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Editorial

Değerli Okuyucular,

Dergimizin 2022 yılındaki ilk sayısı ile sizinle buluşuyor olmaktan dolayı mutluyuz. 2022 yılı itibarı ile dergimiz yeni bir Editörler Kurulu ile devam ediyor. Önceki Editörler Kurulu ve katkıda bulunan herkese en içten teşekkürlerimizi sunarız. Dergiyi bilimsel açıdan en ileri seviyeye çıkarmak için bayrak yarışında bir süre için bu bayrağı taşıma görevini biz devralmış bulunuyoruz.

Dergimize katkısı olan kıymetli yazar arkadaşlarımıza, hakemlere, derginin hazırlanıp sizlerin okumasına hazır hale getirilmesinde desteği olan bütün herkese ve ATUDER (Acil Tıp Uzmanları Derneği) Yönetim Kurulu ile Başkanımız Prof. Dr. Başar Cander'e destek ve katkıları nedeniyle teşekkür ederiz.

Saygılarımızla.

Eurasian Journal of Toxicology Editörler Kurulu

Contents

Letter to Editor

Eurasian Journal of Toxicology

Risk Determination of Acetaminophen Intoxication in Cases Nomogram is not Applicable

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Abstract

The Rumack-Matthew nomogram for acetaminophen toxicity was prepared using the acetaminophen levels of untreated patients and published in 1975. In order to determine the risk, the authors aimed to determine the acetaminophen levels that cause the aminotransferase level to increase to 1,000 IU/L and above. Thus, the line presenting the values above 200 was created. In the study published by Rumack et al. in 1981, the line representing values above 150 was suggested as a safer value. On the other hand, the nomogram was designed on the known intake times of single dose, immediate-release acetaminophen preparations. This causes significant limitations in clinical practice.

Keywords: Pharmacokinetics, toxicology, acetaminophen

Özet

Parasetamol toksisitesi için Rumack-Matthew nomogramı tedavi edilmeyen hastaların asetaminofen düzeyleri kullanılarak hazırlanmış ve 1975 yılında yayınlamıştır. Risk belirlemek için yazarlar aminotransferase seviyesinin 1,000 IU/L ve üzeri değerlere yükselmesine neden olan parasetamol düzeylerini tespit etmeyi amaçlamıştır. Böylelikle 200 üzerindeki değerleri temsil eden cizgi oluşturulmuştur. Rumack ve arkadaşlarının 1981 yılında yayınladıkları çalışmada ise 150 üzerindeki değerleri temsil eden cizgi daha güvenli bir değer olarak önerildi. Öte yandan nomogram tek doz, hızlı cözünen preparatların bilinen alım süreleri üzerine dizayn edildi. Bu klinik uygulamada önemli limitasyonlara neden olmaktadır.

Keywords: Farmakokinetik, toksikoloji, asetaminofen

Dear Editor,

The Rumack-Matthew nomogram for acetaminophen toxicity was prepared using the acetaminophen levels of untreated patients and published in 1975. To determine the risk of mortality, the authors aimed to determine the acetaminophen levels that cause the aminotransferase level to increase to 1.000 IU/L and above1. Thus, the line presenting the values above 200 was created. In the study published by Rumack et al. in 1981, the line representing values above 150 was suggested as a safer value[2]. On the other hand, the nomogram was designed on the known intake times of single dose, immediate-release acetaminophenpreparations. This causes significant limitations in clinical practice.

The first limitation is the risk assessment situation when the time of ingestion is unknown, or it is wider than 24 hours. It is almost always possible to determine at least one window of time during which ingestion occurs. The earliest possible time for ingestion is used as the intake time for risk assessment. If this time window cannot be determined or wider than 24 hours; both acetaminophen and aminotransferase value should be tested. If aminotransferase is elevated, treatment with N-acetylcysteine should be initiated regardless of the acetaminophen level. In cases where the intake time is not completely known and the acetaminophen level can be determined, treatment with N-acetylcysteine should be started, considering that the patient is at risk. If the acetaminophen level is below the toxic level on admission and the aminotransferase is normal, there is no evidence of possible liver damage and N-acetylcysteine therapy is unnecessary[1].

The second limitation is the risk assessment situation after taking extended or modified-release acetaminophen. In taking extended-releaseacetaminophen-containing drugs, serum acetaminophen level can be measured and evaluated according to the nomogram, and the necessity of antidote treatment can be checked. However, the validity of this decision requires further evaluation. Intoxications with short-release and long-release combined preparations require more careful evaluation1. In the study conducted with 2596 patients ingesting slow-release acetaminophen-containing

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drugs were evaluated, it was shown that there was no risk increase between intoxication and immediate-release drug intoxication with the extended-release drug[3].

