	3 (2.4)	0	0.421

ED: Emergency department

Discussion

Although synthetic cannabinoids were originally produced as therapeutic agents, they were sold as marijuana alternatives stuffed in dried plants after being synthesized in laboratories in the early 2000s (12). Although their use is increasingly common, their toxic effects and medical consequences are not fully known (11,13,14).

It is known that all forms of narcotic substance use are common among young males (7,15-17). The median age of our patients was 25 years and 81.2% of them were male. No correlation was found between intoxication and gender or age. We believe that Bonsai use is common among young males, because they frequently spend their time in places where Bonsai use is common, and they perceive drug use as a means to draw attention or a sign of courage. Compared to other substances, being cheap and more easily accessible may also have made Bonsai more popular among young people. We believe that bonsai users are predominantly young, because more potent substances (heroin, cocaine, etc.) are used later in life. A greater mortality rate is associated with their use and users undergo rehabilitation. We opine that intoxication with these substances

is more linked to their properties, amount, and duration of exposure than the age or gender of the patient.

Published reports suggest that although synthetic cannabinoids are generally used in cigarette form, they can be inhaled in vaporized form or taken orally or rectally (2,3,18). In our study, cigarette form was the most common form (94.6%), but the route of use was not significantly correlated to intoxication. Although Bonsai is best suited for inhaled use in cigarette form, we think that some patients may try other forms to cause a change or to get more pleasure. Since both the number of people who tried other forms and the amount of substance used by these routes were small, it did not make a significant difference with regard to intoxication.

Doğan et al. (3) reported that 74.2% of patients, who had a higher rate of liver and renal dysfunction, had a history of substance use, although the difference did not reach statistical significance (2). On the other hand, 90.6% of our patients had been using Bonsai for six months. Intoxication was independent of the duration of repetitive substance use. We believe that the repetitive Bonsai use has gradually increased due to addiction potential and abstinence symptoms. However, the duration of Bonsai use is shorter in Turkey due to its recent introduction to this country, and signs of intoxication more commonly appear in case of hepatic and renal dysfunction caused by worsening hypoxia in the long term.

Synthetic cannabinoids are partial or complete agonists of CB1 receptors. They cause adverse effects such as sweating, nausea, vomiting, appetite disorders, hyper/hypotension, chest pain, tachycardia/bradycardia, respiratory depression, confusion, psychomotor agitation, somnolence, and sedation in addition to their usual effects including euphoria, anxiety, agitation, irritability, psychosis, and altered cognitive skills (2,7,19,20). Barratt et al. (16) reported that 68% of patients experienced at least one side effect, the most common of which was impaired motor coordination (39%). Doğan et al. (3) stated that dizziness and agitation were the most common symptoms. Zimmermann et al. (21) stressed that patients regularly using Bonsai may suffer from signs and symptoms of abstinence syndrome, which include shivering, headache, nightmares, craving, hypertension, and tachycardia. Forrester reported that 48.5% of the patients presented with palpitations and chest pain, and 24.3% with dizziness and vertigo (22). We demonstrated that the most common symptoms among intoxicated patients were agitation, speech disturbance, and altered consciousness. Many symptoms have been linked to Bonsai use in the literature. This may be a result of different CB-1 receptor affinities, potencies, doses, and duration of the effect of different synthetic cannabinoid subgroups. Considering that the patient group with signs of abstinence syndrome also had a high anxiety rate, we think that the symptoms of Bonsai use are largely similar.

At low to moderate doses, cannabinoids induce tachycardia and increase cardiac output by a sympathomimetic effect whereas, at higher doses, they cause bradycardia and hypotension by their parasympathomimetic effect (23,24). Studies conducted so far have shown that affected patients most commonly experienced tachycardia and hypertension, while bradycardia and hypotension were less common (25-28). We could not find any abnormal vital parameters except for tachypnea, and vital parameters were not correlated to intoxication status. We believe that our patients generally used low to moderate doses of Bonsai, and its effects started to wane over time. We think that tachypnea occurred as a result of anxiety in both groups. Anxiety caused similar vital parameters in patients with abstinence symptoms and intoxicated patients.

Former studies have shown glucose, urea, creatinine and CK elevation and hypopotassemia with Bonsai use (29-31). Doğan et al. (3) reported higher CK, CK-MB, AST, ALT and creatinine levels in Bonsai users. In a series of 6 patients, Ergül et al. (32) demonstrated that BUN, creatinine, CK, LDH, AST and ALT levels were elevated. The authors attributed this result to the possibility of a variety of substances being admixed with synthetic cannabinoids, such as agricultural chemicals, fluorescent dust, Veronika and industrial chemicals (32). Altınışık et al. (27) reported that four of 12 patients admitted to intensive care unit after using Bonsai had impaired hepatic and renal function, with renal function recovered in 48 hours but hepatic markers remained elevated for a longer period. It was reported that synthetic cannabinoid use was associated with acute tubular necrosis, resulting in acute renal failure (30,31,33). Sheikh et al. (34) reported hepatocellular necrosis and hepatic failure in a patient using Bonsai.

Our study demonstrated that creatinine and CK-MB were higher in intoxications, that patients admitted to the intensive care unit had a higher heart rate, respiratory rate, glucose, AST, ALT, urea, creatinine, and CK-MB levels, but a lower GCS and that the deceased patients had higher heart rate, respiratory rate, and glucose level, but a lower GCS. We believe that organ injuries develope due to ischemia affecting all tissues, so blood levels increase and GCS falls. The release of stress hormones in response to increased stress levels may explain elevated glucose levels.

The majority of synthetic cannabinoids have an effect period of 2-6 hours, although some may have persistent effects beyond 24 hours (13,17,29,35). Some studies reported that consciousness was regained within 8-12 hours after the Bonsai use unless there were additional complications (29,35). It has been reported that a variety of fatty acids, herbal compounds, preservatives like

benzyl benzoate, and addictive substances like alpha-tocopherol, which are used for synthetic cannabinoid manufacturing or are naturally found in the plant's chemical structure, may extend the duration of action of B2 adrenergic agonists up to 24 hours (36).

In our study, the duration of ED follow-up was eight hours, with the duration for intoxicated patients being significantly longer. Our results are in accordance with the previous literature, and we believe that patients whose symptoms improved were either discharged or admitted for a period of approximately eight hours. We believe that relief of the abstinence symptoms by therapy resulted in a rapid discharge of patients who were free of intoxication.

While synthetic cannabinoids have not been consistently reported to cause respiratory difficulty and/or respiratory arrest (37), pulmonary fluid accumulation and respiratory depression due to long-term synthetic cannabinoid use have been reported (36,38). Altınışık et al. (27) reported that one of 12 patients with loss of consciousness due to Bonsai use needed intubation. Küçük et al. (7) reported that 3% required intubation. Four percent of our patients were intubated. Although all intubated patients were intoxicated, this tendency was not statistically significant. We believe that patients developed respiratory arrest due to increased fluid accumulation in lungs and/or due to other narcotic substances used in combination with Bonsai.

Monte et al. (39) reported that 9% of patients were hospitalized. A domestic study by Küçük et al. (7) showed that 46% of patients were hospitalized, of whom half were monitored in the the intensive care unit Lank et al. (40) reported that the level of knowledge among ED physicians about synthetic cannabinoids was low, which resulted in a high admission rate. Our study demonstrated that 7.4% of patients were admitted to the intensive care unit and 0.6% to a regular ward and that all admitted patients were intoxicated at admission. We believe that patients who were not intoxicated and the majority of intoxicated patients had a relatively stable overall status and were therefore treated in the ED from where they were discharged. The reason for the high rate of intensive care admission may be the impending risk of respiratory arrest during admission.

Among patients who were admitted to the intensive care unit for intoxication, the intensive care follow-up period was reported to be three days (41,42). Altınışık et al. (27) reported that most of the patients admitted to the intensive care unit after synthetic cannabinoid use regained consciousness by 24 hours and the remainders by 48 hours. They reported a follow-up period of three days and recommended a follow-up period of at least three days (27). In our study, the intensive care follow-up period was four days, and the regular ward follow-up period was two days. As synthetic cannabinoid types are variable and their duration of effect is largely unknown, we believe that intensive care unit follow-up should be sufficiently long.

No death occurred among nine patients of Buser et al. (30) and 12 patients of Altınışık et al. (27). According to Turkey Drug Report published in 2013, seven drug-related deaths occurred due to synthetic cannabinoids and three deaths occurred due to the combined use of marijuana and synthetic cannabinoids in the second half of 2012 (43). The overall mortality rate in our study was 2%. Although all deceased patients were also intoxicated, this trend did not reach statistical significance. Deaths may have developed as a result of irreversible injury caused by worsening hypoxia. The major factor giving rise to our higher mortality rate may be the referral of patients with poor overall status to our center from neighboring district hospitals.

Study Limitations

Since the present study had a retrospective design, we could not obtain any information about patient anamnesis, history, family history, and details of additional substance use (Was the patient addicted to any other substance? Which substance, other than Bonzai, was recently taken and when?). Similarly, complete blood count, blood gas analysis, and other biochemical parameters could not be analyzed.

Conclusion

Particularly affecting young people, Bonsai use is characterized by ischemic symptoms and can therefore be fatal. Strict measures should be taken in emergency departments and more robust security policies should be implemented to reduce mortality and morbidity associated with Bonsai use. It is also necessary to prohibit the production and use of Bonsai.

Ethics

Ethics Committee Approval: University of Health Sciences Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Turkey, approval number: 32/06 22.11.2016.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.K., Concept: N.K., U.Y.Ç., Design: N.K., U.Y.Ç., Data Collection or Processing: N.K., H.S., B.D., Analysis or Interpretation: N.K., R.P.K., Literature Search: N.K., U.Y.Ç., R.P.K., H.S., B.D., Writing: N.K.

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References

1. Orsini J, Blaak C, Tam E, Rajayer S, Morante J, Yeh A, et al. The wide and unpredictable scope of synthetic cannabinoids toxicity. Case Rep Crit Care. 2015;2015:542490.
2. Artuç S, Doğan KH, Demirci Ş. Uyuşturucu maddelerde yeni trend: sentetik kannabinoidler. Adli Tıp Bülteni. 2014;19:198-203.
3. Doğan H, Özüçelik DN, Açıksarı K, Avcı A, Yazıcığlu M, Çelikmen MF, et al. New synthetic cannabinoid intoxications in emergency department (It's grass, it's no sin). Anadolu Psikiyatri Derg. 2016;17:18-25.
4. Aoun EG, Christopher PP, Ingraham JW. Emerging drugs of use: clinical and legal considerations. RI Med J (2013). 2014;97:41-5.
5. Office of National Drug Control Policy. (2014). Fact sheet: Synthetic drugs (a.k.a. K2, Spice, bath salts, etc.). http://www.whitehouse.gov/ondcp/ondcp-fact-sheets/synthetic-drugs-k2-spice-bath-salts Son erişim tarihi:01.01.2017.
6. Hudson S, Ramsey J, King L, Timbers S, Maynard S, Dargan PI, et al. Use of high-resolution accurate mass spectrometry to detect reported and previously unreported cannabinomimetics in "herbal high" products. J Anal Toxicol. 2010;34:252-60.
7. Küçük E, Küçük İ, Kirazaldı YY. Acil serviste yeni bir tehlike: Sentetik kannabinoidler (Bonsai, Jameika). Genel Tıp Derg. 2015;25:18-22.
8. Freeman MJ, Rose DZ, Myers MA, Gooch CL, Bozeman AC, Burgin WS. Ischemic stroke after use of the synthetic marijuana "spice". Neurology. 2013;81:2090-3.
9. Thornton SL, Wood C, Friesen MW, Gerona RR. Synthetic cannabinoid use associated with acute kidney injury. Clin Toxicol (Phila). 2013;51:189-90.
10. McKeever RG, Vearrier D, Jacobs D, LaSala G, Okaneku J, Greenberg MI. K2--not the spice of life; synthetic cannabinoids and ST elevation myocardial infarction: a case report. J Med Toxicol. 2015;11:129-31.
11. Eminler AT, Yıldırım M, Uslan Mİ, Köksal AŞ, Parlak E. Sentetik kannabinoidler (BONZAİ) ve gastrointestinal sistem üzerine etkileri: "Kannabinoid Hiperemezis Sendromu". Güncel Gastroentereloji. 2014;18:460-3.
12. Atik SU, Dedeoğlu R, Varol F, Çam H, Eroğlu AG, Saltık L. Cardiovascular side effects related with use of synthetic cannabinoids "bonzai": two case reports. Turk Pediatri Ars. 2015;50:61-4.
13. EMCDDA 2013 Ulusal Raporu (2012 Verileri) Reitox Ulusal Temas Noktası. Türkiye Uyuşturucu Ve Uyuşturucu Bağımlılığı İzleme Merkezi (TUBİM) Ankara 2013.
14. Bozkurt M, Umut G, Evren C, Karabulut V. Sentetik kannabinoid kullanımı nedeniyle polikliniğe başvuran hastaların klinik özellikleri ve laboratuvar sonuçları. Düşünen Adam Psikiyatri ve Nörolojik Bilimler Dergisi. 2014;27:328-34.
15. Hu X, Primack BA, Barnett TE, Cook RL. College students and use of K2: an emerging drug of use in young persons. SubstAbuse Treat Prev Policy. 2011;6:16.
16. Barratt MJ, Cakic V, Lenton S. Patterns of synthetic cannabinoid use in Australia. Drug Alcohol Rev. 2013;32:141-6.
17. Hoyte CO, Jacob J, Monte AA, Al-Jumaan M, Bronstein AC, Heard KJ. A characterization of synthetic cannabinoid exposures reported to the National Poison Data System in 2010. Ann Emerg Med. 2012;60:435-8.
18. Vandrey R, Dunn KE, Fry JA, Girling ER. A survey study to characterize use of Spice products (synthetic cannabinoids). Drug Alcohol Depend. 2012;120:238-41.
19. Schneir AB, Cullen J, Ly BT. "Spice" girls: synthetic cannabinoid intoxication. J Emerg Med. 2011;40:296-9.
20. Castellanos D, Singh S, Thornton G, Avila M, Moreno A. Synthetic cannabinoid use: a case series of adolescents. J Adolesc Health. 2011;49:347-9.
21. Zimmermann US, Winkelmann PR, Pilhatsch M, Nees JA, Spanagel R, Schulz K. Withdrawal phenomena and dependence syndrome after the consumption of "spice gold". Dtsch Arztebl Int. 2009;106:464-7.
22. Forrester MB. Adolescent synthetic cannabinoid exposures reported to Texas poison centers. Pediatr Emerg Care. 2012;28:985-9.
23. Sarımehmetoğlu AC, Helvacı A. Madde Bağımlılığı ve Kardiyovasküler Sistem. Eur Arch Med Res. 2014;30:99-103.
24. Bashour TT. Acute myocardial infarction resulting from amphetamine abuse: a spasm-thrombus interplay? Am J Heart J. 1994;128:1237-9.
25. Ekim M, Ekim H. Sentetik Kannabinoidlerin (Bonzai) Kullanılmasına Bağlı Psişik ve Kardiyovasküler Rahatsızlıklar. Tıp Araştırmaları Dergisi. 2016;14:79-83.
26. Bachs L, Mørland H. Acute cardiovascular fatalities following cannabis use. Forensic Sci Int. 2001;124:200-3.
27. Altınışık U, Altınışık HB, Şimşek T, Doğu T, Şimşek E, Aydın H. Clinical Characteristics of Patients Diagnosed with Synthetic Cannabinoid (Bonsai) Intoxication in ICU. J Turk Soc Intens Care. 2015;13:117-21.
28. Parlakpinar H, Celbis O, Onural Ö, Petekkaya S, Şamdancı E, Ermiş N, et al. Cardiovascular effects of JWH-018 from synthetic cannabinoids. Medicine Science. 2016;5:1049-54.
29. Hermanns-Clausen M, Kneisel S, Szabo B, Auwärter V. Acute toxicity due to the confirmed consumption of synthetic cannabinoids: clinical and laboratory findings . Addiction. 2013;108:534-44.
30. Buser GL, Gerona RR, Horowitz BZ, Vian KP, Troxell ML, Hendrickson RG, et al. Acute kidney injury associated with smoking synthetic cannabinoid. Clin Toxicol (Phila). 2014;52:664-73.
31. Taskiran B, Mutluay R. A Case of Hypokalemia with Synthetic Cannabinoid Use. Medicine Science. 2014;3:1713-8.
32. Ergül DF, Ekemen S, Yelken BB. Synthetic Cannabinoid 'Bonsai'Intoxication: Six Case Series. Turk J Anaesthesiol Reanim. 2015;43:347.
33. Gudsoorkar VS, Perez JA Jr. A new differential diagnosis: synthetic cannabinoids-associated acute renal failure. Methodist Debakey Cardiovasc J. 2015;11:189-91.
34. Sheikh IA, Lukšic M, Ferstenberg R, Culpepper-Morgan JA. Spice/K2 synthetic marijuana-induced toxic hepatitis treated with N-acetylcysteine. Am J Case Rep. 2014;15:584-8.
35. Simmons JR, Skinner CG, Williams J, Kang CS, Schwartz MD, Wills BK. Intoxication from smoking "spice". Ann Emerg Med. 2011;57:187-8.
36. Evren C, Bozkurt M. Synthetic cannabinoids: Crisis of the decade. Düşünen Adam: The Journal of Psychiatry and Neurological Sciences. 2013;26:1-11.
37. Kalyoncu ÖA, Ünlü B, Taştan U. A Dangerous Game That May Harm Kids and Teens: A Review on Synthetic Cannabinoids (Bonzai). Dergisi-Journal of Dependence. 2014;15:150-5.
38. Hopkins CY, Gilchrist BL. A case of cannabinoid hyperemesis syndrome caused by synthetic cannabinoids. J Emerg Med. 2013;45:544-6.
39. Monte AA, Bronstein AC, Cao DJ, Heard KJ, Hoppe JA, Hoyte CO, et al. An outbreak of exposure to a novel synthetic cannabinoid. N Engl J Med. 2014;370:389-90.
40. Lank PM, Pines E, Mycyk MB. Emergency physicians' knowledge of cannabinoid designer drugs. West J Emerg Med. 2013;14:467-70.
41. Özayar E, Değerli S, Güleç H, Sahin S, Dereli N. Retrospective analysis of intoxication cases in the ICU. J Turk Soc Intens Care. 2011;3:59-62.
42. Yağan Ö, Akan B, Erdem D, Albayrak D, Bilal B, Göğüş N. The retrospective analysis of the acute poisoning cases applying to the emergency unit in one year. The Medical Bulletin of Sisli Etfal Hospital. 2009;43:60-4.
43. 2013 Türkiye Uyuşturucu Raporu. http://www.kom.gov.tr/Tr/Dosyalar/2013_turkıye_uyusturucu_raporu.pdf. Son erişim Tarihi:07/01/2017.

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Are the Judicial Reports Prepared in Emergency Services Consistent with Those Prepared in Forensic Medicine Department of a University Hospital?

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Abstract

Aim: This study aimed to analyze the judicial reports prepared in emergency services and to emphasize the importance of forensic medicine education for the physicians working at these services and the reflection of the situation to the judicial authorities.

Materials and Methods: Reports prepared by Forensic Medicine Department of Gaziantep University Medical Faculty were accepted as the gold standard and the judicial reports of the same patients prepared in emergency services were compared retrospectively.

Results: Most reports were found to be prepared as temporary reports. The concepts of general condition, consciousness, life-threatening clinical status and simple medical interventions were frequently mentioned, while other concepts were not mentioned. The success rate of identifying cases with and without life-threatening clinical status in emergency services was 83.49% and 85.52%, respectively. The success rate of identifying cases that could and could not be treated with simple medical intervention was 84.20% and 58.62%, respectively.

Conclusion: It has been determined that the problems in both mentioning basic concepts and accurate report writing cannot be solved in the judicial reports organized in emergency departments. In order to protect themselves, physicians have a tendency to report the consequences more severe than they actually are. However, it should be kept in mind that this tendency may not protect the physician, but also may cause additional legal problems.

Keywords: Judicial report errors, emergency service, forensic medicine

Introduction

Judicial report writing is more than an act of writing to influence the court. It must follow ethical guidelines and practice principles as well as the recommended style and formatting. The most important principle is to remain impartial and not advocate for the referral source (1).

One of the responsibilities of the physicians working in emergency services is to report judicial cases to the authorities and prepare case reports (2,3). The reports prepared by these physicians play an important role in the accurate and rapid progression of judicial procedures (4). Today, the concept of medical error goes beyond examining the physician's ability to interpret information to analyze whether they can accurately utilize the

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available methods and techniques (5). Since the number of forensic specialists in Turkey is insufficient, most judicial cases are examined by physicians who have specialized in areas other than forensic medicine (6,7). In addition to the insufficient importance given to forensic medicine courses during medical education, long working hours, inappropriate conditions for physicians and high number of patients make inaccurate judicial reports unavoidable (2-4,8).

In our country, because of insufficient forensic medicine education in medical faculties and in-service training in public and private hospitals, the insight of emergency physicians in preparing judicial reports cannot be developed effectively, and the consequent errors might have irreversible effects (9,10). Considering problems such as limited information obtained from emergency service patients and limited possible examinations, physicians tend to prepare temporary reports (11-13). However, this does not protect physicians and, on the contrary, leads to prolonged judicial procedures and unnecessary document traffic (14).

In this study, we examined judicial reports referred to Forensic Medicine Department of Gaziantep University Medical Faculty for a final report and investigated the context and errors in these reports. Therefore, we aimed to emphasize the importance of judicial medicine education for emergency physicians and how this is reflected on the cases presented to the judicial authorities.

Materials and Methods

The study population consisted of 631 judicial reports that were prepared in emergency services and that were referred to the Forensic Medicine Department of Gaziantep University between January 1, 2012 - January 1, 2015. The judicial reports prepared by emergency physicians in our region were examined in terms of fundamental criteria, such as whether the present lesions were life-threatening, if they could be treated by simple medical intervention, if the criterion of permanent scar on the face was mentioned and the effects of a bone fracture on vital functions. These reports were also examined in terms of error rates. This study was designed as a descriptive and retrospective study, and the judicial reports that were prepared by our department and sent to judicial authorities were considered as gold standard.

The ethical committee approval of our study was obtained from the Ethical Committee of Clinic Researches of Gaziantep University (approval number: 2016/168).

Statistical Analysis

Numbers and percentages were given as descriptive statistics. Sensitivity, specificity and 95% confidence intervals (CIs) were calculated using Medcalc Version 15.11 to evaluate the correct classification capability of the reports prepared by emergency services. The cases where 50% of data did not fall within the CI of sensitivity and specificity were considered statistically significant.

Results

Eighty percent (n=505) of the cases were male and 20% (n=126) were female. The mean age was 28.41 years (±16.64); the youngest case was a 10-month-old female and the oldest case was an 82-year-old male. It was determined that the majority of the reports (92.1%) were prepared as temporary reports. While the general condition, consciousness, life-threatening clinical status and simple medical intervention concepts were frequently mentioned, cooperation was only mentioned in 62 cases, bone fracture in one case and permanent facial scar in three cases. In the temporary reports, emergency physicians stated that lesions involved life-threatening clinical status in 166 cases (26.3%), that the lesions could not be treated by simple medical intervention in 437 (69.3%) cases and that they requested an analysis for alcohol use in 72 (11.4%) cases (Table 1).

Based on the reports prepared by emergency services, the types of events were as follows: traffic accidents in 210 cases (33.3%), battery/physical violence in 188 cases (29.8%), penetrating stab wounds in 115 cases (18.2%), firearm injuries in 54 cases (8.6%), falling from a height in 14 cases (2.2%), industrial accidents in 10 cases (1.6%), suicide attempt in 5 cases (0.8%) and undefined injuries in 35 cases (5.5%).

Excluding the four cases where life-threatening criteria were not questioned (although there was a life-threatening clinical status), it was determined that, from the aspect of forensic medicine practice, the “life-threatening” statement was accurate in 91 and inaccurate in 14 final and temporary reports prepared in the emergency services. On the other hand, in 75 cases, the report indicated a life-threatening clinical status although there was no life-threatening clinical status. The absence of life-threatening clinical status was accurately diagnosed in 429 cases, and this criterion was not discussed in 14 cases with no life-threatening clinical status. The success rate of emergency services in identifying cases that involved life-threatening clinical status was 83.49% (95% CI=75.16-89.91) and in identifying the absence of life-threatening clinical status was 85.52% (95% CI=82.19-88.44) (Table 2).

The final and temporary reports prepared by emergency services were compared after excluding 23 cases in which the criterion of “simple medical intervention” was not questioned by the judicial authorities. Emergency physicians specified that the lesions could not be treated by simple medical intervention in

341 cases and that the lesions could be treated in 109 cases. This criterion was not discussed in 29 cases, in which the lesions could be treated by simple medical intervention in 19 cases and could not be treated in 10 cases. The reports were prepared incorrectly in 129 cases. The lesions that could be treated by simple medical intervention were reported to be not treatable by simple medical intervention in 84 cases, and those that could not be treated by simple medical intervention were reported to be treatable in 45 cases. The success rate of emergency services in accurately identifying the cases that could not be treated by simple medical intervention was 84.20% (95% CI=80.27-87.61) and in identifying those that could be treated by simple medical intervention was 58.62% (95% CI=51.51-65.47) (Table 2).

Considering the relationship between event types and life-threatening conditions, the reports accurately prepared by emergency services included 166 reports for traffic accidents, 171 reports for physical violence/battery, 96 reports for penetrating stab injuries and 41 reports for firearm injuries. On the other hand, the inaccurate reports included 42 reports for traffic accidents, 10 reports for physical violence/battery, 15 reports for penetrating stab injuries and 11 reports for firearm injuries. The number of reports where these parameters were not discussed was two for traffic accidents, five for physical violence/battery and one for firearm injuries (Table 3). Considering event types with a limited number of cases, reports for falling from a height indicated that there was life-threatening clinical status in four of 14 cases and no life-threatening clinical status in five cases, and three of the five cases without life-threatening clinical status were incorrectly reported and no opinion was reported in two cases. Of the 10 industrial accidents, a life-threatening clinical status was reported in two cases and no life-threatening clinical status was reported in eight reports. Of the five suicide attempt cases, there was a life-threatening clinical status in two cases. Two cases with no life-threatening clinical status was accurately diagnosed, whereas, one case with a life-threatening clinical status was inaccurately reported.

Table 1. Demographic data for case reports prepared by emergency services

Parameters		Number [n (%)]	Parameters		Number [n (%)]
Gender	Female	126/20	**Life-threatening clinical status**	Yes	166 (26.3)
	Male	505/80		No	447 (70.8)
Age*	Min-max (0-82)	28.41±16.64		Not specified	18 (2.9)
General condition†	Yes	472/74.8	**Simple medical treatment**	Untreatable	437 (69.2)
	No	148/23.5		Treatable	164 (26.0)
	N/A	11/1.7		Not specified	30 (4.8)
Consciousness†	Yes	468/74.2	**Alcohol**	Examined	72 (11.4)
	No	152/24.1		Unexamined	559 (88.6)
	N/A	11/1.7	**Report type**	Temporary	581 (92.1)
Cooperation†	Yes	62/9.8		Final	48 (7.6)
	No	556/88.1		Not specified	2 (0.3)
	N/A	13/2.1	-	-	-

*Continuous variables (mean ± standard deviation), †ordinal or binary variable (n/%), min: Minunmum, Max: Maximum

Table 2. Sensitivity and specificity values for vital risk and simple medical intervention

		Reports of forensic medicine department				Reports of forensic medicine department	
	LTCS	**Yes**	**No**		**SMT**	**Untreatable**	**Treatable**
Emergency service reports	Yes	91	75	**Emergency service reports**	Untreatable	341	84
	No	14	429		Treatable	45	109
	Not specified	4	14		Not specified	19	10
Sensitivity (95% CI)=83.49 (75.16-89.91)				Sensitivity (95% CI)=84.20 (80.27-87.61)			
Specificity (95% CI)=85.52 (82.19-88.44)				Specificity (95% CI)=58.62 (51.51-65.47)			

LTCS: Life-threatening clinical status, SMT: Simple medical treatment, CI: Confidence interval

Considering the relationship between event types and simple medical intervention, it was determined that the number of accurately prepared reports was 158 for traffic accidents, 118 for physical violence/battery, 80 for penetrating stab injuries and 46 for firearm injuries. On the other hand, the number of incorrect reports was 35 for traffic accidents, 53 for physical violence/battery, 30 for penetrating stab injuries and three for firearm injuries. The number of reports that did not discuss these parameters was eight for traffic accidents, nine for physical violence/battery, four for penetrating stab injuries and four for firearm injuries (Table 4). Considering the event types with a limited number of cases, of the 12 cases of falling from a height, it was accurately diagnosed that nine cases could and one case could not be treated by simple medical intervention, while two treatable cases were reported to be untreatable by simple medical intervention. It was reported that cases were accurately identified to be untreatable in 10 industrial accidents and that one case was not identified. In four of five suicide attempt cases, the lesions were reported to be treatable by simple medical intervention in parallel with the report of our department, while one report was written incorrectly by emergency physicians.

Interestingly, in the judicial reports prepared by the emergency services, only one case was reported to have a bone fracture, and the injury was not reported to cause any bone fracture or dislocation. A permanent facial scar was reported in three cases, but one lesion was not within the facial borders and the other was wrongly reported to be a permanent scar (in forensic medical practice, a six-month period is required after which the scar is re-assessed and then diagnosed as a permanent scar). The criteria regarding lesions causing a permanent weakening or loss of any of the senses or organs were not discussed in any of the reports.

Discussion

Today, the concept of expert opinion plays an important role in determining the relationship between the behavior and any consequent damage. Considering the increasing number of law suits filed against physicians, especially in recent years, the

Table 3. Comparison of availability of life-threatening clinical status between the reports prepared by our department and emergency services according to event type

Event type			Available [n (%)] / Not available [n (%)]	Reports of forensic medicine department		Total [n (%)]
Traffic accident	Emergency service reports	Life-threatening clinical status	Available	40 (78.4)	32 (20.1)	72 (34.3)
			N/A	10 (19.6)	126 (79.2)	136 (64.8)
			Not specified	1 (2.0)	1 (0.6)	2 (1.0)
		Total		51 (100)	159 (100)	210 (100)
Physical violence/battery	Emergency service reports	Life-threatening clinical status	Available	5 (71.4)	8 (4.5)	13 (7.0)
			N/A	2 (28.6)	166 (92.7)	168 (90.3)
			Not specified	0 (0.0)	5 (2.8)	5 (2.7)
		Total		7 (100)	179 (100)	186 (100)
Penetrating stab injuries	Emergency service reports	Life-threatening clinical status	Available	22 (95.7)	15 (16.5)	37 (32.5)
			N/A	0 (0.0)	74 (81.3)	74 (64.9)
			Not specified	1 (4.3)	2 (2.2)	3 (2.6)
		Total		23 (100)	91 (100)	114 (100)
Firearm injuries	Emergency service reports	Life-threatening clinical status	Available	11 (91.7)	11 (26.8)	22 (41.5)
			N/A	0 (0.0)	30 (73.2)	30 (56.6)
			Not specified	1 (8.3)	0 (0.0)	1 (1.9)
		Total		12 (100)	41 (100)	53 (100)

importance of expert opinion in addition to accurate and on-time patient intervention means that physicians need specific training for preparing accurate judicial reports (15). Even though both clinical and judicial reports require good writing skills and extensive experience (16-18), judicial reports have a different purpose, which is reflected in their impact, quality and style (19,20). When conducting a clinical evaluation, the patient is likely the person being tested. Conversely, in a forensic evaluation, the client is usually the court and referral questions are related to psycho-legal issues (21). Another key difference between judicial and clinical reports is the impact of the report. Judicial reports often have more lasting repercussions than clinical reports. The written report, either alone or with accompanying testimony, often significantly influences the outcome of a legal conflict (16,22). Given that a considerable number of applications to emergency services are judicial cases, the preparation of accurate and legally appropriate reports becomes more important (2,23).

In studies carried out on judicial cases referred by emergency services, the most frequent reason for the application is traffic accidents (3,4,6,9,23-27). In the present study, traffic accidents were the most common reason with 210 cases (33.3%). Despite social awareness-raising efforts and road maintenance works, traffic accidents are still an important problem in our country.

In a study conducted by Turla et al. (24), they reported that there was no information about the general status, consciousness and cooperation in approximately 60% of judicial reports. In our study, the criteria of general status and consciousness were mainly discussed, although cooperation was not mentioned. This result indicates that the importance given to patient consciousness by the physicians has increased but that the concept of cooperation is not given sufficient importance.

In the present study, only 9.2% of the reports were prepared as a final report, and this result is consistent with the tendency of emergency services to handwrite temporary reports (4,26,28,29).

Table 4. Comparison of simple medical treatment between the reports prepared by our department and emergency services according to event type

Event type				Reports of forensic medicine department		Total [n (%)]
				Untreatable [n (%)]	Treatable [n (%)]	
Traffic accident	Emergency service reports	Simple medical treatment	Untreatable	127 (87.0)	21 (38.2)	148 (73.6)
			Treatable	14 (9.6)	31 (56.4)	45 (22.4)
			Not specified	5 (3.4)	3 (5.5)	8 (4.0)
		Total		146 (100)	55 (100)	201 (100)
Physical violence/ battery	Emergency service reports	Simple medical treatment	Untreatable	54 (76.1)	40 (36.7)	94 (52.2)
			Treatable	13 (18.3)	64 (58.7)	77 (42.8)
			Not specified	4 (5.6)	5 (4.6)	9 (5.0)
		Total		71 (100)	109 (100)	180 (100)
Penetrating stab injuries	Emergency service reports	Simple medical treatment	Untreatable	72 (80.9)	17 (68.0)	89 (78.1)
			Treatable	13 (14.6)	8 (32.0)	21 (18.4)
			Not specified	4 (4.5)	0 (0.0)	4 (3.5)
		Total		89 (100.0)	25 (100.0)	114 (100.0)
Firearm injuries	Emergency service reports	Simple medical treatment	Untreatable	46 (90.2)	1 (50.0)	47 (88.7)
			Treatable	2 (3.9)	0 (0.0)	2 (3.8)
			Not specified	3 (5.9)	1 (50.0)	4 (7.5)
		Total		51 (100)	2 (100)	53 (100)

In a study by Demirci et al. (30), emergency physicians were given theoretical and practical training on writing judicial reports, and the rate of "temporary report" declined from 55.5% (prior to training) to 0.5%. Emergency physicians generally prefer not to prepare final reports due to both lack of knowledge and avoidance from legal responsibility. Over time, this leads to spoiling of evidence, prolongation of legal procedures and delay in justice (25). This result was also corroborated in our study and it is necessary to encourage physicians to prepare final reports.

In their study examining a series of 5870 cases, Seviner et al. (25) reported that life-threatening clinical status was discussed in 56.8% of the reports prepared by emergency services. The reported rated was 80.3% in the study of Güven et al. (31) in 1296 cases, 91.5% in the study of Bozkurt (29) in 1218 cases and 97.1% in our study. Therefore, the inclusion of life-threatening clinical status, which is one of the most fundamental criteria that the judicial reports should include, was quite variable. Although there has been an increase in the rate of discussing this parameter in recent years, actual data indicate that emergency physicians lack a basic knowledge of writing judicial reports.

In previous studies, the rate of incorrect life-threatening clinical status was reported to be 13% by Serinken et al. (4) and 6.5% by Türkmen et al. (32). In our study, the life-threatening clinical status was accurately diagnosed in 520 emergency service reports, inaccurately diagnosed in 89 reports and not discussed in 18 reports. The rate of correctly identifying life-threatening clinical status was 83.49% and identifying the absence of life-threatening clinical status was 85.52%. This result shows that, beside the fact that there are significant problems in discussing basic criteria in judicial reports prepared in emergency services, there are also important problems in writing the reports and indicating accurate diagnoses. Considering the importance given to life-threatening clinical status under Turkish Penal Law, it is clear that this is a serious problem with significant consequences.

Bozkurt (29) emphasized that the concept of simple medical intervention was discussed in 66% of judicial reports, and this was 95.2% in the present study. Moreover, from the aspect of simple medical intervention by emergency services, our study determined that accurate diagnoses were made in 450 cases, misdiagnoses were made in 129 cases and no diagnosis was made in 19 reports. For the cases that could not be treated by simple medical intervention, the success rate of accurately identifying this was 84.20% and that of identifying the cases that could be treated by simple medical intervention was 58.62%. The success of physicians in identifying the lesions that could be treated by simple medical intervention was 50%, and it was almost the same for non-physician individuals. This remarkable result clearly indicates that, besides the severe knowledge deficiency, the physicians that prepared the judicial reports and stated that the lesions could not be treated by simple medical intervention did so in order to protect themselves and to avoid taking any legal responsibility. However, when a report that has severe consequences for the counterparty is prepared, the physician that prepared the report may have certain legal responsibilities.

Considering the event types from a general aspect, the most accurate reports are written for cases such as falling from a height, industrial accident, suicide attempt, firearm injury and penetrating stub injuries, where the lesions are visible during a physical examination. This rate decreases for blunt trauma cases such as physical violence/battery, traffic accident and lesions of visceral organs, where the lesions are not visible to the naked eye. Some of the reasons for these observations are that physicians do not have information about writing judicial reports, and that they do not have time for a detailed patient examination and writing the report before examining the patient in detail.

Conclusion

In conclusion, even the scope of judicial reports is very wide, reports prepared by emergency service personnel are expected to accurately and fully describe the lesions, to be written in a more comprehensive language and accurately define the legal concepts such as life-threatening clinical status and simple medical intervention. Because of these important deficiencies, our physicians may be subjected to legal and penal sanctions due to unjust treatments caused by inaccurate reports. Thus, in order to protect physicians from being victimized as a result of their actions and to prevent the victimization of counterparties in a lawsuit, it is necessary to offer students objective-driven education by refining these topics in forensic medical education in medical faculties. It is of great importance to initiate a widespread in-service training campaign by the Ministry of Health, and to repeat training, which will be given by forensic medicine experts, on a regular basis in order to keep abreast with knowledge in this area.

Ethics

Ethics Committee Approval: The ethical committee approval of our study was obtained from the Ethical Committee of Clinic Researches of Gaziantep University (approval number: 2016/168).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.A., V.D., Y.A., Concept: M.A., M.K.A., M.K., Design: M.A., Z.T., Data Collection or

Processing: M.A., V.D., Analysis or Interpretation: S.K., Literature Search: M.A., M.K., Writing: M.A., Y.A., Z.T.

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References

1. Young G. Psychiatric/psychological forensic report writing. Int J Law Psychiatry. 2016;49:214-20.
2. Korkmaz T, Kahramansoy N, Erkol Z, Sarıçil F, Kılıç A. Evaluation of the forensic patients presenting to the emergency department and legal reports. Med Bull Haseki. 2012;50:14-20.
3. Küçük E, Günel C. Demographic characteristics of forensic investigation in emergency service. Sakarya Tıp Dergisi. 2016;6:100-5.
4. Serinken M, Türkçüer İ, Acar K, Özen M. Evaluation of medicolegal reports written by physicians in the emergency unit with regard to deficiencies and mistakes. Ulus Travma Acil Cerrahi Derg. 2011;17:23-8.
5. Christensen AM, Crowder CM, Ousley SD, Houck MM. Error and its meaning in forensic science. J Forensic Sci. 2014;59:123-6.
6. Güven FMK, Bütün C, Beyaztaş FY, Eren ŞH, Korkmaz İ. Evaluation of forensic cases admitted to Cumhuriyet University hospital. Meandros Med Dent J. 2009;10:23-8.
7. Yavuz MF, Yavuz MS. Standardization and deficiencies of forensic reports. Turkiye Klinikleri Journal of Surgical Medical Sciences. 2006;2:28-33.
8. Serinken M, Çımrın A, Ergör A, Cimilli C, Bengi F. Burnout syndrome and emergency service physicians. Toplum ve Hekim. 2002;17:358-65.
9. Fedakar R, Aydiner AH, Ercan İ. A comparison of "life threatening injury" concept in the Turkish Penal Code and trauma scoring systems. Ulusal Travma Acil Cerrahi Derg. 2007;13:192-8.
10. Yavuz MS, Aydın S. Forensic cases and reports in primary health care. Turkish Journal of Family Practice. 2007;8:30-3.
11. Hon KL, Leung TF, Cheung KL, Nip SY, Ng J, Fok TF et al. Severe childhood injuries and poisoning in a densely populated city: Where do they occur and what type? J Crit Care. 2010;25:175.
12. Sever M, Saz EU, Koşargelir M. An evaluation of the pediatric medico-legal admissions to a tertiary hospital emergency department. Ulus Travma Acil Cerrahi Derg. 2010;16:260-7.
13. Çetinel Y, Gülalp B, Karagün Ö, Örel Ö, Seçkin TD, Aldinç H, et al. Pediatric cases that composed temporary legal report; whom? when? JAEM. 2013;12:113-7.
14. Çolak B, Demirbaş İ, Albayrak Ü. The importance of temporary forencis reports. STED Dergisi. 2005;14:161-4.
15. Naveen S, Kumar MV. Preparing medico legal report in clinical practice. Indian J Surg. 2013;75:47-9.
16. Griffith EE, Stankovic A, Baranoski M. Conceptualizing the forensic psychiatry report as performative narrative. J Am Acad Psychiatry Law. 2009;38:32-42.
17. Howes LM, Kirkbride KP, Kelty SF, Julian R, Kemp N. The readability of expert reports for non-scientist report-users: Reports of forensic comparison of glass. Forensic Sci Int. 2014;236:54-66.
18. Sand K, Eik-Nes NL, Loge JH. Readability of informed consent documents (1987-2007) for clinical trials: a linguistic analysis. J Empir Res Hum Res Ethics. 2012;7:67-78.
19. Brannick ME. Guidelines for Forensic Report Writing: Helping Trainees Understand Common Pitfalls to Improve Reports. 2015
20. Kariyawasam U. The impact of peer review on paediatric forensic reports. J Forensic Leg Med. 2016;43:42-7.
21. Karson M, Nadkarni L. Principles of forensic report writing: American Psychological Association. 2013.
22. Reid WH. Writing reports for lawyers and courts. J Psychiatr Pract. 2011;17:355-9.
23. Yavuz M, Baştürk P, Yavuz M, Yorulmaz C. Evaluation of forensic cases admitted to Cerrahpaşa Medical Faculty Emergency Service. Adli Bilimler Dergisi. 2002;1:21-6.
24. Turla A, Aydın B, Sataloğlu N. Mistakes and omissions in judicial reports prepared in emergency services. Ulus Travma Acil Cerrahi Derg. 2009;15:180-4.
25. Seviner M, Kozacı N, Ay MO, Açıkalın A, Çökük A, Gülen M, et al. Analysis of judicial cases at emergency department. Cukurova Medical Journal (Çukurova Üniversitesi Tıp Fakültesi Dergisi). 2013;38:250-60.
26. Hakkoymaz H, Keten HS, Artuç S, Üçer H, Bozkurt S, Okumuş M, et al. Evaluation of medico-legal reports in respect of the Turkish penal code. J Kartal Tr. 2014;25:177-80.
27. Karbeyaz K, Gündüz T, Balcı Y. Forensic medicine approach to bone fractures in the framework of the new Turkish penal code. Ulus Travma Acil Cerrahi Derg. 2010;16:453-8.
28. Çınar O, Acar YA, Çevik E, Kılınç E, Bilgiç S, Ak M, et al. Analysis of forensic cases in the 0-18 years age group that were presented to emergency department. Anatolian Journal of Clinical Investigation. 2010;4:148-51.
29. Bozkurt S. Evaluation of judicial reports which executing on emergency service and fixed deficiencies. Journal of Clinical and Analytical Medicine. 2015;6:331-4.
30. Demirci Ş, Günaydın G, Doğan UDKH, Aynacı Y, Deniz İ. The importance of practical applicatıon in preperation of forensic reports. Journal of Forensic Medicine. 2007;21:10-4.
31. Güven FMK, Bütün C, Beyaztaş FY, Eren ŞH, Korkmaz İ. Evaluation of forensic cases admitted to Cumhuriyet university hospital. Meandros Med Dent J. 2009;10:23-8.
32. Türkmen N, Akgöz S, Çoltu A, Ergin N. Evaluation of legal cases admitted to uludağ university medical school emergency department. Uludağ Medical Journal. 2005;31:25-9.