A third limitation is the risk assessment in patients with symptoms and signs of liver injury after acute intake. N-acetylcysteine therapy should be initiated promptly in patients with symptoms and signs of liver injury after acute ingestion. Aminotransferase and serum acetaminophen measurement should be done. In the presence of high aminotransferase level and serum acetaminophen level detected below the treatment line, the history should be taken again regarding the time of administration and repeated doses of very high acetaminophen. N-acetylcysteine therapy should continue until the causes of liver failure and elevated aminotransferase values are clearly identified[1,4].

Another limitation is the risk assessment after repeated intake. Usually, the rate of serious acetaminophen toxicity after repeated doses is very low5. Serious acetaminophen toxicity may occur following high doses or after prolonged high-dose intake. In normal adults, as with alcoholics, the highest dose of chronic ingestion of 4 g/day is generally safe6. Since hepatotoxicity risk is affected by patient-related factors, amount of intake and duration of intake, a safe cutoff value for hepatotoxicity has not yet been determined for repeated doses. In the presence of toxicity risk after repeated high doses of acetaminophen, screening tests including acetaminophen and aminotransferase and additional tests may be required depending on their results and clinical features.

As a conclusion, emergency medicine specialists and anesthesiologists should keep in mind that the nomogram does not meet all scenarios in paracetamol intoxication and should be prepared for scenarios where the nomogram cannot be used.

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Original Article

Eurasian Journal of Toxicology

CBRN Incident Awareness of Healthcare Professional Working in Public and University Hospitals

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Abstract

Objectives: The aim of this study is to investigate the perception, information and experiences of healthcare professionals working in public and university hospitals who will respond to the CBRN incidents in order to raise awareness for requirements of knowledge, training and practice about this topic.

Materials and Methods: Our study was a survey study. Data acquisition was carried out between the dates 10.05.2021-10.11.2021. The questionnaire was applied to health care professionals working in public and university hospitals. There were 26 questions in our questionnaire. Questions were prepared to be short, clear and understandable. Each question was provided with 3 options as "Yes/No/Partially".

Results: A total of 103 people participated to the study. 65 (63.1%) of the participants were male, 38 (36.9%) were female. The ages of the participants were categorically evaluated and 44 (42.7%) were in age group 26-35, 38 (36.9%) were in 18-25, 17 (16.5%) were in 36-45, and 4 (3.9%) were above 46. When the answers were evaluated according to education status, people with bachelor's degree answered "Yes" to the question "Injured people with possible exposure to an CBRN agent are accepted to the emergency service after decontamination process in the health care facility I work in" significantly higher than the other groups (p:0.04). The question of "I have come across with hospitalized injured in the region I work" were answered as "No" by 17 doctors, 41 nurses, and "Yes" by 1 doctor and 1 nurse, while the majority of people answering "Yes" to this question were emergency medical technician and paramedics. The difference was statistically significant (p<0,001).

Conclusion: As a conclusion, we think that healthcare professionals do not have the required interest and awareness for preparation of CBRN incidents and it is crucial to determine and eliminate the deficiencies in this topic.

Keywords: Awareness, CBRN, disaster, emergency medicine.

Özet

Amaç: Bu çalışmanın amacı KBRN olaylarına müdahale edecek kamu ve üniversite hastanesinde görev alan sağlık çalışanlarının KBRN konusundaki algıları, bilgi ve deneyimlerini araştırarak bu konudaki bilgi, eğitim ve tatbikat ihtiyaçları konusunda farkındalık oluşturmaktır.

Gereç ve Yöntem: Çalışmamız bir anket çalışmasıdır. Veri toplama 10.05.2021-10.11.2021 tarihleri arasında gerçekleştirilmiştir. Anket kamu ve üniversite hastanelerinde çalışan sağlık profesyonellerine uygulanmıştır. Anketimizde 26 soru vardır. Sorular kısa, açık ve anlaşılır olacak şekilde hazırlanmıştır. Her soruya "Evet/Hayır/Kısmen" şeklinde 3 seçenek sunulmuştur.

Bulgular: Çalışmaya toplam 103 kişi katıldı. Katılımcıların 65 (%63,1) kadın, 38 (%36,9) ise erkekti. Ankete katılanların yaş verileri kategorik olarak değerlendirilmiş olup 44 (%42,7) kişi 26-35 yaş arasında 38(%36,9) kişi 18-25 yaş arasında, 17(%16,5) 36-45 yaş arasında, 4 (%3,9) kişi de 46 ve üzeri yaş grubundaydı. Sorulara verilen yanıtlar eğitim durumu ile karşılaştırılarak değerlendirildiğinde, çalıştığım sağlık kuruluşunda olası bir KBRN ajanına maruz kalan yaralı/yaralılar dekontaminasyon işlemi gerçekleştirildikten sonra acil servise kabul edilmektedir ifadesine lisans mezunu olanların diğer gruplara kıyasla istatistiksel olarak anlamlı derecede daha çok evet cevabı verdiği belirlendi (p:0,04). Görev yaptığım bölgede KBRN ajanına maruziyet nedeniyle hastaneye başvuran yaralılar ile karşılaştım sorusuna 17 doktor hayır 1 doktor evet, 41 hemşire hayır, 1 hemşire evet cevabını verirken evet cevabını verenlerin çoğunluğunun ATT ve paramedik olduğu belirlendi. Bu farklılık istatistiksel olarak anlamlı değerlendirildi (p<0,001).

Sonuç: Sonuç olarak KBRN olaylarına hazırlık konusunda sağlık çalışanlarının ihtiyaç duyulan ilgi ve farkındalığa sahip olmadığı bu konudaki eksikliklerin belirlenerek giderilmesinin oldukça önem arz ettiği düşünülmektedir.

Keywords: Farkındalık, KBRN, afet, acil servis

Introduction

CBRN is a natural or man-made disaster which gives rise to dangerous and harmful situations for humans and environmentand cannot be handled by local facilities, is happened by chemical, biological, radiological and nuclear materials and which affects the area it happens either in long or short periods[1].

Various CBRN incidents have happened form past to present[2]. Societies are still in a position to be injured or dead due to any accident or attack resulting from any CBRN agent[3].

Technology today has developed very much due to rapid progress of knowledge and equipment and has eased the human life[4]. Although it makes life easier, CBRN materials used and stored in nuclear energy power plants and industrial plants

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may accompany extensional disasters due to a mistake during the co-use of them with burnable and explosive materials[5].

People exposed to CBRN agents during the incidents usually apply to health care services by themselves in the shortest time possible. Asymptomatic or people not exposed to agents might cause unnecessary use of hospital sources. Health care professionals working in the emergency services who are the first responders to the exposed or injured people are the riskiest ones in terms of secondary contamination.

Medical response to a possible CBRN incident after the provision of necessary occupational health and security, protection of health care professionals and injured people from possible harmful effects of CBRN agent, managing the scene, determination of the CBRN agent, triage of injured people exposed to CBRN agent, first aid in CBRN incidents, medical decontamination processes and further diagnosis and treatment of injured people exposed to CBRN agent have a significant importance.

It is predicted that CBRN incidents cause panic and disorder, and a burden to health services, it is time consuming and hard to respond to people exposed to the agent, the first responder healthcare professionals are under risk, and it is required to use PPE (personal protective equipment) in CBRN incidents and decontamination should be carried out. Possible CBRN incidents and conditions during the incidents can be predicted. Most real-like projection of possible situations, raising awareness about CBRN via trainings and practices, keeping the stuff ready for emergency and disasters, and developing necessary knowledge, skills and attitude are very important[6].

Relevant institutions and organizations must plan the things to be done during the incidents in advance and prepare to disaster plans which they can apply in case of extensional disasters via training.

Disaster management is a polity to be designed for the disasters as a whole, which requires specialized knowledge and which plans preparations prior to disasters, and correct actions in the course and after the disaster. As it is valid for modern disaster management, for CBRN incidents detailed and multidimensional plans should be prepared to carry out risk reduction, preparation, response and recovery practices affectively by taking possible damages into consideration and specially trained and kitted up crew should respond to the CBRN incidents[7]. In order to provide the fastest and most effective response to eliminate the negative effects of the CBRN agents which are highly dangerous for human and environmental health, CBRN trainings should be provided to the society and should be trained with CBRN educations, and enough number of well-equipped responder teams should be formed[2,8].

The aim of this survey study was to investigate the perception, information and experiences of healthcare professionals working in public and university hospitals who will respond to the any CBRN incidents in order to raise awareness for requirements of knowledge, training and practice about this topic.