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Epidemiologic Evaluation and Clinical Aspects of Superficial Corneal Foreign Body Injuries at a Tertiary Referral Center in İstanbul

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Abstract

Aim: To assess the demographic characteristics and clinical aspects of superficial corneal foreign body (CFB) trauma, as well as to estimate the impact of awareness of CFB scar on wearing protective goggles (PG).

Materials and Methods: A total of 238 patients were enrolled in this prospective study. Four groups were designated, namely group 1-metal industry workers, group 2-construction workers, group 3-workers with different occupations who had considerable risk for CFB trauma and group 4-miscellaneous patients with low risk for CFB trauma.

Results: There were 234 (98.3%) men and four (1.7%) women in the study. The mean age was 33.96±10.54 years (range, 3-69 years). There were 126 patients (52.9%) in group 1, 53 patients (22.3%) in group 2, 27 patients (11.3%) in group 3 and 32 patients (13.4%) in group 4. Seventy-nine patients (38.4%) did not use PG, while, 67 patients (32.5%) occasionally used PG, 34 patients (16.5%) frequently used PG and 26 patients (12.6%) routinely used PG. Awareness of CFB scar was significantly lower in patients who did not use PG ($p<0.05$).

Conclusion: The awareness of CFB scar was significantly lower among patients who never used PG. This could be avoided by arranging training programs for workers.

Keywords: Corneal foreign body, epidemiology, protective goggle use, trauma

Introduction

Corneal foreign body (CFB) trauma is a common eye injury in the emergency departments (ED) (1). The CFB trauma is mostly associated with occupational accidents frequently seen in construction and metal industry workers (2). Metal CFBs carry the risk of corneal scarring with decreased visual quality if the injury lies within the visual axis or the risk of a secondary infection (3). Furthermore, CFB trauma also causes an economic burden. A study in Turkey stated that unregistered employment is relatively higher and this forces workers to remove CFBs by themselves (4). Several studies have been reported on demographic and clinical characteristics of CFB trauma. Using protective goggles (PG) has been suggested to prevent workers from CFB trauma (5).

In the present study, we aimed to evaluate the demographic and clinical characteristics of the patients who suffered from CFB trauma and who were treated in the ED. We also aimed to estimate the impact of awareness of CFB scar on wearing PG.

Materials and Methods

This study was conducted in patients presenting to the ED with CFB between July 2015 and November 2015. The mean

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number of daily ED admissions and emergency eye department admissions were means 1300 and 30, respectively. Patients with an eye emergency who were consulted from ED were examined in Ophthalmology Department at the same hospital. Only patients with CFB were included in the study. Patients who had eye emergency other than CFB trauma, including open globe injuries such as penetrating and/or perforating ocular trauma with or without a intraocular foreign body, blunt ocular trauma, eyelid trauma, chemical ocular trauma and orbital fractures were excluded from the study. All patients signed written informed consent before taking part in the study and a local ethical approval was obtained. The study followed the principles outlined in the Declaration of Helsinki.

Patients with CFB trauma were subjected to a routine ophthalmic examination. All examinations were performed by an ophthalmologist. The location of the CFB on the cornea was noted considering the quadrants (central, superonasal, superotemporal, inferonasal or inferotemporal). The size of the CFB was measured with its largest diameter under slit-lamp biomicroscopic examination. The number of hours from injury to presentation was recorded. A questionnaire was also filled out for all patients regarding age, gender, occupation, type of CFB, number of previous CFB removal, PG use and awareness of CFB scar.

Management of CFB was performed in a standard manner. After applying topical anesthetic drop (proparacaine hydrochloride 0.5%), CFB was removed with a 26-gauge needle under slit-lamp. Topical antibiotic treatment (lomefloxacin) was ordered four times daily for four days after the procedure. Eye patching was not suggested in any of the patients (6). Patients were controlled two days after treatment.

Four groups were designated in the study, namely group 1-metal industry workers, group 2-construction workers, group 3-workers in different occupations who had considerable risk for CFB trauma (sweeper, technician, junk dealer and electrician) and group 4-miscellaneous patients with low risk for CFB trauma (student, engineer, housewife and children).

Statistical Analysis

Statistical Package for the Social Sciences (SPSS 22.0) program was used for the statistical analysis. Descriptive statistical methods were expressed as mean and standard deviation. Anova and Kruskal-Wallis tests were used to compare quantitative data according to distribution. Pearson and Spearman's rho correlation methods were performed to assess the relationship between the parameters according to the distribution. Chi-square test was used for comparison of the rates. $p<0.05$ was considered statistically significant.

Results

A total of 238 patients were included in the study. There were four women (1.7%) and 234 men (98.3%) in the study. The mean age of the study population was 33.96±10.54 years (range, 3-69 years). There were 126 patients (52.9%) in group 1, 53 patients (22.3%) in group 2, 27 patients (11.3%) in group 3 and 32 patients (13.4%) in group 4. No significant difference was found between the groups in terms of age ($p=0.719$). The CFB was found in the right eye in 112 patients (47.1%) and in the left eye in 126 patients (52.9%). The type of the CFBs in each group is summarized in Table 1.

The CFB was located in the central cornea in 77 patients (32.4%), in the inferotemporal quadrant in 68 patients (28.6%), in the inferonasal quadrant in 44 patients (18.5%), in the superotemporal quadrant in 30 patients (12.6%) and in the superonasal quadrant in 19 patients (8%). No significant difference was observed between the groups in terms of CFB location ($p>0.05$) (Table 2).

The mean CFB size was 0.30±0.22 mm (range, 0.02-1.20 mm) in the study. The mean time from the CFB injury to presentation was 28.44±32.77 hours (range, 0.3-240 hours). The time from the CFB injury to presentation was significantly associated with the number of previous CFB removals. Increasing number of CFB removals was associated with decreased time from CFB trauma to presentation ($r=0.150$; $p=0.021$).

Regarding the use of PG among patients with a risk of CFB trauma, 79 patients (38.4%) never used PG. Sixty-seven patients (32.5%) occasionally used PG, 34 patients (16.5%) frequently used PG and 26 patients (12.6%) routinely used PG.

Table 1. The types of corneal foreign bodies

	Group 1	Group 2	Group 3	Group 4	p
Metal	121 (96%)	40 (75.5%)	25 (92.6%)	24 (75%)	0.001[a]
Stone	5 (4%)	13 (24.5%)	2 (7.4%)	7 (21.9%)	
Wood	0 (0%)	0 (0%)	0 (0%)	1 (3.1%)	

Group 1: Metal industry workers, Group 2: Construction workers; Group 3: Workers with different occupations who had considerable risk for corneal foreign body trauma, Group 4: Patients with low risk for corneal foreign body trauma

[a]Chi-square $p<0.01$

Table 2. Localization of corneal foreign body

	Group 1 n (%)	Group 2 n (%)	Group 3 n (%)	Group 4 n (%)	p
Inferotemporal	31 (24.6%)	17 (32.1%)	10 (37%)	10 (31.3%)	
Inferonasal	25 (19.8%)	9 (17%)	5 (18.5%)	5 (15.6%)	
Central	46 (36.5%)	19 (35.8%)	7 (25.9%)	5 (15.6%)	
Superotemporal	15 (11.9%)	4 (7.5%)	4 (14.8%)	7 (21.9%)	0.407[a]
Superonasal	9 (7.1%)	4 (7.5%)	1 (3.7%)	5 (15.6%)	

Group 1: Metal industry workers, Group 2: Construction workers; Group 3: Workers with different occupations who had considerable risk for corneal foreign body trauma; Group 4: Patients with low risk for corneal foreign body trauma

[a]Chi-square test

Table 3. The relationship between protective goggle use with the number of corneal foreign body removal and awareness of corneal foreign body scar

	Number of CFB removal (mean ± SD)	p	Awareness of CFB scar		p
			Yes n (%)	No n (%)	
Routine PGU	5.65±6.41	0.001[a]	15 (57.7%)	11 (42.3%)	0.001[b]
Frequent PGU	9.06±17.25		16 (47.1%)	18 (52.9%)	
Occasional PGU	6.78±13.79		16 (23.9%)	51 (76.1%)	
No PGU	3.70±5.93		10 (9%)	101 (91%)	

[a]Kruskal-Wallis test, $p<0.05$, [b]chi-square test, $p<0.05$

CFB: Corneal foreign body, PGU: Protective goggle use, SD: Standard deviation

Table 4. Relationship of occupation with the awareness of corneal foreign body scar

	Awareness of CFB scar		p
	Yes	No	
	n (%)	n (%)	
Group 1	39 (31%)	87 (69%)	0.056
Group 2	9 (17%)	44 (83%)	
Group 3	5 (18.5%)	22 (81.5%)	
Group 4	4 (12.5%)	28 (87.5%)	

Group 1: Metal industry workers, Group 2: Construction workers, Group 3: Workers with different occupations who had considerable risk for corneal foreign body trauma; Group 4: Patients with low risk for corneal foreign body trauma

Chi-square test, CFB: Corneal foreign body

Regarding the awareness of CFB scar, pairwise comparisons showed that the rate of the awareness of CFB scar was significantly lower in patients who never used PG compared to patients who used PG occasionally (p=0.006), frequently (p=0.001) and routinely (p=0.001). Also, the rate of the awareness of CFB scar was significantly lower in patients who used PG occasionally compared to patients who used PG routinely (p=0.002) and frequently (p=0.018). There was no statistically significant difference in terms of CFB scar awareness among patients using PG routinely and frequently (Table 3). No significant difference was noted among the study groups in terms of the awareness of corneal scar after CFB removal (p=0.056) (Table 4).

Discussion

In the present study, we assessed epidemiological and clinical characteristics of 238 patients with CFB trauma, including 234 men with a mean age of 34 years. Our study population mainly consisted of metal industry and construction workers. These findings are compatible with previous literature stating that CFB trauma occurs mainly in young men working in the metal industry and in construction. Although the majority of CFB trauma comprised work-related injuries, 13.4% of our study population consisted of individuals who did not work.

It has been shown that CFB is often located in the central cornea (4). Although the majority of CFBs were found in the central cornea in our study, this finding did not reach a statistically significant level between the groups. We also found a mean time of 28 hours from CFB injury to CFB removal in the present study. One reason for this delay might be that patients tried to remove the CFB themselves, so that such an effort could lead to corneal ulcer formation eventually (4). Furthermore, we observed

that higher number of previous CFB removals was related to decreased time from CFB trauma to presentation to hospital. A shorter interval of hospital admission can be a protective factor for the patient from possible future harmful effect of a CFB, such as corneal ulcer or corneal scar.

It has been stated that the use of PG can protect most of the workers from CFB trauma, as well as from possible scarring in the cornea (1). It has also been shown that leaving the CFB for more than 24 hours causes the rust ring to result in a corneal scar eventually (7). We observed that only 12.6% of patients at risk of CFB trauma always wore PG during working. Vast majority of such patients (91%) who did not wear PG during working were not aware of the possible scar of the CFB. These findings may indicate that majority of the subjects do not have enough knowledge of whether they are at risk of CFB scar whether or not while working. Actually, this represents an important issue for occupational health. An experienced on-site physician should inform the workers about such occupational accident, irrespective of their social and educational status. Also, the employer should be informed in order to take preventive measures for CFB injury.

Several methods have been used in an attempt to remove the rust ring of the CFB, including an electric burr or a hypodermic needle (8,9). The electrical burr has been demonstrated to be associated with deeper stromal damage after CFB removal (9). In our study, we successfully used a 26-gauge hypodermic needle in order to remove the CFB and its rust.

Studies did not suggest a routine eye patch for corneal abrasions, because it does not have any effect on healing time and pain (10). It has also been indicated that smaller abrasions, as in CFB trauma, could be treated only with antibiotic ointments (11). Following CFB removal, all patients in the current study were prescribed ocular antibiotic drops without eye patching, and then patients were re-assessed two days after the procedure. We found that such treatment approach seems to be a safe and practical method for CFB injuries in terms of avoiding secondary infection and providing patient rehabilitation.

Study Limitations

The inclusion of relatively small number of patients can be one of the drawbacks of the study.

Conclusion

Corneal foreign body trauma is a preventable healthcare problem. Our study demonstrated that patients were relatively unaware of the further complications related to CFB. Such injuries and related complications can be better avoided by taking preventive measures at workplaces and by informing individuals on this issue.

Ethics

Ethics Committee Approval: Ümraniye Training and Research Hospital, approval number: B.10.1.TKH.4.34.H.GP.0.01/41.

Informed Consent: N/A.

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Authorship Contributions

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

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References

1. Zimmerman DR, Shneor E, Millodot M, Gordon-Shaag A. Corneal and conjunctival injury seen in urgent care centres in Israel. Ophthalmic Physiol Opt. 2019;39:46-52.
2. Ramakrishnan T, Constantinou M, Jhanji V, Vajpayee RB. Corneal metallic foreign body injuries due to suboptimal ocular protection. Arch Environ Occup Health. 2012;67:48-50.
3. Sayegh JS, Lahham S, Woodhouse L, Seong J, McCoy CE. Creation of a Realistic Model for Removal of a Metallic Corneal Foreign Body for Less than $75. West J Emerg Med 2017;18:121-5.
4. Ozkurt ZG, Yuksel H, Saka G, Guclu H, Evsen S, Balsak S. Metallic corneal foreign bodies: an occupational health hazard. Arq Bras Oftalmol. 2014;77:81-3.
5. Ahmed F, House RJ, Feldman BH. Corneal Abrasions and Corneal Foreign Bodies. Prim Care. 2015;42:363-75.
6. Lim CH, Turner A, Lim BX. Patching for corneal abrasion. Cochrane Database Syst Rev. 2016;7:CD004764.
7. Brock G, Gurekas V. The occasional corneal rust ring removal. Can J Rural Med. 2013;18:140-2.
8. Fraenkel A, Lee LR, Lee GA. Managing corneal foreign bodies in office-based general practice. Aust Fam Physician. 2017;46:89-93.
9. Brown N, Clemett R, Grey R. Corneal rust removal by electric drill. Clinical trial by comparison with manual removal. Br J Ophthalmol. 1975;59:586-9.
10. Menghini M, Knecht PB, Kaufmann C, Kovacs R, Watson SL, Landau K, et al. Treatment of traumatic corneal abrasions: a three-arm, prospective, randomized study. Ophthalmic Res. 2013;50:13-8.
11. Segal KL, Fleischut PM, Kim C, Levine B, Faggiani SL, Banerjee S, et al. Evaluation and treatment of perioperative corneal abrasions. J Ophthalmol. 2014;2014:901901.

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Lipid Emulsion Therapy in Lipophilic or Hydrophilic Drug Intoxication: The Last Weapon in Our Arsenal

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Abstract

Aim: Previous case reports have described the administration of lipid emulsion therapy in lipophilic drug intoxication cases. In this study, we wanted to contribute to the literature that lipid emulsion therapy could also be given lipid as the last weapon in not only lipophilic drug intoxication but also all intoxication cases with worsening general condition.

Materials and Methods: A total of 65 patients, who presented to the emergency room and received lipid therapy between January 1, 2014 and January 1, 2017, were included in this study. Each patient was given a 20% ClinOleic (Baxter) infusion of 1.5 mL/kg for 1-3 minutes and then 100 mL/h (0.025 mL/kg/min). Toxic drugs were divided into low or high permeability groups according to their lipid/water partition coefficients (LogP).

Results: Of the 65 patients, 55.4% (n=36) were female and 44.6% (n=29) were male. These patients were grouped according to a lipid/water cut-off value of 1.72. The lipid therapy was administered in addition to antidotal therapy in two patients in the hydrophilic group and in five patients in the lipophilic group. The only variable that was significantly restored 12 hours after the lipid therapy was the respiratory rate, which was 16.0 (range, 15.5-17.3)/min in the hydrophilic group and 20.0 (range, 18.0-22.0)/min in the lipophilic group (p=0.003).

Conclusion: We believe that lipid therapy can be used as a last resort in intoxication cases, especially in patients with low Glasgow coma scale scores and worsened vital signs despite antidotal and extracorporeal therapies, regardless of whether the causative agent is hydrophilic or lipophilic.

Keywords: Lipophilicity, lipid emulsion therapy, toxicity, hydrophilicity, lipid/water partition coefficient, emergency service

Introduction

For the first time in 1998, the infusion of soybean oil used in total parenteral nutrition solutions showed that it could prevent cardiovascular collapse resulting from an overdose of bupivacaine in anesthetized rats and could improve resuscitation (1). In another experimental model, spontaneous circulation was restored in all lipid-treated animals following a bupivacaine challenge, but it was not restored in any of the saline-treated control subjects (2). The first case report describing the use of intravenous lipid emulsion (ILE) therapy as a rescue or antidotal therapy for acute intoxication was published in 2006 (3). In recent years, it has become one of the most recommended treatment methods for patients who have experienced cardiac arrest or those with high hemodynamic risk following xenobiotic toxicity (4).

The mechanism of action of ILE in the management of intoxication is not yet fully understood; however, numerous mechanisms are thought to contribute to its activity. The emulsion acts as a lipid sink that surrounds and neutralizes a lipophilic drug molecule. Several *in vitro* and *in vivo* studies have confirmed the benefits of the lipid sink impact (5-7). The *in vitro* models have suggested

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that the mechanism underlying ILE binding depends on the lipid/water partition coefficient and distribution volume. The lipid/water coefficient defines how easily a drug moves between the water and lipid medium (8). Drugs with a LogP >1.72 are classified as having high permeability and those with a LogP <1.72 are considered to have low permeability (9,10).

In this retrospective study, we aimed to share the demographic data and outcomes of patients treated with ILE therapy based on lipophilicity in the emergency department in the light of the literature. We were especially interested in patients with poor general status despite ongoing initial antidotal and extracorporeal therapies, regardless of the lipophilicity of the toxic agent.

Materials and Methods

Trial Design and Participants

A total of 73 patients, who were admitted to the emergency room and received ILE therapy between January 1, 2014 and January 1, 2017, were retrospectively evaluated with the approval of the local ethics committee (53043469-050.04.04/2017-1071). A total of 65 patients with accessible data were included in this research.

According to the dosing scheme recommended by the American College of Medical Toxicology, each patient was administered a bolus of 20% ClinOleic (Baxter) at 1.5 mL/kg for 1-3 minutes (11). The infusion continued at 100 mL/h (0.025 mL/kg/min) until the hemodynamic variables returned to normal. The lipid/water partition coefficients (LogP) of the drugs taken at toxic doses were determined and they were divided into hydrophilic and lipophilic groups (9,10).

Follow-up

All patients were followed-up in the emergency intensive care and emergency observation units. Demographics, admission data, intensive care follow-up, extracorporeal treatments and outcomes were evaluated. Since the patients receiving ILE therapy in our service were followed-up for one month, any additional complaints were evaluated for one month after discharge.

Statistical Analysis

The normality of continuous variables was evaluated by Kolmogorov-Smirnov test. The descriptive statistics of the normally distributed variables were expressed as mean ± standard deviation, and an Independent Samples t-test was used for comparisons between the groups. The descriptive statistics of the non-normally distributed variables were expressed as median (25%-75%), and Mann-Whitney U test was used for comparisons between the groups. P value <0.05 was considered statistically significant.

Results

Among the 73 patients who underwent ILE therapy due to intoxication, the data of 65 patients was obtained. Of these patients, 55.4% (n=36) were females and 44.6% (n=29) were males. The mean age was 32.5±12.6 years for females and 35.0±14.7 years for males.

The cut-off value for lipid/water partition coefficient was 1.72, and the patients were divided into hydrophilic and lipophilic groups accordingly (Table 1). Of the 59 patients in the lipophilic

Table 1. Intoxication agents and their LogP values

Lipophilicity	Toxic agent	LogP
Lipophilic, LogP ≥1.72 (1,2)	Tetrahydrocannabinol	7.22
	Amitriptyline	4.81
	Imipramine	4.80
	Biperiden	4.28
	Fluoxetine	4.05
	Paroxetine	3.70
	Dexibuprofen	3.67
	Opipramole	3.45
	Clozapine	3.23
	Bupropion	3.12
	Escitalopram	3.08
	Phenytoin	2.47
	Olanzapine	3.00
	Valproic Acid	2.75
	Warfarin	2.70
	Mirtazapine	2.70
	Alprazolam	2.65
	Carbamazepine	2.45
	Venlafaxine	2.38
	Malathion	2.36
	Amlodipine	2.22
	Quetiapine	2.09
	Metoprolol	1.87
	Bisoprolol	1.87
	Amphetamine	1.85
Hydrophilic, LogP <1.72 (1,2)		
	Paracetamol	0.46
	Methylphenidate	0.20
	Theophylline	-0.13
	Monocrotophos	-0.40
	Pregabalin	-0.55

Table 2. Distributions of length of hospitalization, Glasgow coma scale scores, mean arterial pressures and respiratory rates according to toxic agent group

	Lipophilic	Hydrophilic	p
Length of hospitalization			
Emergency intensive care	2.0 (1.0-4.0) (n=59)	2.5 (0.8-6.0) (n=6)	0.670
Observation unit	1.0 (1.0-2.0) (n=59)	1.5 (1.0-2.5) (n=6)	0.479
Total (day)	3.0 (2.0-5.0) (n=59)	3.5 (2.8-7.0) (n=6)	0.365
GCS			
Admission	13.0 (4.5-15.0) (n=48)	15.0 (8.5-15.0) (n=5)	0.213
Post-treatment 12th hour	15.0 (14.0-15.0) (n=48)	15.0 (11.0-15.0) (n=5)	0.867
Post-treatment 24th hour	15.0 (14.0-15.0) (n=48)	15.0 (14.0-15.0) (n=5)	0.955
Mean arterial pressure			
Admission	88.9±16.3 (n=45)	95.7±18.0 (n=5)	0.388
Post-treatment 12th hour	83.3±14.2 (n=45)	83.3±10.8 (n=5)	0.997
Post-treatment 24th hour	83.4±15.1 (n=45)	90.7±10.6 (n=5)	0.302
Respiratory rate			
Admission	20.0 (18.0-22.0) (n=51)	16.0 (15.5-17.3) (n=6)	0.003
Post-treatment 12th hour	18.0 (16.0-21.0) (n=51)	21.0 (15.5-25.5) (n=6)	0.255
Post-treatment 24th hour	19.0 (15.5-22.0) (n=51)	18.0 (14.0-20.0) (n=6)	0.417

GCS: Glasgow coma scale

group, 56 presented with intake of only lipophilic drugs and three presented with intake of both hydrophilic and toxic lipophilic drugs. Of the six patients in the lipophilic group, two presented with intake of only hydrophilic drugs and four presented with intake of both lipophilic and toxic hydrophilic drugs.

The length of hospitalization, Glasgow coma scale (GCS) score, mean arterial pressure (MAP) and respiratory rate of the patients are shown in Table 2. The respiratory rate was significantly higher in the lipophilic group than in the hydrophilic group (p=0.003). Thirty-six patients were in the mono-drug group and 29 were in the poly-drug group. Three patients died during treatment and one patient developed pancreatitis. Mortality occurred due to insecticides in two patients and quetiapine in one patient. When the patients were classified according to the administered extracorporeal therapy, plasmapheresis was administered in one patient in the hydrophilic group and in two in the lipophilic group. Hemoperfusion was administered in four patients, hemofiltration in one patient, and hemodialysis in one patient in the lipophilic group.

ILE therapy was administered in addition to antidotal therapy in two patients in the hydrophilic group and five patients in the lipophilic group. The reasons for the ILE administration in addition to the antidotal therapy were low GCS score in three patients, the development of tachypnea in two patients and hypotension in two patients.

The vital signs and examination results of the patients at the time of admission were compared between the lipophilic and hydrophilic groups. The only statistically significant finding was the respiratory rate, which was 16.0 (range, 15.5-17.3)/min in the hydrophilic group and 20.0 (range, 18.0-22.0)/min in the lipophilic group (p=0.003). The only variable that was restored after the neurological and vital sign examinations 12 hours after admission was the respiratory rate.

Discussion

One of the results making this study unique was the fact that ILE therapy could be applied regardless of whether the patient was overdosed with a lipophilic or hydrophilic substance. The other reason was that the respiratory rate could be used to evaluate the response of a patient to ILE administration. The only variable restored was the respiratory rate, which improved at 12 hours in the lipophilic group and 24 hours in the hydrophilic group. The delayed elevation of the respiratory rate in the hydrophilic group could be explained by late passage of drugs into the central nervous system. However, the decrease in the respiratory rate 24 hours after the ILE therapy could be attributed to the indication of lipid activity in the hydrophilic group.

One theory suggested that local anesthetics suspended the transport of fatty acids to cardiac mitochondria, thus decreasing the energy supply. Fatty acids provide a readily available energy resource for the myocardium, thus improving the function of the heart (12). However, this theory is insufficient to explain the effects of ILE therapy that we encountered in the non-local anesthetic and LogP <1.72 drug intoxication patients. We believe that this effect is associated with all drugs according to the LogP value of the toxic agent.

In their study, Levine et al. (13) reported a case of acute pancreatitis and acute respiratory distress in a 13-year-old female patient who was given a lipid emulsion dose recommended by the American Society of Regional Anesthesia and Pain Medicine following tricyclic antidepressant overdose. The lipase level peaked at 1.849 U/L on the 5th day of lipid administration. In our series of 65 patients, one patient among the patients who received IV organophosphate as a complication had a mild amylase increase. In addition, allergy developed in one patient who had escitalopram overdose.

In their review, Cao et al. (14) classified the drugs taken according to the LogP=2 classification. According to this study, metoprolol remained in the hydrophilic group, even though it was described as moderately lipophilic in the literature (15-18). In our study metoprolol remained in the lipophilic part of the classification.

No significant difference was found between the groups in terms of length of hospitalization, GCS and MAP values at 12 and 24 hours. However, there was an increase in the GCS score 12 hours after ILE administration compared to the admission scores in both groups. Although some of the case reports stated that ILE therapy was administered at lower GCS scores, the overall evaluation of the GCS scores was another important part of our study.

Poly-drug intake is unknown in the literature. In our study, 44.6% (n=29) of the patients given ILE therapy presented with poly-drug intake. Four of the six patients in the hydrophilic group were admitted with lipophilic drug intake in addition to the intake of toxic hydrophilic drugs. This indicates that patients can receive additional lipophilic drugs despite the fact that the causative agent was hydrophilic, and thus, the toxic picture might worsen.

Three of the patients died during the treatment, and of those, the mortality occurred due to insecticide intake in two patients and quetiapine intake in one patient. It has been reported in the literature that low-dose lipid therapy could be useful in case of quetiapine and insecticide intoxications (19,20). In our study, the reasons for the response failure of ILE therapy could be the low GCS scores at admission (3,4,3) and late presentation to emergency service.

In one study, combined use of ILE therapy and extracorporeal treatment methods did not provide additional benefits in clinical practice (21). The patients were classified based on the administered extracorporeal therapy: plasmapheresis was administered in three patients, hemoperfusion in four patients, hemofiltration in one patient, and hemodialysis in one patient. Lipid therapy was applied in patients in whom the extracorporeal therapy would be delayed.

Filter occlusion was not observed in any of the patients because ILE was discontinued one hour before the extracorporeal therapy. The ILE therapy was administered in addition to the antidotal treatment in seven patients due to low GCS scores in three patients, the development of tachypnea in two patients, and hypotension in two patients.

Study Limitations

This study had several limitations. For example, it was designed as a retrospective study without pediatric patients. In addition, time from drug intake to hospital admission and time from admission to decontamination were not determined.

Conclusion

In conclusion, we believe that ILE therapy can be used as a last resort treatment regimen in cases of delayed antidotal and extracorporeal treatments, regardless of the lipophilicity of the toxic agent, especially in patients with a poor general status. In addition, the respiratory rate can be used to assess the response of a patient to ILE therapy. Further large-scale studies are needed both for the demonstration of the action mechanism and implementation in practice.

Ethics

Ethics Committee Approval: A total of 73 patients, who were admitted to the emergency room and received ILE therapy between January 1, 2014 and January 1, 2017, were retrospectively evaluated with the approval of the local ethics committee (53043469-050.04.04/2017-1071).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

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

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References

1. Weinberg GL, VadeBoncouer T, Ramaraju GA, Garcia-Amaro MF, Cwik MJ. Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats. Anesthesiology. 1998;88:1071-5.
2. Weinberg G, Ripper R, Feinstein DL, Hoffman W. Lipid emulsion infusion rescues dogs from bupivacaine-induced cardiac toxicity. Reg Anesth Pain Med. 2003;28:198-202.
3. Jamaty C, Bailey B, Larocque A, Notebaert E, Sanogo K, Chauny JM. Lipid emulsions in the treatment of acute poisoning: a systematic review of human and animal studies. Clin Toxicol (Phila). 2010;48:1-27.

4. Christian MR, Pallasch EM, Wahl M, Mycyk MB. Lipid rescue 911: Are poison centers recommending intravenous fat emulsion therapy for severe poisoning? J Med Toxicol. 2013;9:231-4.
5. Weinberg G, Lin B, Zheng S, Di Gregorio G, Hiller D, Ripper R, et al. Partitioning effect in lipid resuscitation: further evidence for the lipid sink. Crit Care Med. 2010;38:2268-9.
6. Mazoit JX, Le Guen R, Beloeil H, Benhamou D. Binding of longlasting local anesthetics to lipid emulsions. Anesthesiology. 2009;110:380-6.
7. Samuels TL, Willers JW, Uncles DR, Monteiro R, Halloran C, Dai H. In vitro suppression of drug-induced methaemoglobin formation by Intralipid(®) in whole human blood: observations relevant to the 'lipid sink theory'. Anaesthesia. 2012;67:23-32.
8. French D, Smollin C, Ruan W, Wong A, Drasner K, Wu AH. Partition constant and volume of distribution as predictors of clinical efficacy of lipid rescue for toxicological emergencies. Clin Toxicol (Phila). 2011;49:801-9.
9. Kasim NA, Whitehouse M, Ramachandran C, Bermejo M, Lennernäs H, Hussain AS, et al. Molecular properties of WHO essential drugs and provisional biopharmaceutical classification. Mol Pharm. 2004;1:85-96.
10. Takagi T, Ramachandran C, Bermejo M, Yamashita S, Yu LX, Amidon GL. A provisional biopharmaceutical classification of the top 200 oral drug products in the United States, Great Britain, Spain, and Japan. Mol Pharm. 2006;3:631-43.
11. American College of Medical Toxicology. ACMT Position Statement: Interim Guidance for the Use of Lipid Resuscitation Therapy. J Med Toxicol. 2011;7:81-2.
12. Gueret G, Pennec JP, Arvieux CC. Hemodynamic effects of intralipid after verapamil intoxication may be due to a direct effect of fatty acids on myocardial calcium channels. Acad Emerg Med. 2007;14:761.
13. Levine M, Brooks DE, Franken A, Graham R. Delayed-onset seizure and cardiac arrest after amitriptyline overdose, treated with intravenous lipid emulsion therapy. Pediatrics. 2012;130:432-8.
14. Cao D, Heard K, Foran M, Koyfman A. Intravenous lipid emulsion in the emergency department:a systematic review of recent literature. J Emerg Med. 2015;48:387-97.
15. Westerlund A. Central nervous system side-effects with hydrophilic and lipophilic beta-blockers. Eur J Clin Pharmacol. 1985;28(Suppl):73-6.
16. Ahmed AI, van Mierlo PJ, van Waarde JA, Jansen PA. Hallucinations and vivid dreams by use of metoprolol. Tijdschr Psychiatr. 2010;52:117-21.
17. Cove-Smith JR, Kirk CA. CNS-related side-effects with metoprolol and atenolol. Eur J Clin Pharmaco. 1985;28(Suppl):69-72.
18. Sirois FJ. Visual hallucinations and metoprolol. Psychosomatics. 2006;47:537-8.
19. Purg D, Markota A, Grenc D, Sinkovic A. Low-dose intravenous lipid emulsion for the treatment of severe quetiapine and citalopram poisoning. Arh Hig Rada Toksikol. 2016;67:164-6.
20. Turkdogan KA, Duman A, Avcil M, Akoz A, Canakcı SE, Kantekin B. Treatment methods following suicidal self-administration of IV organophosphate: What can additional lipid administration change? Am J Emerg Med. 2017;35:1388.
21. Karaman K, Türkdoğan KA, Deniz AT, Canakcı SE. Which is the best in carbamazepine overdose? Clin Case Rep. 2017;5:1612-5.

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Predictive Values of Serum Uric Acid, Mean Platelet Volume and Plateletcrit on Benign Paroxysmal Positional Vertigo

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Abstract

Aim: There are conflicting study results on correlation of serum uric acid (SUA) with benign paroxysmal positional vertigo (BPPV). In this study, it was aimed to evaluate predictive values of SUA, mean platelet volume (MPV) and plateletcrit (PTC) on BPPV.

Materials and Methods: After the approval of the ethics committee, the files of all patients with BPPV who were admitted to the Emergency Department of Ufuk University between 01.01.2015 and 01.01.2016 were examined retrospectively. White blood cell, MPV, PTC and SUA levels of patients were evaluated.

Results: There was no statistically significant difference between the groups in terms of gender distribution ($p>0.05$). The mean age of the control group (31.25±11.46 years) was lower than the vertigo group (44.71±19.38 years), but this difference was not statistically significant ($p>0.05$). The difference between two groups in terms of MPV, PTC and SUA parameters was statistically significant ($p<0.05$). The sensitivity was found to be 92.1% and the specificity was 47.8%. For a PTC value of 0.224%, the sensitivity was 23.7% and the specificity was 87%. For SUA, area under curve was 71.6% indicating that SUA had a predictive value for peripheral vertigo ($p<0.01$). The sensitivity of SUA was 55.3% and the specificity was 21.7% for a SUA value of 4.1. The sensitivity of SUA was 15.8 and the specificity was 87% for a SUA value of 6.55.

Conclusion: Analysis results were in accordance with volume ure in which SUA is suspected in idiopathic BPPV. In addition, PTC was also correlated with BPPV.

Keywords: Serum uric acid, mean platelet volume, plateletcrit, benign paroxysmal positional vertigo

Introduction

Benign paroxysmal positional vertigo (BPPV) is a common healthcare problem in the elderly. BPPV is characterized by short vertigo episodes with movement of the head (1). BPPV has a high incidence rate, approximately 17-20% of peripheral vertigo (2). Most BPPV cases are idiopathic. However, some risk factors such as ear surgery, labyrinthitis, vestibular neuritis, and head trauma are common causes for BPPV. In addition, the symptoms and prevalence increase with age (3). The common diagnostic procedure includes visualization of nystagmus and medical history of the patient (4). The prevalence of BPPV is reported as 25% in older people over 70 years with complaints of more than one year (5). More than 90% of BPPV patients can be treated with maneuvers. Most patients with vertigo state that closing the eyes reduces the symptoms (6). Current treatments include manual repositioning procedures such as Gufoni, Semont, Epley or Barbecue procedures (2).

Serum uric acid (SUA) is a purine metabolism product. Some studies have shown that SUA may be an important biomarker for specific motor features (7). Its association with diabetic peripheral neuropathy (8), cardiovascular diseases (9,10), ischemic stroke (11) and many other clinical syndromes was reported. Similar to SUA, mean platelet volume (MPV) and plateletcrit (PTC) have been reported as biomarkers for some health problems.

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In this study, it was aimed to evaluate predictive values of SUA, MPV and PTC in BPPV patients who applied to our emergency clinic.

Materials and Methods

Patient files of all patients who were admitted to the emergency department of Ufuk University with BPPV between 01.01.2015 and 01.01.2016 were examined retrospectively. White blood cell (WBC), MPV, platelet distribution width (PDW) and SUA values of patients were evaluated. This study was conducted in accordance with World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013). No consent form was obtained from the patients due to retrospective nature of the study. This study was approved by the Ethics Committee of Ufuk University with a number of 26022016-2 and a date of 26.02.2016.

Statistical Analysis

Nominal and binary parameters were described with frequency analysis. The values for research parameters were described as mean ± standard deviation. Chi-square analysis was used for nonparametric nominal parameter differences. Kolmogorov-Smirnov test was used to examine the normality of scale parameters. Since all parameters showed non-normal distribution, Mann-Whitney U test was used to define differences between control and vertigo groups. ROC Curve analysis was used to define sensitivity and specificity of the parameters. All analyzes were performed using SPSS 17.0 for Windows (Chicago, Illinois) at 95%-99% CI levels.

Results

The results of gender and age distribution and difference analysis for patient groups are given in Table 1.

Fifty-two point two percent of the subjects in the control group were female and 47.8% were male. There were 26 women (68.4%) and 12 men (31.6%) in the vertigo group. The difference between the groups in terms of gender distribution was not statistically significant (p>0.05). The mean age of the control group (31.25±11.46 years) was lower than the vertigo group (44.71±19.38 years), but this difference was not statistically significant (p>0.05). The results of some blood parameters in the control and vertigo groups and difference analysis are given in Table 2.

Table 1. The gender and age distribution of groups

	Control (n=24)	Vertigo (n=38)	p
Gender			
Female, n (%)	12 (52.2)	26 (68.4)	0.204[a]
Male, n (%)	11 (47.8)	12 (31.6)	
Age, Mean ± SD	31.25±11.46	44.71±19.38	0.074[b]

[a]Chi-square test, [b]Mann-Whitney U test, SD: Standard deviation

WBC, MPV, PDW and SUA levels of the control group were higher than the vertigo group. PTC level of the vertigo group was higher than the control group. The difference between two groups in terms of MPV, PTC and SUA parameters were statistically significant (p<0.05). The results of the ROC analysis for examining the predictive values of the significant parameters on vertigo are given in the Figure 1.

The area under the curve was found to be 0.969. The predictive power of PTC was found to be 69.6%. The results of ROC analysis were statistically significant (p>0.05). For a PTC value of 0.1565, the sensitivity was 92.1% and the specificity was 47.8%. For a PTC value of 0.224%, the sensitivity was 23.7% and the specificity was 87%. For SUA, the area under the curve was 71.6% indicating that uric acid had a predictive value for peripheral vertigo (p<0.01). The sensitivity of SUA was 55.3% and the specificity was 21.7% for a SUA value of 4.1. The sensitivity of SUA was 15.8% and the specificity was 87% for a SUA value of 6.55. The results of univariate and multiple regression analysis are given in the Table 3.

Univariate and multiple regression analysis results showed that only SUA (p<0.01) and MPV (p<0.05) had a predictive value for

Table 2. The blood parameters and comparison of the control and vertigo groups

Parameters[a]	Control (n=24)	Vertigo (n=38)	p[b]
WBC	7.61±1.41	7.55±2.65	0.240
MPV	8.20±2.13	7.23±1.40	0.036
PDW	17.84±3.60	17.30±3.26	0.829
PTC	0.19±0.10	0.21±0.07	0.011
Uric acid	5.39±1.19	4.45±1.43	0.005

[a]Mean ± standard deviation, [b]Mann-Whitney U test, WBC: White blood cell, MPV: Mean platelet volume, PDW: Platelet distribution width, PTC: Plateletcrit

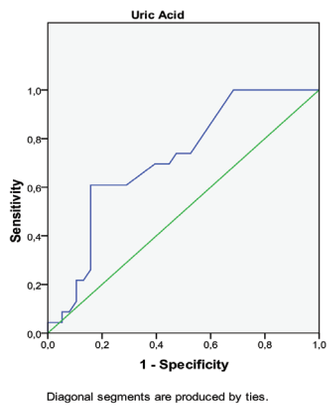

Figure 1. The results of the ROC analysis to examine the predictive value of significant parameters on vertigo

Table 3. Univariate and multiple regression analysis results

Variables	Univariate		Multiple	
	OR (95% CI)	p	OR (95% CI)	p
Gender	2.00 (0.818-4.89)	0.129	-	-
WBC	1.042 (0.862-1.259)	0.674	-	-
MPV	0.738 (0.555-0.981)	0.036	0.668 (0.474-0.942)	0.022
PDW	0.984 (0.857-1.130)	0.818	-	-
Uric acid	0.614 (0.425-0.886)	0.009	0.592 (0.399-0.880)	0.01

WBC: White blood cell, MPV: Mean platelet volume, PDW: Platelet distribution width, CI: Confidence interval, OR: Odds ratio

single parameter level, whereas MPV and SUA had predictive value at multiple parameter levels. These results showed that SUA had a predictive value for vertigo.

Discussion

Vertigo is one of the most important and common health problems in emergency services. In addition, vertigo significantly reduces the quality of life in patients. Thus, there have been researches on the diagnosis and treatment of vertigo. In emergency services, its diagnosis is more important and researches on this area focus on diagnosis in order to prevent misuse of medical agents. The SRM-IV vestibular function diagnosis and treatment procedure helps in the diagnosis and treatment of BPPV (2). Moreover, oxidative stress has been reported to induce pathogenesis of BPPV (12). Thus, it can be argued that BPPV has a complex diagnostic procedure and risk factors. Some researchers reported that vertigo has a significant correlation with age, BMI and gender (13). In our study, gender and age distributions of patient groups were not statistically significant. This shows that the study cohort does not include age and gender effects on vertigo and this increases the reliability of the analysis results.

In the literature, researches on the relationship between BPPV and SUA can be classified into two groups. In the first group, researches argue that SUA is correlated with BPPV. In the second group, researches argue that BPPV patients have lower SUA levels, but the correlation is insignificant. Celikbilek et al. (14) reported that SUA level was positively correlated with BPPV. Similarly, Chang et al. (15) reported a relationship between vertigo and SUA. Yuan et al. (16) reported that SUA was lower in BPPV patients, but the difference was not statistically significant. In another research conducted by Yuan et al. (1), SUA levels of BPPV patients were found to be lower with an insignificant risk factor for BPPV. Jeong and Kim (17) reported that SUA was not a risk factor for idiopathic BPPV. In our study, PTC levels were lower in the vertigo group. The other blood parameters (WBC, MPV and PDW) were higher in the control group. Thus, it is recommended to evaluate SUA with MPV at multiple variables level.