Material and Methods

Our study was a survey study and ethical principles presented in Helsinki declaration were followed. Data acquisitions were carried out in between the dates of 10.05.2021-10.11.2021. The study was conducted as multi centered and applied to healthcare professionals working in public and university hospitals.

Informed consent forms were obtained from all participants prior to the questionnaire. There was a total of 26 questions in our questionnaire. Personal information was not asked from the participants while the first 4 questions were descriptive for socio-demographic information. Other questions were aimed for determination of knowledge and attitude. Questions were short, clear and understandable. Each question was provided with 3 options as "Yes/No/Partially". The questions were about: "what an CBRN agent is, applications to be carried out in hot, cool and cold zones during CBRN incidents, what the emergency plan and applications for CBRN incidents are, what "Orange Code" training is, whether the CBRN training and practices are enough or not, if ever encountered any CBRN injured people applying to hospital, whether taken part in an CBRN response team before or not, whether there are protective materials against CBRN incidents, enough antidotes and medications or not, decontamination process for an CBRN agent and where this process would be done, whether to accept CBRN emission injured people to emergency service after contamination control or not, where the locations and access paths to CBRN shelters are, what the warning and alarm signs (Yellow Warning, Red Alarm, Black Alarm, White Warning) used for CBRN incidents are, what the usage and planning of isolation and quarantine rooms used for CBRN exposed injured people are, decontamination process for equipment and dressing during hospital phase and in decontamination tent, whether improper collection of dangerous wastes spreading around after the CBRN decontamination process increases CBRN infection risk or not, whether there is any risky industrial plants proximal to settlements of the working place or not, planning and response phases for secondary disasters to occur as a result of a possible CBRN emission around the work place, whether a farmer knows what an organophosphate exposure, a worker of automobile industry knows what it is to be affected from exhaust gas or not, organizations and contact numbers in case of a possible CBRN incident". Questionnaires were delivered to the participants via internet.

Statistical Analysis

Obtained data were saved and analyzed with PASW Statistics 18.0 for Windows (Predictive Analytics Software) statistical package program. Prior to the study, approval from Namık Kemal University Faculty of Medicine Non-invasive Clinical Researches Ethical Council (decree no: 27.04.2021-31432) was obtained.

Results

A total of 103 people participated to the study. 65 (63.1%) of the participants were male, 38 (36.9%) were female. The ages of the participants were categorically evaluated and 44 (42.7%) were in age group 26-35, 38 (36.9%) were in 18-25, 17 (16.5%) were in 36-45, and 4 (3.9%) were above 46.

The first question "I have enough knowledge and practicum about CBRN agents" was answered as "partially" by 52 (52.5%) of the participants, as "no" by 29 (28.2%), and the ones answering "yes" was a minority.

The expression "I have enough information about emergency plans and applications for CBRN incidents in the healthcare organization where I work" was answered as "no" by 44 (42.7%) of the participants, while answered "partially" by 35 (34%) people.

The expression "Regular Orange Code trainings are carried out in the healthcare organization where I work" was answered as "no" by 72 (69.9%), while "partially" by 18 (17.5%).

Among the participants, 60(58,3%) "I think that CBRN training and practices carried out in the healthcare organization where I work are enough" answered as "no". The same question was answered as "partially" by 35 (34%) and "yes" by 8 (7.8%).

The expression "I have encountered injured people because of CBRN agent exposure in my working region" was answered as "no" by 79 (76.6%), while "I have participated in a CBRN response team" was answered as "no" by 90 (87.4%) people.

"There is protective material, enough antidote and medications in the healthcare organization where I work" was answered as "partially" by 44 (42.7%) and as "yes" by 33 (32%) participants.

4 (39.8%) of the participants answered to the expression "I have sufficient information about the decontamination process of a possible CBRN agent and how/where this process should be carried out" as "no", while 32 (31.1%) answered as "partially", and 30 (29.1%) as "yes".

The expression "The injured people exposed to a possible CBRN agent are accepted to the emergency service of the healthcare organization where I work after a decontamination process" was answered as "yes" by 56 (54.4%) participants.

"I have sufficient information about the locations and how to access to the CBRN shelters in the healthcare organization where I work" was responded as "no" and "partially" by 64 (62.1%) and 22 (21.4%) participants, respectively.

The question about the knowledge and awareness level of the participants about the warning and alarm signs (Yellow Warning, Red Alarm, Black Alarm, White Warning) was answered as "partially" by 39 (37.9%), "no" by 39 (36.9%), and "yes" by 26 (25.2%) participants.