Conclusion

In literature, there are studies arguing whether SUA is a risk factor for BPPV. In our study, analysis results are in accordance with the literature suggesting that SUA predicts idiopathic BPPV. In addition, PTC was also correlated with BPPV. On the other hand, both literature research groups with significant or insignificant correlation stated that SUA levels were lower in the BPPV patients. In this respect, it can be argued that the increasing number of researches and meta-analysis in this issue, and the increasing number of patient population may change the direction of the literature towards the significant correlation results. For emergency clinics, SUA for BPPV patients may help physician to predict or suspect for BPPV.

Ethics

Ethics Committee Approval: The research has been approved by the Ufuk University Ethics Committee on 26.02.2016 and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments (approval number: 26022016-2).

Informed Consent: No consent form was obtained from the patients due to retrospective nature of the study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

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

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

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References

1. Yuan J, Chen Y, Chen Y, Niu S, Li S, Dong Q, et al. Relationship between serum level of uric acid and benign paroxysmal positional vertigo. Zhonghua Yi Xue Za Zhi. 20153;95:344-8.
2. Wang N, Zhou H, Huang H, Geng D, Yang X, Yu C. Efficacy of SRM-IV Vestibular Function Diagnosis and Treatment System in Treating Benign Paroxysmal Positional Vertigo. Iran J Public Health. 2018;47:641-7.
3. Saeed BMN, Omari AF. Climatic variations and benign paroxysmal positional vertigo. J Otol. 2016;11:33-7.
4. Ferreira MM, Ganança MM, Caovilla HH. Subjective visual vertical after treatment of benign paroxysmal positional vertigo. Braz J Otorhinolaryngol. 2017;83:659-64.
5. Ribeiro KF, Oliveira BS, Freitas RV, Ferreira LM, Deshpande N, Guerra RO. Effectiveness of Otolith Repositioning Maneuvers and Vestibular

Rehabilitation exercises in elderly people with Benign Paroxysmal Positional Vertigo: a systematic review. Braz J Otorhinolaryngol. 2018;84:109-18.

6. Chin S. Visual vertigo: Vertigo of oculomotor origin. Med Hypotheses. 2018;116:84-95.
7. Huang X, Ng SY, Chia NS, Acharyya S, Setiawan F, Lu ZH, et al. Serum uric acid level and its association with motor subtypes and non-motor symptoms in early Parkinson's disease: PALS study. Parkinsonism Relat Disord. 2018;55:50-4.
8. Lin X, Xu L, Zhao D, Luo Z, Pan S. Correlation between serum uric acid and diabetic peripheral neuropathy in T2DM patients. J Neurol Sci. 2018;385:78-82.
9. Wu AH, Gladden JD, Ahmed M, Ahmed A, Flippatos G. Relation of serum uric acid to cardiovascular disease. Int J Cardiol. 2016;213:4-7.
10. Jun JE, Lee YB, Lee SE, Ahn JY, Kim G, Jin SM, et al. Relation of serum uric acid to cardiovascular disease. Atherosclerosis. 2018;272:233-9.
11. Bayar N, Küçükseymen S, Güven R, Erkal Z, Köklü E, Yüksel İÖ, et al. Association between serum uric acid and ischemic stroke in patients with non valvular paroxysmal atrial fibrillation. Int J Cardiovascular Academy. 2017;3:118-21.
12. Güçlütürk MT, Ünal ZN, İsmi O, Çimen MB, Ünal M. The Role of Oxidative Stress and Inflammatory Mediators in Benign Paroxysmal Positional Vertigo. J Int Adv Otol. 2016;12:101-5.
13. Filippopulos FM, Albers L, Straube A, Gerstl L, Blum B, Langhagen T, et al. Vertigo and dizziness in adolescents: Risk factors and their population attributable risk. PLoS One. 2017;12:e0187819.
14. Celikbilek A, Gencer ZK, Saydam L, Zararsiz G, Tanik N, Ozkiris M. Serum uric acid levels correlate with benign paroxysmal positional vertigo. Eur J Neurol. 2014;21:79-85.
15. Chang CC, Chang WN, Huang CR, Liou CW, Lin TK, Lu CH. The Relationship between Isolated Dizziness/Vertigo and the Risk Factors of Ischemic Stroke: A Case Control Study. Acta Neurol Taiwan. 2011;20:101-6.
16. Yuan J, Dai J, Li WA, Hu W. Factors Associated with Benign Paroxysmal Positional Vertigo: A Chinese Case-Control Study. Med Sci Monit. 2017;23:3885-9.
17. Jeong SH, Kim JS. The Effect of Serum Uric Acid in Generating Idiopathic Benign Paroxysmal Positional Vertigo. Research in Vestibular Science. 2010;9:27-31.

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Investigation of Aspiration Pneumonia and Respiratory Tract Complications in Cases Presenting to the Emergency Service with Intoxication: A Prospective Study

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Abstract

Aim: In this study, we aimed to investigate the frequency of aspiration pneumonia (AP) and factors affecting AP development in patients presenting to the emergency department with intoxication.

Materials and Methods: This single-center prospective study was conducted during one year in patients admitted to the emergency service of a tertiary hospital for intoxication within the first two hours. The data obtained during the study were analyzed statistically using the Statistical Package for Social Sciences (SPSS version 22.0). The results were expressed as mean ± standard deviation. Univariate statistical analysis was performed using chi-square test for categorical variables and Mann-Whitney U test for non-parametric data.

Results: Of the 50 acute poisoning cases included in the study, pneumonia developed in two cases (4%) in the study group within the first seven days and none of the patients in the control group had AP or respiratory complications. No significant difference was found between the study group and the control group in terms of AP development (p=0.113).

Conclusion: Based on the results of this study, it was considered that gastric lavage and activated charcoal administration were more closely associated with AP development in patients presenting with intoxication compared other AP risk factors such as age, lower Glascow coma scale, and antidepressant or antipsychotic overdose. Therefore, emergency physicians should be sensitive to such cases in order to reduce the duration of treatment and hospitalization of these patients.

Keywords: Aspiration pneumonia, intoxication, gastric lavage, activated charcoal

Introduction

Aspiration pneumonia (AP) is defined as acute lung infection following aspiration of high-pH oropharyngeal or upper gastrointestinal contents (1). The protective mechanisms deteriorate in case of altered consciousness that may occur in intoxication, gastric irrigation and activated charcoal administration; resulting in aspiration. In this study, we aimed to investigate the frequency of AP and the factors affecting AP development in patients presenting to the emergency department with intoxication.

Materials and Methods

For this single-center prospective study, the ethics committee approval was obtained from the Clinical Trials Ethics Commission (2011-61/2). The study was conducted during one year in patients admitted to the emergency service of a tertiary hospital for intoxication within the first two hours. The study group consisted of 50 patients with intoxication who underwent gastric lavage and activated charcoal administration in the emergency department, and the control group included 30 people who were referred to the same service with non-intoxication complaints and who did

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not undergo gastric lavage or activated charcoal administration. Written informed consent was obtained from patients who agreed to participate in the study. Cases associated with corrosive substances or inhalation, those under the age of 18 and those who did not agree to participate in the study were excluded (Figure 1).

Age, gender, absence or presence of risk factors for AP, time between intoxication and presentation to the emergency service, state of consciousness at admission, poisoning agent, complaints, vital signs, glasgow coma scale (GCS), treatment method, need for intubation, physical examination-laboratory findings within the first seven days and chest radiographs were recorded.

In the study group, the presence of at least one of the findings of rales, rhonchi, wheezing and purulent secretion on physical examination and leukocytosis in laboratory tests within the first seven days in addition to detection of infiltration on chest radiography were accepted as AP (2).

The data obtained during the study was analyzed statistically using the Statistical Package for Social Sciences (SPSS version 22.0). The results were expressed as mean ± standard deviation. Univariate statistical analysis was performed using chi-square test for categorical variables and Mann-Whitney U test for non-parametric data.

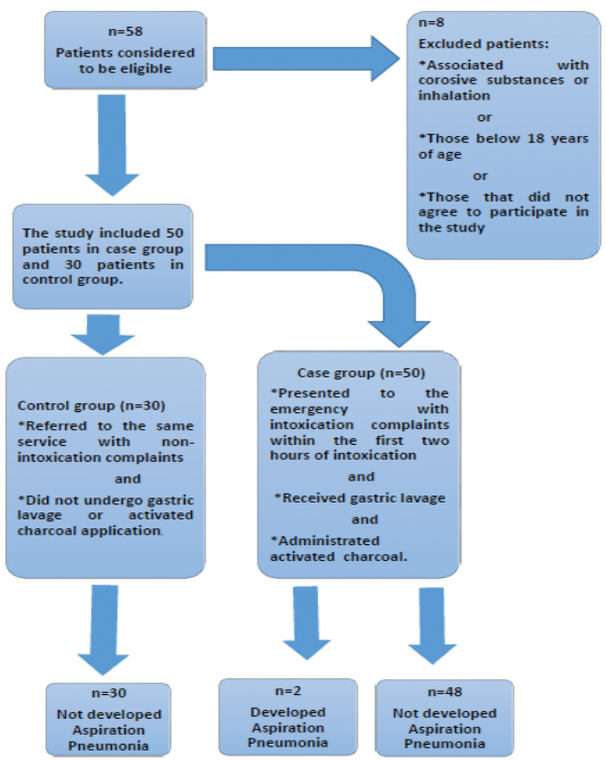

Figure 1. Flow chart

Results

Of the 50 acute poisoning cases included in the study, 80% (n=40) were female and 20% (n=10) were male. The age of the patients ranged from 18 to 76 years and the overall mean age was 28.12±11.20 years, with a mean age of 27.3±11.64 years in females and 30±9.56 years in males. Pneumonia developed in two patients (4%) in the study group within the first seven days, and none of the patients in the control group had AP or respiratory complications.

The cause of intoxication was noted as non-steroidal anti-inflammatory drugs or paracetamol in 38% (n=19), antidepressants or antipsychotics in 34% (n=17), antihypertensive drugs in 10% (n=5) and other drugs in 14% (n=7). The active substance of the drug could not be identified in the remaining two patients (4%).

The complaints of the patients in the study group were nausea in 44% (n=22), drowsiness in 22% (n=11), abdominal pain in 10% (n=5), palpitation in 4% (n=2), clouding of consciousness in 14% (n=7) and other symptoms in 6% (n=3).

Regarding vital signs of the intoxication cases, the mean systolic blood pressure was 110.3±18.25 mmHg and diastolic blood pressure was 69±12.49 mmHg. The mean heart rate was 89.66±14.78 beats per minute (bpm), with 89.43±15.65 bpm for women and 90.6±11.28 bpm for men. Of the 50 cases, 14 (28%) were followed up in the emergency department and 36 (72%) were hospitalized for treatment. Of the 36 patients admitted to the hospital, 29 (80.5%) were treated in the internal medicine service and seven (19.5%) were treated in the intensive care unit (Table 1).

In the control group, 56% of the patients (n=17) were female and 44% (n=13) were male. No pneumonia findings were detected in the first seven days in this group. The mean age of the control group was 33.77±13.86 years; with a mean age of 34.12±12.43 years for women and 33.42±11.25 years for men. For these patients, the reason for referral to the emergency department was headache in 40% (n=12), nausea and vomiting in 36% (n=11), minor trauma in 10% (n=3) and other causes in 13% (n=4).

In the group presenting to the emergency service with drug intoxication, GCS was 12 in two patients (4%), 13 in five patients (10%), 14 in six patients (12%), and 15 in 37 patients (74%). The GCS did not drop below 8 in any of the patients at admission or during follow-up and there were no problems with the preservation of the respiratory system, so intubation was not required for any of the patients.

All cases of acute intoxication were treated with gastric lavage and activated charcoal. The mean age was calculated as 26±13

years in patients without AP and 49.25±21 years in AP patients. It was determined that the patients who developed AP had an overdose of antidepressants and antipsychotics. In two AP cases, the GCS was 12. Eighty-six percent of drug intoxication cases (n=43) were in the 18-40 years age group. Radiological, laboratory or physical examination findings supporting AP were present in two cases (4%) with acute intoxication.

Table 1. Patient characteristics

Variable	Cases (n=50)
Age, years (min-max, mean age)	18.0-76.0, 28.12±11.20
Gender	
Female	80% (n=40)
Male	20% (n=10)
The causes of intoxication	
NSAIDs or paracetamol	38% (n=19)
Antidepressants or antipsychotics	34% (n=17)
Antihypertensive drugs	10% (n=5)
Other drugs	14% (n=7)
Unidentified	4% (n=2)
The complaints of the patients	
Nausea	44% (n=22)
Drowsiness	22% (n=11)
Abdominal pain	10% (n=5)
Palpitation	4% (n=2)
Clouding of consciousness	14% (n=7)
Other	6% (n=3)
Vital signs of the intoxication cases	
Mean systolic blood pressure (mmHg)	110.3±18.25
Diastolic blood pressure (mmHg)	69±12.49
Mean heart rate (beat/min)	89.66±14.78
Hospitalization	
Treated in the emergency department	28% (n=14)
Treated in the internal medicine service	58% (n=29)
Treated in the intensive care unit	14% (n=7)
Glasgow coma scale	
12	2 (4%)
13	5 (10%)
14	6 (12)
15	37 (74%)

NSAIDs: Nonsteroidal anti-inflammatory drugs

Table 2. The rate of aspiration pneumonia development in patients that presented to the emergency service with intoxication and treated with gastric lavage and activated charcoal

		Study group (n=50) (%)		Control group (n=30) (%)		p
AP	Present	2	4.0	0	0.0	0.113
	Absent	48	96	30	100	
	Total	50	100	30	100	

AP: Aspiration pneumonia

As a result of this study, no significant difference was found between the intoxication group including patients admitted to the emergency service with intoxication and treated with gastric lavage and activated charcoal, and the control group who did not undergo any procedures in terms of AP development (p=0.113) (Table 2).

Discussion

In two different studies investigating acute intoxication cases associated with drug overdose, the frequency of AP has been reported as 29-50% (3,4). In most cases of intoxication, it is not possible to know what type of substance(s) the patients had been exposed to at the time of presentation to the emergency service, immediate intervention and treatment (5). One of the primary objectives in the treatment of acute intoxication is to remove the toxic substance from the patient's body (6). For this purpose, irrigation of the stomach is an important treatment step to be undertaken within 30 minutes to one hour in symptomatic patients who have ingested the poison orally (7). However, gastric irrigation is contraindicated in cases where intoxication is caused by smaller amount of drugs, corrosive substances and hydrocarbons, and when there is a long period between intoxication and referral to the hospital and the airway is not well protected (8).

Pulmonary complications of gastric content aspiration are divided into three groups as particle-related, acid-related, and bacterial. Although the characteristic radiographic localization of AP may be observed in all segments of bedridden patients, it is most commonly seen in the upper segments of the lower lobes and the posterior segments of the upper lobes. However, it mostly develops in the basal segments of the lower lobes in non-bedridden patients (8). Sometimes bilateral or interstitial patterns may be seen. On chest radiographs, the findings are non-specific and may not be detected within a few hours (9). It may take 48-72 hours for the infiltration to become radiographically visible.

AP is not common in cases of acute intoxication, but it significantly increases mortality and morbidity (10). The diagnosis of AP is based on the presence of an infiltrative appearance on chest radiography accompanied by one of the clinical signs or risk factors of AP (11). In different studies, the rate of AP in acute intoxication cases was reported to be between 1.6% and 29%. In one study, the rate of AP development was reported as 29% in patients presenting with drug overdose (12). In another study by Isbister et al. (10), who examined 4,562 acute intoxication cases,

AP development rate was calculated as 1.6%. This rate was 4% in our study.

The risk of AP development is higher in older age than in younger people (8). It has been reported that dysphagia and dysmotility may be the causative agents in elderly patients with higher incidence of AP (13). Isbister et al. (10) noted the mean age as 44 years for patients with AP and 33 years for those who did not develop this complication. In the current study, patients over 40 years of age constituted 12% of all cases and 75% of patients who developed AP. We determined that the mean age of the patients with and without AP was 49.25±21 and 26±13 years, respectively.

There are many publications suggesting a close relationship between reduced consciousness and aspiration. It has been reported that the risk of AP development increases with decreased consciousness (14). Adnet and Baud (12) found that the rate of AP was 29% in drug overdose cases and that 85% had GCS below 15. Isbister et al. (10) reported that 95.9% of the acute intoxication cases had a GCS of 15 and that AP rate was 1.6%. The coughing and retching reflexes are important in protecting the patient from aspiration. These reflexes can be suppressed by altered level of consciousness. However, the relationship between the GCS and protective reflexes remains unclear. In their study, Adnet and Baud (12) reported that seven of 12 patients with a GCS of 3 had an intact cough reflex and that there was no relationship between the GCS and protective reflexes. In contrast, in another study, it was found that the retching reflex was not maintained even in cases with a relatively high GCS and that 15.4% of the patients with a GCS of 9 to 14 presented with symptoms indicative of AP (15). In cases where the airway is not well protected, the risk of AP increases despite high GCS values (12). In our study, two patients that developed AP had a GCS of 12, which is consistent with the literature.

In acute intoxication cases, gastric lavage is used to remove the toxic substance from the body. A review argues that the gastric lavage should not be done routinely for the treatment of poisoned patients and that it should only be done by appropriately trained or expert persons in rare cases where gastric lavage is required (16). It has been reported that endotracheal intubation is important in the prevention of aspiration in coma patients and that it should be taken as a preventive measure in patients with a GCS of 8 or below (17). The sample of the current study included patients referred to the emergency service within two hours, as this was the maximum period for the administration of activated charcoal. The lowest GCS was 12 and therefore, there was no need for intubation in any patient at admission or during follow-up (18).

Improper placement of a nasogastric tube also increases the risk of aspiration (8). In a study by Karataş (19), 3.4% of patients without nasogastric tube developed AP, but the rate of this complication increased threefold (10.7%) in cases where nasogastric tube was used. In the current study, the rate of AP development was determined as 4% in patients who underwent nasogastric intubation and activated charcoal administration.

Although activated charcoal is generally regarded as an inert substance, experimental research has shown that aspirated activated charcoal can cause parenchymal injury or bronchiolar obliteration in the lungs (16). Despite being rare, aspiration of activated charcoal results in a clinical picture that leads to respiratory failure and even death, and therefore, activated charcoal should not be administered to patients before initial checking and airway protection. In a study of patients who were poisoned with tricyclic antidepressants, activated charcoal was detected in bronchial secretions of one-fourth of the intubated cases (20). Some complications of activated charcoal in the gastrointestinal system have also been shown to be associated with aspiration (21).

Spontaneous or conscious vomiting is common in patients with acute intoxication. Vomiting is a protective reflex, as well as a treatment method in this patient group. Eighteen percent of the patients in our study vomited at least once at admission or after admission to the emergency service. However, there was no significant difference in AP development between the groups with and without a history of vomiting.

Study Limitations

The most important limitation of the study is related to single-center design. Another limitation is that all patients had a GCS of 12 or above. Furthermore, due to the sample selection criterion of referral to the emergency department within the first two hours for the administration of gastric lavage and activated charcoal, the toxic effect of the ingested drug was not sufficient to further reduce GCS. Another factor for higher GCS may be the developed prehospital health services and transportation facilities in our province, possibly reducing the time between intoxication and admission to the hospital.

Conclusion

In this study, there was no significant difference between the study group that presented to our emergency service with intoxication and received gastric lavage and activated charcoal and the control group in terms of the risk of AP development. However, two patients that developed AP were older and had a lower GCS than the patients without AP. In addition, both AP cases were intoxicated by antidepressants and antipsychotics. Therefore, physicians should consider the possibility of AP development in cases of advanced age, lower GCS, and

antidepressant or antipsychotic overdose. It should also be remembered that although the possibility of AP development is higher in patients with a GCS of 8, this complication can also occur in individuals with a normal level of consciousness, and that endotracheal intubation may not always fully protect the respiratory tract. Unnecessary nasogastric tube insertion, gastric lavage and activated charcoal administration can also increase the risk of AP development in acute intoxication cases.

Based on the results of this study, it is considered that gastric lavage and activated charcoal administration are more closely associated with development of AP compared to the other AP risk factors such as age, lower GCS, and antidepressant or antipsychotic overdose in cases presenting with intoxication. Therefore, emergency physicians should be sensitive to such cases in order to shorten the duration of treatment and hospitalization of patients.

Acknowledgements

This study was produced from the thesis prepared by the first author under the supervision of the second author. In addition, this study was presented as an oral presentation at the 23rd İstanbul Emergency Medicine Winter Symposium held between 15-17 February 2019 in İstanbul.

Ethics

Ethics Committee Approval: Haydarpaşa Numune Training and Research Hospital Clinical Trials Ethics Commission (2011-61/2).

Informed Consent: It was taken.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: İ.T., A.D.A., Concept: İ.T., A.D.A., Design: İ.T., A.D.A., Data Collection or Processing: İ.T., A.D.A., Analysis or Interpretation: İ.T., A.D.A., Literature Search: İ.T., A.D.A., Writing: İ.T., A.D.A.

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

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References

1. DiBardino DM, Wunderink RG. Aspiration pneumonia: A review of modern trends. J Crit Care. 2015;30:40-8.
2. Liisanantti J, Kaukoranta P, Martikainen M, Ala-Kokko T. Aspiration pneumonia following sever self poisoning. Resuscitation. 2003;56:49-53.
3. Montassier E, Le Conte P. Aspiration pneumonia and severe self-poisoning: About the necessity of early airway management. J Emer Med. 2012;43:122-3.
4. Marik PE, Careau P. The role of anaerobes in patients with ventilator-associated pneumonia and aspiration pneumonia: A prospective study. Chest. 1999;115:178-83.
5. Erickson TB, Thompson TM, Lu JJ. The approach to the patient with an unknown overdose. Emerg Med Clin Nort Am. 2007;25:249-81.
6. Frithgen IL, Simpson WM Jr. Recognition and management acute medication poisoning. Am Fam Physician. 2010;81:316-23.
7. Stan KB, Jason EW, Douglas SM. Applied pharmacology: Toxicology. USA, Saunders; 2011.p.59-74.
8. Maloney G, Anderson E, Yealy DM. Pneumonia and Pulmonary Infiltrates In: Tintinalli JE, Stapczynki JS, Ma OJ, Yealy DM, Meckler GD, Cline DM, editors. Emergency Medicine A Comprehensive Study Guide. 8th ed. New York: McGraw-Hill; 2016.p.445-56.
9. Raghavendran K, Nemzek J, Napolitano LM, Knight PR. Aspiration-induced lung injury. Crit Care Med. 2011;39:818-26.
10. Isbister GK, Downes F, Sibbritt D, Dawson AH, Whyte IM. Aspiration pneumonitis in overdose population: Frequency, predictors and outcomes. Crit Care Med. 2004;32:88-93.
11. Russell CD, Koch O, Laurenson IF, O'Shea DT, Sutherland R, Mackintosh CL. Diagnosis and features of hospital-acquired pneumonia: a retrospective cohort study. J Hosp Infect. 2016;92:273-9.
12. Adnet F, Baud F. Relation betvveen Glasgow coma scale and aspiration pneumonia. Lancet. 1996;348:123-4.
13. Marik PE. Aspiration pneumonitis and aspiration pneumonia. N Engl Med. 2001;344:665-71.
14. Chang HS, Jin WH, Dong WS, Bum JO, Kyoung SL, Won YK. Aspiration Pneumonia in Carbon Monoxide Poisoning Patients with Loss of Consciouness: Prevalence, Outcomes, and Risk Factors. Am J Med. 2017;130:1465.
15. Moulton C, Pennycook AG. Relation betvveen Glasgow coma score and cough reflex. Lancet. 1994;343:1261-2.
16. Rotheray KR, Cheung PSY, Cheung CSK, Wai AKC, Chan DYS, Rainer TH, et al. What is the relationship between the Glasgow coma scale and airway protective reflexes in the Chinese population? Resuscitation. 2012;83:86-9.
17. Benson BE, Hoppu K, Troutman WG, Bedry R, Erdman A, Höjer J, et al. Position paper update: gastric lavage for gastrointestinal decontamination. Clin Toxicol (Phila). 2013;51:140-6.
18. Eizadi-Mood N, Saghaei M, Alfred S, Zargarzadeh AH, Huynh C, Gheshlaghi F, et al. Comparative evaluation of Glasgow Coma Score and gag reflex in predicting aspiration pneumonitis in acute poisoning. J Crit Care. 2009;24:470.
19. Karataş AD. Akut Zehirlenme Olgularında Aspirasyon Pnömonisi Sıklığı ve Nedenleri. Samsun Ondokuz Mayıs Üniversitesi Acil Tıp ABD Uzmanlık Tezi; 2006.
20. De Weerdt A, Snoeckx A, Germonpre P, Jorens PG. Rapid-onset adult respiratory distress syndrome after activated charcoal aspiration. A pitch-black tale of a potential to kill. Am J Respir Crit Care Med. 2015;191:344-5.
21. Eroğlu F, Yavuz L, Topal M et al. Pulmonary aspiration during treatment by activated charcoal. SDÜ Tıp Fak Derg. 2009;16:29-31.

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Bangladesh National Drug Policy 1982-2016 and Recommendations in Policy Aspects

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Abstract

Science is progressing a lot in recent years. Remarkable advances have been achieved in the field of health care technology. However, unfortunately, medicines are still the only hope for treating diseases for thousands of people in developing countries around the world. An effective National Drug Policy might be a lifesaving step for many people in these countries. Fortunately, that happened in Bangladesh after the 1982 Drug Policy. In the meantime, the country has further editions of that policy, which were National Drug Policy 2005 & 2016. In this article, this research will discuss the comparative impact scenario of these policies in Bangladesh. Readers will know the past and present of the National Drug Policy of Bangladesh and will be able to assume the future of this policy in Bangladesh.

Keywords: Bangladesh, National Drug Policy, 1982, 2005, 2016

Introduction

This study used the search terms "National Drug Policy (NDP), Bangladesh", "NDP Bangladesh", "Bangladesh National Drug Policy" etc. for searching in PubMed and Google scholar search engine for the literature review. Researchers also collected information from different books collected from Bangabandhu Sheikh Mujib Medical University, National Institute of Preventive and Social Medicine, Gonoshasthaya Kendra library of Dhaka, Bangladesh.

National Drug Policy

The World Health Organization (WHO) defines NDP as "a comprehensive framework in which each component plays an important role in achieving one or more of the general objectives of the policy (access, quality, and rational use)" (1). The policy must have the self-assurance of the several penalty area and purposes, generating a comprehensive and reliable existence. The system should address access to essential medicines (EMs). Essential medicine was defined in 1977 as "medicines that are of utmost importance, and are basic, indispensable and necessary for the health needs of the population" (2). In 2002, EMs were again redefined as "EM are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence of efficacy, safety, and comparative cost-effectiveness. EM are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. The implementation of the concept of EMs is intended to be flexible and adaptable to many different situations; exactly which medicines are regarded as essential remains a national responsibility" (2). It is often explained that such access to EM could be achieved through the promotion of rational use of medicines (RUM), reasonable prices, workable sponsoring, and consistent health and supply systems. Similarly, RUM depends on various issues, such as the careful and scientific selection of medicines, regulatory procedures, informative and

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educational interventions, and financial enticements (1). A NDP has also been described as "an assurance to an objective and an escort for a struggle to ensure the rights of the people". The NDP states the medium- to long-term goals of the national government for the pharmaceutical industries and ascertains the principal line of attack for achieving the aims. It offers an outline in which the accomplishments of the pharmaceutical sector can be synchronized. The NDP deals with both public and private segments of pharmaceutical issues and comprises all the notable thespians of this medicine-producing arena (3).

Why Does the Country Need a National Drug Policy?

Medicines play the most critical role in the care, protection, and reestablishment of the health of the citizens of any country. All governments around the world are highly concerned about the availability of medicines with appropriate quality, adequate amounts and in affordable price for ordinary people especially in low and middle-income countries (LMIC) (4-6). There are reports of irrational prescribing and drug use with poor availability of EMs, particularly in LMIC, and this also applies to poorer communities of the developed world (7-10). Moreover, about 90% of citizens of developing and emerging countries obtain medication from their out-of-pocket expenses when compared to developed nations (11,12). Thereafter, the most important requirements for a NDP are to present different government commitments, to define pharmaceutical sector goals and objectives, to identify priority areas of action, to identify national strategies to achieve national goals, to identify stakeholders of implementation and finally to organize a national forum of discussion on the priority issues (3).

According to WHO, the General Objectives of a National Drug Policy are to Ensure

- Access: equitable availability and affordability of EMs.
- Quality: the quality, safety, and efficacy of all medicines.
- Rational use: the promotion of a therapeutically sound and cost-effective method of drugs by health professionals and consumers (1,13).

National Drug Policy of Bangladesh

Bangladesh won its independence on December 16, 1971. During the birth of the country, the socio-economic infrastructural situation was fragile. Before independence, it was reported that 60-70% of drugs were imported from West Pakistan, because most of the pharmaceutical industry were mainly located in the western part of Pakistan (14). After independence, it became a great challenge for the Government of Bangladesh to ensure the availability and accessibility of EMs. Despite this crisis due to lack of drug policy, the market was full of unnecessary drugs. The plight of EMs was first critically identified in the country's first five-year plan in 1973 (14). After this blueprint, multiple industries started importing finished medicine products on a large scale that were packaged and marketed locally in Bangladesh. These local industries were actually representing and acting for some overseas pharmaceutical companies. Additionally, poor quality control was observed, mainly for drugs with doubtful efficacy and counterfeit medicine (15). The country has gone through several stages of policy development programs for drug policy, which ultimately delivered a deep-seated, comprehensive, public-friendly NDP in 1982, as the effort made in 1973 did not work efficiently (16-18). The honorable attempt in 1973 to formulate the drug policy to improve the situation failed due to the tragic assassination of the country's father of the nation and President Bangabandhu Sheikh Mujibur Rahman in 1975 (15).

Bangladesh National Drug Policy 1982

Bangladesh NDP 1982 is an epoch-making event in the history of Bangladesh. Before 1982, there was no NDP in Bangladesh (19). The medicine market in Bangladesh was filled with unnecessary, harmful, and unsafe medicines before NDP 1982 and multinational companies were controlling the pharmaceutical markets of Bangladesh (17,20). Only 14 countries, including Bangladesh, had NDP in 1982 (21,22). On April 27, 1982, an expert committee was formed. Expert Committee consisted of renowned academicians, regulatory personnel, and health activists (23). Bangladesh NDP 1982 was highly praised by WHO and other international organizations at that time (15,20). After that, the glory of Bangladesh has increased in relation to the policy (13).

The Work (Report) of the Expert Committee

A highly knowledgeable, proficient and professional commission was formed to develop NDP. This commission worked very methodically, spending over 1000 business hours to build the policy, which was tabled to the Ministry of Health on the auspicious day May 11, 1982 (15).

This commission undisputedly formulated 16 principles to appraise all currently available medical, medicinal, pharmacological and therapeutic products, and new drugs applied for cataloging or approved (15).

The Sixteen Principles

1. The combination of antibiotics will be prohibited. The combination of antibiotics with glucocorticoid or other similar active ingredients will be banned. Harmful liquid forms of antibiotics (e.g., tetracycline) will be banned. Tetracycline may hamper bone growth and may cause discoloration of teeth of a child. Combinations of antibiotics have no therapeutic advantage; instead, it promotes more adverse effects.

2. The combination of analgesics will be prohibited. The combination of analgesics with iron, vitamins, or alcohol will also be banned. Analgesic combinations promote adverse events, and their therapeutic value is dubious in nature. Another problem in combination medicine is if a dose adjustment is required in case of any single or multiple elements, then it would be impossible as the components remain is fixed strength in combination forms.

3. Due to the risk of addiction or dependency, any combination form of codeine will not be allowed.

4. In general, combinations can be allowed if there is absolutely no alternative single drug available for treatment or if no alternative single drug is cost-effective, for the purpose.

5. Certain exceptions will be made in the cases of eye, skin, respiratory and hemorrhoidal preparations, co-trimoxazole, oral rehydration salts, antimalarial, iron-folic, etc., as well as certain vitamin preparations, allowing combinations of more than one active ingredient in one product.

6. Vitamins must be formulated as a particular/individual component products, except for B complex. B12 should always be produced as a single-ingredient injectable product. The combining of Vitamins with any other ingredient such as minerals, glycerophosphate, etc., will also be prohibited. The liquid form of vitamins was prohibited in order to prevent the wastage of resources used to produce liquid vitamins, because it has no beneficial impacts on health.

7. Cough syrups, throat pastilles, gripe water, alkalis, and etc. production will be prohibited due to their questionable scientific efficacy.

8. The sale of tonics, enzyme mixtures/preparations, and alleged recuperative and invigorating products should be discontinued. However, pancreatin and lactase may be manufactured and/or imported as single-ingredient products. Tonics were prohibited because there was a significant amount of alcohol in tonics that may cause addiction or dependency.

9. Me-too drugs will not be allowed. Me-too drugs are those drugs that have the same or almost the same efficacy but have non-significant structural dissimilarity.

10. Medicine with uncertain, petite or no healing and beneficial significance, and to a certain degree, from time to time detrimental, dangerous for human health, and often increases the possibility of misuse, will be debarred and proscribed.

11. All prescription chemicals and galenical preparations, which are included in the latest edition of the British Pharmacopeia or the British Pharmaceutical Codex, will be approved.

12. Considering the favorable risk:benefit ratio; certain medicine, despite known severe adverse effects and the possibility of misapplication, may be manufactured in a small amount for limited and regulated use. These medicines will be prescribed by medical specialists only.

13. The medicines, which can be produced by national medicine industry, should not be imported in order to protect the medicine industry of Bangladesh. However, if local production is far short of need, this condition may be relaxed in some cases.

14. A primary pharmaceutical raw material, which is locally manufactured, will be given protection by disallowing it or its substitute to be imported if sufficient quantity is available in the country. The role of multinationals in providing medicine for this country is acknowledged with appreciation. In view of the caliber of machinery and technical know-how which lies in their hands for producing important and innovative drugs for the country. Easily producible drugs such as antacids and vitamins will be produced by only national companies. So that the large transnationals and corporations can focus their energies and capitals on those medicines not so straightforwardly manufactured by smaller domestic pharmaceutical industries.

15. Foreign brands were not allowed to manufacture under authorization in any pharmaceutical industry in Bangladesh if the identical or comparable medicines are existing/manufactured in Bangladesh, as this leads to superfluously high prices and imbursement of royalties. In the light of this policy, all existing licensing agreements should be reviewed.

16. According to the policy, “Third Party Licensing” will not be allowed. Under the third party licensing a company can manufacture and distribute drugs in the market.

The first eleven principles were established completely on scientific perceptive, although, the Principle 14 was based on political and economic thoughts. The remaining four principles (12, 13, 15, and 16) were considered for the assistance and growth of the homegrown, domestic pharmaceutical manufacturing plant. There were 166 approved medicinal and therapeutic products available in Bangladesh during the development and promotion of NDP-1982. Interestingly, 122 multinational pharmaceutical industries were exporting medicines to the country from 23 countries. Additionally, 4,340 medicinal products were approved. These products were either produced locally or imported. The commission banned 1,742 medicinal products by utilizing 16 principles of NDP-1982, as these medicines were either ineffective or non-essentials.

These banned 1,742 medicines were placed in one of three categories (15):

Schedule I: Production of these drugs was to be stopped immediately and stocks were to be collected from pharmacies and destroyed within three months of the acceptance of the report.

Schedule II: These drugs were to be reformulated within six months on the basis of the guidelines suggested by the committee.

Schedule III: A maximum of nine months was allowed for using up stocks of these drugs.

Importation of raw materials for Schedule I and II drugs was prohibited (15).

Significant Recommendations of NDP-1982 (15)

1. Establish an essential list of 150 EMs and a supplementary list of 100 specific drugs. The basic list was subdivided into three levels of use: 12 drugs for village workers; 45 medications for primary health care; and all 150 drugs for tertiary care,

2. Use generic names for the manufacture,

3. Prepare and publish a National Formulary by 1983,

4. Eliminate product patents and limit the use of process patents,

5. Revise the 1940 Drugs Act to include:

a. A registration system for Ayurvedic, Unani and homeopathic medicines;

b. Implementation of good manufacturing practices (GMP), together with ample quality control;

c. Regulating labeling and promotional activities;

d. Price control;

e. Prescription control of toxic/poisonous and abusing medicine;

f. Establishing of specialized medicine courts and substantial punishments;

g. Regulation of technology transfer and licensing agreements with foreign collaborators;

h. Restriction of ownership of retail pharmacies to professional pharmacists only;

6. Set up a National Drug Control Laboratory by 1985,

7. Commission report advised to ban multinational pharmaceutical industry from manufacturing simple medicine like common analgesics, vitamins, antacids,

8. All public hospitals should institute registered retail pharmacies under the supervision of qualified pharmacists,

9. Strengthen the Drug Administration administrative capacity by educational interventions among drug inspectors up to the lowest public administrative level of the country (15).

Impacts of National Drug Policy 1982 (16)

1. Local production of allopathic, traditional and complementary alternative drugs increased substantially.

2. Availability of EMs also increased remarkably with the increase in the volume of local production of all types of recognized drugs, the monetary value of which grew from Taka 1730 million in 1981 to about Taka 41000 million in 2002.

3. Local companies increased their production share from 30% in 1970 to more than 80% in 2002.

4. Drug prices stabilized, increasing (practically a drop-in cost in real times) by only 20%, compared to an increase of 179% in the consumer price index. This made drugs more affordable to consumers.

5. The quality of the products was improved, and the proportion of substandard drugs fell from 36% in 1970 to just 2% in 2002.

6. The volume of imported drugs and medicine in the country reduced drastically.

7. Commendable progress occurred in the research, education, and manufacturing of Unani, Ayurvedic, and Homeopathic-Biochemic systems of medicine.

8. The less dependency on imports and prioritization of useful drugs saved the country approximately US$ 600 million every year.

9. Bangladesh, a drug importing country, has become a drug exporting country (16).

According to NDP-1982, producers were compelled to produce EMs. There was a specific instruction that 60% of their total production would be EMs and price of EMs were fixed by the Government of Bangladesh. The cost of medicine depends on elements of expenditure on production and other factors. During the 1982 policy, experts considered five categories of elements of expenditure to fix up the price of EMs. NDP-1982 has effectively ended to transfer pricing and over-invoicing for imports of capital machinery, raw materials, and packaging materials. Without scientific evidence, combination of drugs was strictly prohibited in NDP-1982. Transnational Companies were strictly prohibited from producing medications that can be produced with more accessible technology. It was implemented according to NDP-1982 to promote the growth of national pharmaceutical market (15,24,25).

National Drug Policy 2005

Price protection was relaxed in Bangladesh by NDP-2005 (26,27). Afterward, the pharmaceutical owners and manufacturers took the opportunity to increase the prices of medicines, including EMs, to maximize their profit. Moreover, drug pricing in middle, and low-income countries is an essential and antagonistic issue. Since most patients do not have or cannot afford any insurance coverage and need to pay in person for their medicine, pricing proportionate with income status is significant to bear the cost (28). The third-party licensing restriction was relaxed to encourage the expansion of the pharmaceutical industry. The national companies started facing a tremendous challenge. NDP-2005 committee consisted of mainly pharmaceutical industrialists. The Committee focused principally on expanding their business without considering safety, efficacy, and affordability of EMs. There were no specific obligations regarding EMs production (27). Also, there were no special instructions regarding EMs pricing in NDP-2005 (27). Similarly, there was no clear-cut direction regarding combination drugs in NDP-2005, but the combination drugs were banned in NDP-1982 except for an exceptional need (27). In 1995, the government made a list of 117 EMs by a special communiqué. This meant that 33 type of EMs remained out of the EMs list and these drugs became open to price increases by the pharmaceutical industries. There were no specific instructions on the prohibition of production of medicines that could easily be produced by national companies in NDP-2005. There were no clear instructions regarding combination drug production in NDP-2005. Nevertheless, policymakers argued that if any combination medicine could be used in developed countries, then it could enter into national drug market. Finally, it can be concluded that the purity of NDP-1982 was destructed by NDP-2005 (14,23).

National Drug Policy 2016

In NDP-2016, Bangladesh government made a list of priority medicines consisting of 285 medicines (29,30). It also included ayurvedic, herbal, and homeopathic medicines. It was not a scientifically sound decision. NDP-2016 discourages registration of combination drugs. However, there is no clear-cut restriction on the production of combination drugs. There are no specific restrictions in NDP-2016, on not including pharmaceutical industrialists in the policy revision committee (27).

A Few Recommendations for Improving the Situation

Bangladeshi consumer needs to be aware of availability, accessibility, safety, and the efficacy of EMs for the successful implementation of an NDP. A community awareness campaign can be initiated to create community demand. To ensure good manufacturing practice, "Directorate of Drug Administration" should be strengthened by providing manpower, adequate lab facilities, commanding and administration power and financial resource flow, so that they can perform sustainably. We can reinforce our "Essential Drug Company Limited" by proving adequate manpower and logistics. Routine update list of EMs by "Expert Committee" consists of scientists, pharmacologists, and economists. Implementation of strict price controlling mechanism by the Government of Bangladesh is required. Currently, Bangladesh imports 80-90% active pharmaceutical ingredients, and it is the primary component that increases drug price in the country (31,32). The country should produce APIs locally; otherwise, self-sufficiency will not be achieved.

Ethics

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.E.M., M.H., Concept: M.E.M., M.H., Design: M.E.M., M.H., Analysis or Interpretation: M.E.M., M.H., Literature Search: M.E.M., M.H., Writing: M.E.M., M.H.

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References

1. World Health Organization. How to Develop and Implement a National Drug Policy. Second Edition. 2001. Available at http://apps.who.int/medicinedocs/en/d/Js2283e/4.1.3.html [Accessed December 2, 2018]
2. World Health Organization. The selection and use of essential medicines. Report of the WHO Expert Committee, 2002 (including the 12th Model list of EMs). World Health Organ Tech Rep Ser. 2003;914:1-126.
3. World Health Organization. Making Drug Policy a Development Priority A Strategy Paper & Six Country Stories. 1995. Available at: http://apps.who.int/medicinedocs/en/m/abstract/Js19174en/ [Accessed November-16-2018]
4. Ahmadiani S, Nikfar S. Challenges of access to medicine and the responsibility of pharmaceutical companies: a legal perspective. Daru. 2016;24:13.
5. Hoebert JM, van Dijk L, Mantel-Teeuwisse AK, Leufkens HG, Laing RO. National medicines policies - a review of the evolution and development processes. J Pharm Policy Pract. 2013;6:5.
6. Kanji N, Hardon A, Harnmeijer JW, Mamdani M, Walt G. Drugs Policy in Developing Countries. London: Zed Books; 1992.p.136.
7. Frisher M, Martino O, Crome I, Croft P. Trends in drug misuse recorded in primary care in the UK from 1998 to 2005. J Public Health (Oxf). 2009;31:69-73.
8. Mao W, Vu H, Xie Z, Chen W, Tang S. Systematic review on irrational use of medicines in China and Vietnam. PLoS One 2015;10:e0117710.
9. Ofori-Asenso R, Agyeman AA. Irrational Use of Medicines-A Summary of Key Concepts. Pharmacy (Basel). 2016:4.
10. Zaidi S, Bigdeli M, Aleem N, Rashidian A. Access to Essential Medicines in Pakistan: Policy and Health Systems Research Concerns. PLoS One. 2013;8:e63515.

11. Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. Lancet. 2009;373:240-9.
12. Kanavos P, Das P, Durairaj V, Laing R, Dele Olawale Abegunde DO. Options for financing and optimizing medicines in resource-poor countries. World Health Report (2010) Background Paper, No 34. Health System Financing. The Path of Universal Coverage. World Health Organization. 2010. Available at http://www.who.int/healthsystems/topics/financing/healthreport/34Medicinesrev.pdf [Accessed December 2, 2018]
13. Chowdhury FR, Ahasan HA, Rahman MM. National Drug Policy of Bangladesh: Some Pitfalls in Implementation. J Coll Physicians Surg Pak. 2006;16:368-70.
14. Islam N. Purity Poisoned. 1st ed. Dhaka: Momin Offset Press, 2007.
15. Chowdhury Z. Bangladesh: A Tough Battle for a National Drug Policy. Available at: http://apps.who.int/medicinedocs/documents/s19176en/s19176en.pdf [Accessed December 3, 2018]
16. Ministry of Health & Family Welfare. Governments of Peoples of the Republic of Bangladesh. National Drug Policy 2005. Bangladesh Gazette, 440-453, 2005. Available at http://apps.who.int/medicinedocs/documents/s17825en/s17825en.pdf [Accessed December 3, 2018]
17. Islam N. On a national drug policy for Bangladesh. Trop Doct. 1984;14:3-7.
18. Azam M. Intellectual Property And Public Health In The Developing World. Cambridge, UK: Open Book Publishers, 2016. Available at http://biblio.unibe.ch/download/eldiss/14azam_m.pdf [Accessed December 3, 2018]
19. Srinivasan S. 'Singing about the Dark Times': Bangladesh Drug Policy. Econ Polit Wkly. 1996;31:1252-5.
20. Reich MR. Bangladesh pharmaceutical policy and politics. Health Policy Plan. 1994;9:130-43.
21. Chowdhury FR, Bari MS, Khan MI. Implementation of National Drug Policy in Different Countries: An Appraisal and Experience from Bangladesh. J Bangladesh Coll Phys Surg. 2011;29:177-9.
22. Chowdhury FR, Muktadir MA, Chowdhury MA. National drug policy of Bangladesh 1982 & 2005-effective implementation is must for peoples will (Bengali Article). Journal of Bangladesh Asiatic Society. 2007; 15 (Winter): 297-308. Available at https://www.researchgate.net/publication/277662077_National_drug_policy_of_Bangladesh_1982_2005-effective_implementation_is_must_for_peoples_will_Bengali_Article [Accessed December 4, 2018]
23. Chowdhury Z. The Politics of Essential Drugs. The Makings of a Successful Health Strategy: Lessons from Bangladesh. London: 1st ed. Zed Press; 1995.
24. Chowdhury N, Kabir ER. Per pill price differences across therapeutic categories: A study of the essential drug brands marketed by multinational and local pharmaceutical companies in Bangladesh. Afr J Mark Manage 2009;1:220-6.
25. Sarowar MG, Bhattarai N, Jain P, Bochenek T. The characteristics of the current drug policies in India, Nepal, and Bangladesh. Leki Za Granic 2008; 6 (1-2): 43-51. Available at http://www.ejournals.eu/sj/index.php/ZNOZ/article/viewFile/5862/5784 [Accessed December 4, 2018]
26. Ministry of Health and Family Welfare, Bangladesh. National Drug Policy, 2005. Public Health Section-1. 2005. Available at http://www.clcbd.org/document/download/53.html [Accessed on December 4, 2018]
27. Hamid SA. Drug Policy of 1982. The foundation of the industry was created. Special Number / Development Omnibus 2, Bonik Barta, 2018 [Accessed December 5, 2018]
28. Danzon PM, Mulcahy AW, Towse AK. Pharmaceutical pricing in emerging markets: effects of income, competition, and procurement. Health Econ. 2015;24:238-52.
29. Directorate General of Drug Administration (DGDA), Ministry of Health & Family Welfare. National Drug Policy 2016. DGDA. Ministry of Health & Family Welfare, Bangladesh. Available at http://www.dgda.gov.bd/index.php/2013-03-31-05-16-29/guidance-documents/205-national-drug-policy-2017-with-essential-drug-list-and-otc-list/file [Accessed December 4, 2018]
30. Tusher HJ. Updated drug policy Okayed by the cabinet. The Daily Star, 2016. Available at https://www.thedailystar.net/frontpage/cabinet-okays-updated-drug-policy-1332568 [Accessed December 4, 2018]
31. Muyeen NM. The growth of Pharmaceutical Company in Bangladesh. Bachelor's Thesis. Department of Pharmacy, Daffodil International University. Available at http://dspace.daffodilvarsity.edu.bd:8080/bitstream/handle/20.500.11948/1866/P05743.pdf?sequence=1&isAllowed=y [Accessed on December 4, 2018]
32. Islam S, Rahman A, Al-Mahmood AK. Bangladesh Pharmaceutical Industry: Perspective and Prospects. Bang J Med Sci. 2018;17:519-25.

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Bougie-facilitated Intubation in Penetrating Neck Injury

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Abstract

A young male patient with a history of schizophrenia was admitted to the emergency department after suicide attempt. He slashed his neck with a broken glass and this resulted in a wound in zone II exposing laryngeal structures. The vocal cords could be visualized through the wound. Intubation over a bougie was successful after well tropicalizing the patient's airway. The patient was taken for immediate tracheostomy and reconstruction.

Keywords: Penetrating, neck, intubation

Introduction

Airway management is a continuous learning experience. Trauma victims form a significant number of challenging cases in emergency departments (1-3). Penetrating neck trauma is a scenario in which the emergency physician needs to be proactive to improvise certain tricks that may save a patient's life (4-6).

Case Report

The present case was a 30-year-old male patient with a history of schizophrenia. He had suicidal thoughts until the night before his presentation to the emergency department. He was taken to his psychiatrist to address this issue, however, the physician changed his medications and discharged him.

On the following day, the patient broke a glass bottle and attempted suicide by slashing his neck. The patient's family found him in his room, still breathing in a pool of blood. Emergency medical service was called and he was transferred to our department.

Upon arrival to the emergency department, the patient was surprisingly quiet, with a GCS of 12, heart rate of 110 bpm, blood pressure of 105/70 mmHg, respiratory rate of 20/min, O_2 saturation of 96% with 10 liters face mask. There was a big dressing on his neck to cover the wound.

Upon exploration of the wound, there was no active bleeding or hematoma. However, a leaking air sound was noticed, which turned our to be a damaged laryngeal structure. Multiple cartilage debris was found in the explored wound.

At this point, the team decided to secure the patient's airway immediately. The following steps were done:

- Exploring the wound for foreign bodies and removal of those that could be aspirated through the damaged larynx. These included parts of the laryngeal cartilage.
- Pre-oxygenation: A non-rebreather oxygen mask was applied on patient's face. As the patient was breathing through the damaged larynx, we applied another non-rebreather oxygen mask over the neck wound.
- As the vocal cords were visualized, topicalization with lidocaine spray was started through the open wound.
- Gentle introduction of Bougie stylet through the visualized vocal cords. When the tracheal rings were felt, a size 7, cuffed endotracheal tube was introduced.

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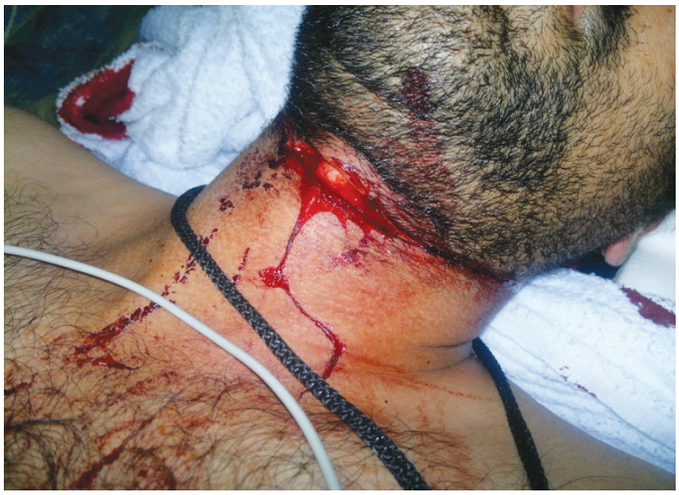

Figure 1. The patient's neck upon exposure, showing a cut wound with exposed larynx

- Sedation and muscle paralysis were initiated.
- Placement was secured and air leaks were tested negative.

The patient was taken to operating room by the surgical team to secure a tracheostomy, which was done successfully. Multiple reconstructive surgeries were performed to reconstruct the laryngeal structure using cartilage implants. His tracheostomy was closed after a few months. His psychiatric status was controlled by more aggressive therapeutic interventions.

This case had the IRB approval no RJ13/025/J, and the article was written in accordance with methods/methodical section of the Ethical Principles for Medical Research (amended in October 2013).

Discussion

The injuries affecting soft tissues during penetrating or blunt trauma can result in soft tissue distortion, damage to major structures, and thus lead to lethal results if not addressed in a timely and accurate manner. Neck trauma with airway injuries is a critical condition requiring immediate action to secure the airway in the best and fastest possible way. Timely interventions to keep the airway intact are the cornerstone of obtaining positive results with no organ or function loss (7,8).

Ethics

Ethics Committee Approval: Ethical Principles for Medical Research (amended in October 2013).

Informed Consent: It was taken.

Peer-review: Externally and internally peer-reviewed.

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

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

References

1. Evans C, Chaplin T, Zelt D. Management of Major Vascular Injuries: Neck, Extremities, and Other Things that Bleed. Emerg Med Clin North Am. 2018;36:181-202
2. Tessler RA, Nguyen H, Newton C, Betts J. Pediatric penetrating neck trauma: Hard signs of injury and selective neck exploration. J Trauma Acute Care Surg. 2017;82:989-94.
3. Madani A, Pecorelli N, Razek T, Spicer J, Ferri LE, Mulder DS. Civilian Airway Trauma: A Single-Institution Experience. World J Surg. 2016;40:2658-66.
4. Madsen AS, Laing GL, Bruce JL, Clarke DL. A comparative audit of gunshot wounds and stab wounds to the neck in a South African metropolitan trauma service. Ann R Coll Surg Engl. 2016;98:488-95.
5. Verdonck P, de Schoutheete JC, Monsieurs KG, Van Laer C, Vander Poorten V, Vanderveken O. Penetrating and blunt trauma to the neck: clinical presentation, assessment and emergency management. B-ENT. 2016;(Suppl 26):69-85.
6. Nasr A, de Oliveira JT, Mazepa MM, de Albuquerque CL, Martini GS, Nazario M, et al. Evaluation of the use of tomography in penetrating neck trauma. Rev Col Bras Cir. 2015;42:215-9.
7. Madsen AS, Laing GL, Bruce JL, Oosthuizen GV, Clarke DL. An audit of penetrating neck injuries in a South African trauma service. Injury. 2016;47:64-9.
8. Youssef N, Raymer KE. Airway management of an open penetrating neck injury. CJEM. 2015;17:89-93.

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Case Report
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Iatrogenic Post-intubation Tracheal Injury: An Emergency Room Presentation in a 17-year-old Girl

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Abstract

Iatrogenic tracheal injury is a rare complication after endotracheal intubation. Mucosal injury should be identified, and it is important to rule out pneumomediastinum and pneumothorax. The diagnosis is based on clinical and endoscopic findings and chest computed tomography. Broad-spectrum antibiotics should be given to avoid mediastinitis. We report a patient with a 5 mm tracheal laceration and significant subcutaneous emphysema after endotracheal intubation. The true incidence of this complication is unknown and early recognition warrants better outcomes.

Keywords: Tracheal injury, endotracheal intubation, bronchoscopy

Introduction

Iatrogenic tracheal injury has catastrophic consequences. In such a case, endotracheal tube (ETT) should be secured proximal to the defect with low volume ventilation. This will assist in reducing the stress on the tear. It is associated with female gender and mechanical factors such as incorrectly sized ETTs, cuff over-inflation, head movement or vigorous coughing. It causes longitudinal lacerations of the posterior membranous trachea (1).

Diagnostic validation is done by fiber-optic bronchoscopy, which will reveal the extent and location of the injury. The preferred treatment is early surgical repair for large lacerations, but conservative management may be a feasible substitute for patients with small lacerations or who are unfit for surgery. However, the criteria for both the managements are unclear (2).

Case Report

A 17-year-old girl with Tetralogy of Fallot presented to our emergency department with complaints of generalized tonic clonic seizures, fever, lethargy and respiratory distress. On admission, she had two episodes of seizures followed by a deteriorated consciousness. She was tachycardic and she had post-ictal confusion. To maintain her airway, rapid sequence intubation was performed using a 7 millimeter (mm) diameter cuffed ETT with a stylet. Intravenous broad-spectrum antibiotics and anti-epileptics were given.

After 90 minutes of intubation, patient became hypoxic and the low-lying ETT was readjusted, but the hypoxia did not resolve. Crackling subcutaneous emphysema was the first clinical sign noticed in the cervical region and upper part of the chest suggesting tracheal injury, so patient was rushed to computed tomography (CT) scan. Head CT scan showed subarachnoid hemorrhage. A 5 mm tear was detected along the left lateral wall of the trachea in chest CT (Figure 1). This tear was complicated with significant emphysema in the neck extending along erector spinae muscles, bilateral axilla and lateral chest wall, causing pneumomediastinum, pneumopericardium and pneumoperitoneum. In addition, chest CT revealed pulmonary embolism and splenic infarcts and patient was given anti-coagulants and analgesics.

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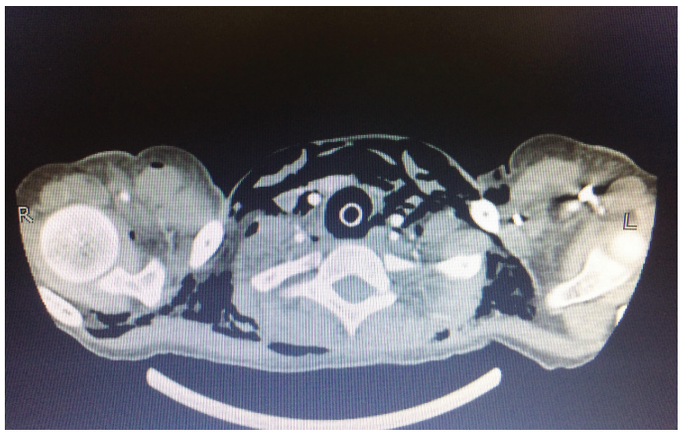

Figure 1. Computed tomographic image of tracheal tear along the left lateral wall measuring 5 mm

The patient was admitted to the intensive care unit, where she remained sedated and was kept on mechanical ventilation. Fiberoptic bronchoscopy showed evidence of a 5 mm laceration 4 cm away from the vocal cords in the membranous wall of the proximal third of the cervical trachea. There was no apparent active bleeding. Conservative treatment was chosen due to the acute neurological status of the patient. An orotracheal tube was inserted with its cuff positioned distally to the lesion, and antibiotic therapy effective on tracheobronchial tree pathogens was initiated. Subcutaneous emphysema was gradually decreased.

Cardiothoracic team consultation suggested managing conservatively as the patient was not stable enough for surgery due to multiple comorbidities. Empirical broad-spectrum antibiotic therapy was administered to prevent mediastinitis, chest physiotherapy was initiated, and mechanical ventilation settings were adjusted to low airway pressure and positive end-expiratory pressure. She remained stable and was weaned uneventfully. High-calorie diet was initiated and she was discharged in stable condition after drug optimization.

Discussion

Signs and symptoms of tracheal injury include subcutaneous emphysema, pneumothorax, dyspnea and hemoptysis. Diagnosis is made by tracheobronchoscopy, which reveals the location and extent of the lesion.

Diagnosis requires the identification of tracheal injury, its extent and depth. There is a controversy regarding surgical versus conservative management. The criteria for conservative management in selected cases include cardiovascular stability, the absence of sequelae such as progressive air leaks or sepsis, and no esophageal injury (3).

Supportive measures are essential in terms of avoiding mediastinitis in which early broad-spectrum antibiotics are indicated. A multidisciplinary approach is needed with risk stratification that permits conservative management even in large and non-bridgeable tears (4).

Early bronchoscopy is essential to confirm the diagnosis and to assess the injury. Conservative management is recommended in patients without rapidly progressing subcutaneous or mediastinal emphysema or mediastinitis (4). In our patient, laceration was approximately 5 mm and was complicated by subcutaneous emphysema. From this and other reported cases, we conclude that surgical repair is the best option for these patients, but patients with multiple comorbidities usually have an extremely high risk for surgery. Early surgical repair is preferred in patients with large lacerations, but conservative therapy can be used in patients with major medical problems.

Regarding treatment, very superficial lesions are usually treated conservatively and surgery is seen as a gold standard in which the lesions are repaired through right-sided posterolateral thoracotomy or a cervical approach (4). However, accumulating evidence challenges this conventional approach with more surgeons choose to adopt a medical approach to management. Yet, the criteria to guide which patients will benefit from medical treatment remain poorly defined and there is an increasing need for clear guidance. Selection criteria for conservative management are a matter of debate. Some authors stress the fact that there should be no evidence of respiratory or hemodynamic instability, while others consider the length or depth of the laceration as an important criterion (5).

Depending on the tracheal injury levels, the patients were managed either conservatively with medical treatment or surgically. Level I or II tracheal injuries should be managed non-surgically, provided that pneumothorax is promptly resolved, the patient has stable vital signs and an adequate respiratory status has been achieved (through either mechanical or spontaneous ventilation). Level IIIA tracheal injuries with adequate respiratory status can be managed conservatively in selected institutions only, because they represent high-risk tracheal lesions. Any tracheal injury associated with esophageal injury or mediastinitis (level IIIB) should be treated with open surgery as soon as possible (5).

The purpose of surgery is to achieve closure of the defect in order to restore effective ventilation, to prevent mediastinitis secondary to contamination from the airways and to reduce the risk of subsequent healing complications or long-term tracheal stenosis. The prevention of mediastinitis is a key goal of the physician dealing with such injuries. In this case report, we emphasized that prevention, early recognition and management

are the key features to deal with the dreaded complications of post-intubation tracheal injuries.

Ethics

Ethics Committee Approval: Aga Khan University Hospital, Karachi, Pakistan.

Informed Consent: Verbal consent taken by the patient.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

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

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

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References

1. Prunet B, Lacroix G, Asencio Y, Cathelinaud O, Avaro JP, Goutorbe P. Iatrogenic post-intubation tracheal rupture treated conservatively without intubation: a case report. Cases J. 2008;1:259.
2. Borasio P, Ardissone F, Chiampo G. Post-intubation tracheal rupture. A report on ten cases. Eur J Cardiothorac Surg. 1997;12:98-100.
3. Grillo HC. Tracheal and Bronchial Trauma. In: Grillo HC, editor. Surgery of the Trachea and Bronchi. Lewiston: BC Decker; 2004.p.274-5.
4. Spaggiari L, Rusca M, Carbognani P, Solli P. Tracheobronchial laceration after double-lumen intubation for thoracic procedures. Ann Thorac Surg. 1998;65:1837-9.
5. Tapias LF, Mathisen DJ. Prevention and management of complications following tracheal resections-lessons learned at the Massachusetts General Hospital. Ann Cardiothorac Surg. 2018;7:237-43.

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An Unusual Case of Bacterial Meningitis

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Abstract

Bacterial meningitis is a medical emergency that requires prompt identification and treatment in the emergency department (ED). Medical management is the mainstay of treatment. However, some patients may require neurosurgical intervention. Furthermore, neurological complications may develop, causing significant morbidity and mortality. We present a case report of a 42-year-old Chinese gentleman who presented to the ED and was subsequently diagnosed with pneumococcal meningitis. In addition to routine medical management, he also underwent emergent extraventricular drainage procedure to alleviate increased intracranial pressure. He subsequently developed stroke, seizure and sensorineural hearing loss. Not seizure-related hearing loss. After a comprehensive rehabilitation program, he showed good response and recovered without focal neurological deficit. A high index of suspicion and timely interventions in ED are important in minimizing morbidity and mortality from bacterial meningitis. The help of neurosurgeons may be necessary in selected cases. Dexamethasone has an important role in the prevention of neurological complications, as well as in their treatment.

Keywords: Emergency department, meningitis, neurosurgical procedure

Introduction

Bacterial meningitis (BM) is an inflammation of the leptomeninges and tissues surrounding the brain and spinal cord due to a bacterial infection - most commonly due to *Streptococcus pneumonia* and *Neisseria meningitidis*, which results in an elevated number of white blood cells in cerebrospinal fluid (CSF) (1). The incidence of BM is estimated to be around 0.6 to 4 per 100,000 adults per year, with higher incidence in developing countries (2). Fortunately, the availability of vaccines for BM has resulted in a significant reduction in overall incidence.

Nonetheless, BM still remains a medical emergency associated with significant morbidity and mortality, especially in the older population. The failure rate of treatment is high, especially with delay in diagnosis and treatment. Furthermore, neurological complications including altered mental status, cerebral edema, increased intracranial pressure, hydrocephalus, seizure, sensorineural hearing loss, focal neurological deficit, cerebrovascular abnormalities and intellectual impairment have been reported in approximately 30% patients with BM (3). Therefore, it is important for emergency physicians to promptly diagnose this condition and institute timely management for patients. However, this is difficult as patients often present with non-specific signs and symptoms, with the classical triad of fever, headache and nuchal rigidity present in only 44% of patients (4).

Medical management is the mainstay of treatment for BM. The patient should be resuscitated and have airway, breathing and circulation stabilized. Blood and CSF samples should be obtained as soon as possible, followed by the administration of empirical antimicrobial therapy (5) (Figure 1). In addition, acyclovir may be added to the regimen when herpes simplex virus or varicella zoster virus is suspected as the causative organism, and dexamethasone may be added to known or suspected pneumococcal meningitis to reduce the incidence of hearing loss and other neurological complications. Computed tomography (CT) of the brain should be considered before lumbar puncture if the patient has any

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of these: severely impaired consciousness, focal neurological deficit, seizure, signs of increased intracranial pressure such as papilledema, or if the patient is immunocompromised (5).

However, some patients may require neurosurgical interventions that are uncommon in the management of BM. Therefore, we present a 42-year-old Chinese gentleman who presented to the ED and was subsequently diagnosed with pneumococcal meningitis. We aimed to highlight the need for emergency physicians to be cognizant of the indications for neurosurgical referral. This will ensure that timely referrals can be made to minimize delay and prevent adverse outcomes for these patients.

Case Report

A 42-year-old Chinese gentleman with no past medical history was admitted to ED by ambulance. He was found in a confused state on the floor next to his bed by his wife. He had fever with runny nose, sore throat and non-vertiginous giddiness of one day duration. He had no cough, headache, neck pain, photophobia, nausea or vomiting.

He was febrile with a body temperature of 39.1 °C. His heart rate was 87 beats per minute with a blood pressure of 124/59 mmHg. His respiratory rate was 28 breaths per minute with an oxygen saturation of 99% in room air. He was agitated with a glasgow coma scale (GCS) of 11 (E4V2M5). His pupils were equal at 3 mm and reactive to light. The neck was supple with negative Brudzinski's and Kernig's signs. There was no focal neurological deficit. No rash and external injuries were noted. The rest of the examination was unremarkable.

Bedside blood glucose level was 12.4 mmol/L. Complete blood count result was as follows: hemoglobin=14.1 g/dL, white blood cell count=28.5x10^3/uL (92.6% neutrophils) and platelet count=186x10^3/uL. C-reactive protein was 176.6 mg/L, procalcitonin was 8.86 ng/L and lactate was 11.2 mmol/L. Other blood examinations were unremarkable. CT of the brain revealed global cerebral edema with diffuse sulcal and basal cisternal effacement. There was also a subtle hypodensity with loss of gray-white matter differentiation in the right high parietal lobe due to focal edema. Tonsils were at the level of foramen magnum (Figures 2, 3). Chest x-ray and urine culture were unremarkable.

He received empirical treatment with intravenous ceftriaxone, vancomycin, acyclovir and dexamethasone. During his stay in ED, his GCS fell to 9 (E3V2M4) with anisocoria - 6 mm left pupil and 2 mm right pupil. He was intubated due to decline in GCS and impending brain herniation due to increased intracranial pressure. Hypertonic saline was started and urgent neurosurgery consultation was performed. He was taken to the emergency operation theatre for external ventricular drainage. Intraoperatively, the CSF pressure was high and its appearance was cloudy. Analysis of the CSF showed 996 white blood cells per mm^3 with neutrophil predominance at 70%, and glucose level of 4.0 mmol/L and protein level of 2.23 g/L. Gram staining revealed

Patient Profile	Common Pathogen	Empirical Antibiotics
Patients who are 50 years old or less AND immunocompetent	Neiserria meningitidis, Streptococcus pneumoniae	Ceftriaxone or cefotaxime AND Vancomycin
Patients who are more than 50 years old	Streptococcus pneumoniae, Neiserria meningitidis, Listeria monocytogenes	Ceftriaxone or cefotaxime AND Vancomycin AND Ampicillin
Patients who are immunocompromised	Streptococcus pneumoniae, Neiserria meningitidis, Listeria monocytogenes, Pseudomonas aeruginosa	Cefepime or meropenem AND Vancomycin AND Ampicillin
Patients who have severe beta-lactam allergy		Moxifloxacin AND Vancomycin

Figure 1. Empirical antibiotics for community-acquired meningitis
Note: Empirical antibiotics may vary according to institutional practice

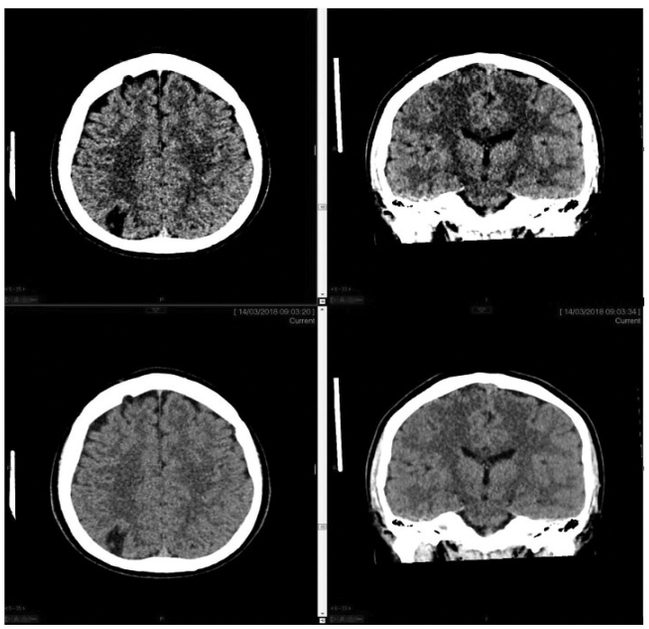

Figure 2. Brain computed tomography demonstrating loss of gray-white matter differentiation in the right high parietal lobe due to focal edema

gram-positive cocci with *Streptococcus pneumoniae* detected in the PCR assay. CSF and blood cultures were positive for pan-sensitive *Streptococcus pneumoniae*.

He was admitted to the intensive care unit. During his hospitalization, he developed a new onset left sided weakness due to stroke as a vascular complication of meningoencephalitis. Magnetic resonance imaging of the brain showed acute infarcts in the right parietal and occipital lobes as well as the right centrum semi-ovale (Figure 4). He had subsequent seizure and levetiracetam was started for seizure control. Bilateral hearing loss was detected. He underwent extensive inpatient rehabilitation for his deconditioning and stroke. He was eventually discharged on day 30 with independent function and performance in Activities of Daily Living.

Informed consent was obtained from the patient for this case report.

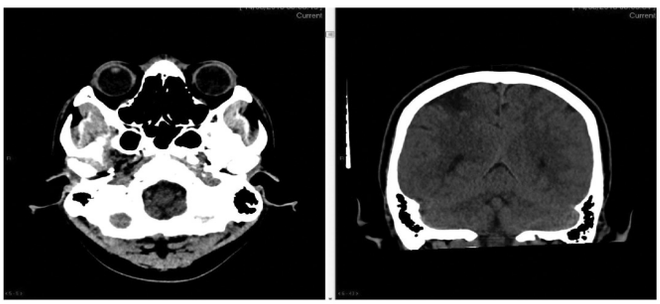

Figure 3. Brain computed tomography demonstrating global cerebral edema with diffuse sulcal and basal cisternal effacement and tonsils are seen at the level of foramen magnum

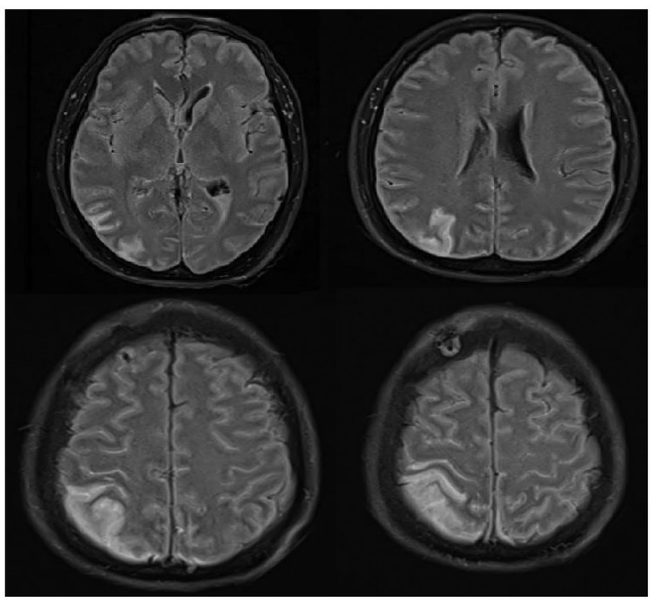

Figure 4. Brain magnetic resonance imaging demonstrating acute infarcts in the right parietal and occipital lobes

Discussion

A neurosurgery consultation should be performed if meningitis is associated with a surgically treatable lesion identified in brain CT, development of neurological complications such as increased intracranial pressure or hydrocephalus, or inadequate treatment response to appropriate antibiotic therapy (6). Among these, the first two indications are more relevant to the setting of the ED.

Our patient was referred to neurosurgery department due to concerns of increased intracranial pressure with impending brain herniation. This was attributable to the global cerebral edema without any space-occupying lesion in brain CT. Cerebral edema occurs in BM as a result of three mechanisms: vasogenic edema from increased permeability of the blood-brain barrier, cytotoxic edema from release of cytokines from neutrophils and bacteria, and interstitial edema from abnormal absorption of cerebrospinal fluid from the subarachnoid space (5). While dexamethasone is associated with worse outcome in other conditions of increased intracranial pressure such as in head injury and cerebral infarction, dexamethasone given for BM can reduce intracranial pressure and increase vascular perfusion. Therefore, in addition to other standard therapies such as head elevation, sedation and hypertonic saline or mannitol administration, treatment for increased intracranial pressure may be given based on suspicion on clinical ground prior to imaging.

Other neurological complications that may require neurosurgery consultation in ED include cerebrovascular abnormalities such as intracranial hemorrhage, hydrocephalus, mycotic aneurysm and brain abscess. The emergency physician must actively assess for these complications, so that timely intervention by neurosurgeons can improve patient outcomes.

The incidence of neurological complications is higher in patients with meningitis due to *Streptococcus pneumonia* than other organisms (3). This was the case in our patient who developed left hemiparesis, seizure and bilateral hearing loss. In BM, stroke is most commonly due to arterial infarction and occurs in about one third of the patients. Among these, more than half have blood vessel abnormalities such as wall irregularities, arterial occlusion, as well as focal dilatations and bleeding, suggestive of vasculitis (7). Therefore, dexamethasone should be used instead of standard treatment with thrombolytics. Fortunately, most patients recover with resolution of their neurological deficits following successful treatment.

Similarly, about one third of patients with BM develop seizures due to the presence of bacterial toxins and the neurochemical changes following inflammation, both lowering the seizure threshold (8). In addition to the use of routine anti-epileptics,

dexamethasone should also be administered to reduce the inflammatory response. These patients may develop recurrent seizures and therefore, anti-epileptics should be continued until a seizure-free period of three months.

Approximately 20% of patients with BM develop sensorineural hearing loss as a result of direct bacterial invasion and inflammatory response causing damage to the eighth cranial nerve, cochlea or labyrinth (9). Once again, dexamethasone has a therapeutic role in these cases.

Although dexamethasone appears to be a useful drug for the prevention and treatment of neurological complications in BM, it should be noted that its efficacy varies in different patient populations. In developing countries, dexamethasone did not show significant benefit in BM due to poor nutrition, delayed presentation, presence of chronic diseases such as infection with Human Immunodeficiency Virus and inadvertent inclusion of cases of tuberculous meningitis (10). Therefore, the practice of administrating dexamethasone with antibiotics may be limited to the developed countries.

Conclusion

BM is a medical emergency that requires early diagnosis and timely management. While the mainstay of management is medical, selected patients may require neurosurgical intervention. The emergency physician should be aware of these rare but important indications so that patients may benefit from early referrals and have better clinical outcomes. Although the etiology of meningitis may not be obvious in ED, dexamethasone should be administered early with antibiotics for suspected cases of meningitis in developed countries given its important role in the prevention and treatment of neurological complications.

Ethics

Ethics Committee Approval: This case report did not require approval as per Institutional Review Board guidelines.

Informed Consent: The patient gave informed consent for this case report for publication.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: J.H.P., Concept: J.H.P., Design: J.H.P., Literature Search: M.J.L., J.H.P., Writing: M.J.L., J.H.P.

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

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

References

1. Kottapally M, Josephson SA. Common neurologic emergencies for nonneurologists: when minutes count. Cleve Clin J Med. 2016;83:116-26.
2. Fitch MT, van de Beek D. Emergency diagnosis and treatment of adult meningitis. Lancet Infect Dis. 2007;7:191-200.
3. Durand ML, Calderwood SB, Weber DJ, Miller SI, Southwick FS, Caviness VS Jr, et al. Acute bacterial meningitis in adults. A review of 493 episodes. N Engl J Med. 1993;328:21-8.
4. van de Beek D, de Gans J, Spanjaard L, Weisfelt M, Reitsma JB, Vermeulen M. Clinical features and prognostic factors in adults with bacterial meningitis. N Engl J Med. 2004;351:1849-59.
5. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis. 2004;39:1267-84.
6. Namani SA, Koci RA, Kuchar E, Dedushi KH. Surgical treatment of neurologic complications of bacterial meningitis in children in Kosovo. J Trop Pediatr. 2012;58:139-42.
7. Pfister HW, Borasio GD, Dirnagl U, Bauer M, Einhäupl KM. Cerebrovascular complications of bacterial meningitis in adults. Neurology. 1992;42:1497-504.
8. Feldman WE. Relation of concentrations of bacteria and bacterial antigen in cerebrospinal fluid to prognosis in patients with bacterial meningitis. N Engl J Med. 1977;296:433-5.
9. Kastenbauer S, Pfister HW. Pneumococcal meningitis in adults: spectrum of complications and prognostic factors in a series of 87 cases. Brain. 2003;126:1015-25.
10. Scarborough M, Gordon SB, Whitty CJ, French N, Njalale Y, Chitani A, et al. Corticosteroids for bacterial meningitis in adults in sub-Saharan Africa. N Engl J Med. 2007;357:2441-50.

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An Unusual Side Effect of Dabigatran Etexilate Use - Acute Renal Failure

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Abstract

Dabigatran etexilate is a prodrug with anticoagulant effect through inhibition of thrombin. Although it does not require laboratory monitoring and has minimal food-drug interaction, its disadvantages are bleeding, common GIS-related side effects and the need for dosage adjustment according to the severity of liver/renal failure. We aimed to present and discuss an unusual side effect of dabigatran etexilate.

Keywords: New oral anticoagulant drugs, acute renal failure, creatinine clearance

Introduction

Anticoagulants are effective drugs in the prevention and treatment thromboembolic events. In recent years, novel oral anticoagulants (NOACs) such as dabigatran etexilate, rivaroxaban, apixaban, edoxaban have started to take part in treatment guidelines and daily clinical practice. These drugs do not require dosage monitoring, have minimal food-drug interactions and are at least as effective as warfarin (1-3). Dabigatran etexilate is an oral prodrug that is converted to its fully active form by esterases, that reaches its peak plasma value at the 2nd-3rd hours, and that is a quite specific competitive direct thrombin inhibitor (1). It has a rapid effect (1-2 hours), short half-life (12-17 hours) and it is mostly (80%) excreted through kidneys. Since NOACs, particularly dabigatran etexilate, have varying rates of renal excretion, the renal functions of the patients should be routinely monitored when using the drug (2-4). NOACs are not recommended for patients with creatinine clearance below 30 ml/min and patients with prosthetic heart valves, and the drug requires a dose adjustment when the creatinine clearance is between 30-49 mL/min (5). Ecarin clotting time, thrombin time and activated partial thromboplastin time (aPTT) are the tests used to evaluate the therapeutic effect of the drug, and these time periods are prolonged in patients using dabigatran etexilate. A normal aPTT level indicates that dabigatran etexilate has no clinically significant effect (6). The only Food and Drug Administration (FDA)-approved antidote for dabigatran etexilate is idarucizumab, a NOAC-specific antidote (7). In this study, we aimed to emphasize that monitoring the side effects and complications of dabigatran etexilate that does not require routine coagulation monitorization may be beneficial by using creatinine clearance (CrCl), especially in elderly patients.

Case Report

A 75-year-old female patient presented to our emergency department with shortness of breath and poor general condition. The patient had a medical history of congestive heart failure, atrial fibrillation and hypertension, and she was on diltiazem, furosemide and sertraline. Recently, dabigatran etexilate (150 mg, twice daily) was added to these drugs. The patient stated that she had not urinated in the last three days.

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Her physical examination findings were as follows: GCS=15, blood pressure=70/40 mmHg, pulse=90 beats/min, respiratory rate=24/min, SO_2=88%, body temperature=36.6 °C, pretibial edema=-/-. The ECG revealed atrial fibrillation and bilateral effusion was observed in posterior-anterior chest X-ray. Urine flow was 20 cc / hour. The laboratory results were as follows: pH=7.46, HCO_3=25.6 mmol/L, international normalized ratio (INR)= 9.16, aPTT=110.2 sec, Hgb=6.1 g/dL, PLT=390 10^3/µL, creatinine=4.51 mg/dL, urea=103 mg/dL, Na=137 mEq/L and K=4.4 mEq/L. The creatinine clearance was calculated as 9 mL/min. Inotropic support and 1 unit of fresh frozen plasma were administered. Since the patient had neither liver nor hematological disorder that would increase the INR value, it was assumed that NOAC created a false-positive increase in INR value. As the patient's previous creatinine level was 0.93 mg/dL, urea level was 50.3 mg/dL and creatinine clearance was 61.16 mL/min during her last follow-up, the new onset increased creatinine level was thought to be associated with dabigatran etexilate and dabigatran etexilate treatment was ceased. The patient was admitted to the intensive care unit of internal medicine department for monitoring. The follow-up examination revealed that urea level was 46.5 mg/dL, creatinine level was 0.99 mg/dL and creatinine clearance was 56.31 mL/min. Subsequently, the patient was discharged with full recovery after eleven days of hospitalization with recommended follow-up control visits.

Discussion

NOACs are oral anticoagulants that have been in use in recent years with the purpose of prevention and treatment of thromboembolic events. These drugs are considered safe and effective since they have an FDA-approved antidote, they do not require dose monitoring and food-drug interaction is minimal (2,3). However, gastrointestinal safety profiles and bleeding rates have not yet been entirely identified. There are two groups of NOACs for clinical application, namely oral direct thrombin inhibitors (dabigatran etexilate) and oral direct factor Xa inhibitors (rivaroxaban, apixaban, edoxaban).

The recommended dose for dabigatran etexilate is 150 mg 2 times a day, according to the FDA and EMA regulations. The Turkish drug license of dabigatran etexilate indicates that it should not be used when creatinine clearance is below 30 mL/min, and this is listed among its contraindications (8). It has also been suggested that the dose should be reduced in cases of moderate renal failure (CrCl: 30-50 mL/min). According to the RE-LY (Randomized Evaluation of Long-Term Anticoagulation Therapy) study, the most common side effects are dyspepsia and gastrointestinal hemorrhage, followed by dyspnea, coughing, dizziness, arthralgia, peripheral edema, and fatigue (9).

Conclusion

To conclude, acute renal failure has not been reported within the side effect profile of dabigatran etexilate, which has a high rate of renal excretion and its dosage is controlled by using the creatinine clearance level. Dabigatran etexilate does not require routine coagulation monitoring, and its dosage adjustment is not made according to coagulation tests. However, we believe that it may be useful to monitor dabigatran etexilate treatment through creatinine clearance, particularly in elderly patients.

Ethics

Informed Consent: The manuscript is merely a case report, and no research was performed necessitating obtaining an informed consent. Also, there was no need to apply to the Research Ethics Committee of the Medical Faculty. The case report has written in an anonymous characteristic, thus secret and detailed data about the patient has removed. Following discharge of the patient from our hospital, she has not presented for her follow-up control examinations. When we decided to present the patient as a case report, we were not able to get in touch for obtaining her consent. Therefore, we have not been able to present any patient consent for publication in your journal up to now.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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References

1. Gnoth MJ, Buetehorn U, Muenster U, Schwarz T, Sandmann S. In vitro and in vivo P-glycoprotein transport characteristics of rivaroxaban. J Pharmacol Exp Ther. 2011;338:372-80.
2. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, Parekh A, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361:1139-51.
3. Camm AJ, Lip GY, De Caterina R, Savelieva I, Atar D, Hohnloser SH, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Eur Heart J. 2012;33:2719-47.
4. Granger CB, Alexander JH, McMurray JJ, Lopes RD, Hylek EM, Hanna M, et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med. 2011;365:981-92.
5. Heidbuchel H, Verhamme P, Alings M, Antz M, Hacke W, Oldgren J, et al. European Heart Rhythm Association pratical guide on the use of new oral

anticoagulants in patients with non-valvular atrial fibrillation. Europace. 2013;15:625-51.

6. Liew A, Eikelboom JW, O'Donnell M, Hart RG. Assessment of anticoagulation intensity and management of bleeding with old and new oral anticoagulants. Can J Cardiol. 2013;29(7 Suppl):34-44.
7. Pollack CV Jr, Reilly PA, Eikelboom J, Glund S, Verhamme P, Bernstein RA, et al. Idarucizumab for Dabigatran reversal. N Engl J Med. 2015;373:511-20.
8. PRADAXAR 75 mg sertkapsul. Boehringer Ingelheim İlacTicaret A.Ş. RuhsatTarihi: 14.03 2011 KUB Tarihi: 13.05.2011 Available from:http: //www.iegm.gov.tr/Folders/KubKT/.
9. Kaiser C. Pradaxa Benefit Outweighs Bleeding Risk, FDA Says. Dec 7, 2011; Available from: http: //abcnews.go.com/Health/ HeartDiseaseNews/pradaxa-benefit-outweighs bleedingriskfda/story?id=15106519#.TuUOJdXiVHQ.