"I have sufficient information about the usage and planning of isolation and quarantine rooms used for CBRN exposed injured people in the work place where I work" was responded as "no" by 54 (52.4%) participants. "I have sufficient information about the decontamination process for equipment and dressing during hospital phase and in decontamination tent." was responded as "no" by 41 (39.8%) participants.

The expression "Improper collection of dangerous wastes spreading around after the CBRN decontamination process increases CBRN infection risk" was answered as "yes" by 77 (74.8%) participants.

"There are no risky industrial plants proximal to settlements of the working place" was replied as "no" by 42 (40.8%), and "yes" by 35 (34%) participants.

44(42.7%) of the participants expressed that they have partially sufficient information about planning and response phases for secondary disasters to occur as a result of a possible CBRN emission around the work place, while 43 (41.7%) expressed that they do not have sufficient information.

"Application of a farmer to the hospital after application of organophosphate pesticide and being affected by it is an example of an CBRN incident" expression was confirmed by 75 (72.8%) participants. "A worker in an automobile industry being affected by the exhaust gas is not an CBRN incident" expression was responded as "yes" by 48 (46.6%), and as "no" by 41 (39.8%). Moreover, 50 (48.5%) participants expressed that they do not have sufficient information about organizations and contact numbers in case of a possible CBRN incident, while 28 (27.2%) said they have "partial" information.

The final question in the questionnaire was "Investigation, search and rescue, and sampling are carried out in hot zone, decontamination (purification/washing/cleaning) is carried out in cool zone, and medical treatment is carried out in the cold zone during CBRN incidents" was answered as "yes" by 62 (60.2%) participants.

There was no statistically significant difference according to sex in any of the questions.

When the answers were evaluated according to the education status, the expression "The injured people exposed to a possible CBRN agent are accepted to the emergency service of the healthcare organization where I work after a decontamination process" was answered as "yes" significantly higher by participants with a bachelor's degree compared to the other groups (p:0.04). (Table 1)

When the answers were evaluated according to the occupational groups; "I have encountered injured people because of CBRN agent exposure in my working region" was replied as "no" by 17 doctors and 41 nurses, "yes" by 1 doctor and 1 nurse, while most f the participants answering "yes" were emergency medical technicians and paramedics. The difference was statistically significant ($p<0.001$).

In the same way, the occupational group who expressed to take place in an intervention team to an CBRN incident was composed of emergency medical technician and paramedics (p: 0.01).

"I have sufficient information about the decontamination process of a possible CBRN agent and how/where this process should be carried out" was answered as "no" by 13

Table 1: The relationship between the education status of the participants and the answers to the questions

Question	**In the health institution where I work, the casualty exposed to a possible CBRN agent is admitted to the emergency room after the decontamination process is performed.**				
Educational status	**n(%)**	**yes**	**no**	**partly**	**p**
secondary education	5(4.9)	3	1	1	
associate degree	10(9.7)	6	4	0	
Bachelor's degree	68(66)	38	9	21	0.004
Master degree	12(11.7)	4	6	2	
Doctorate	8(7.8)	5	0	3	
Questions:	**Previously, I took part in the response team to the CBRN incident.**				
Educational status	**n(%)**	**yes**	**no**	**partly**	**p**
secondary education	15(14.6)	5	10	0	
associate degree	50(48.5)	1	18	0	
Bachelor's degree	19(18.4)	1	47	2	<0.001
Master degree	9(8.7)	3	6	0	
Doctorate	10(9.7)	1	9	0	

and "yes" by 3 doctors; while it was answered as "yes" by 10 nurses and "no" by 21 nurses. Majority of the emergency medical technicians and paramedics answered "yes" to this question. The difference between the groups was statistically significant (p: 0.002).

In the same way," I have sufficient knowledge and awareness level of the participants about the warning and alarm signs (Yellow Warning, Red Alarm, Black Alarm, White Warning) used in a possible CBRN incident" was answered as "yes" mostly by the emergency medical technicians. The intergroup differences were statistically significant (p:0.01). (Table 2)

When the healthcare department of the participants were compared according to the answers;"I have encountered injured people because of CBRN agent exposure in my working region" was answered as "yes" and "no" by 12 and 13 ambulance personnel, respectively. There was no "yes" answer among the emergency service personnel. There were no personnel from the hospitalization service, while 1 personnel working in intensive care unit answered "yes". Difference among the groups was statistically significant (p<0.001). 9 out of 11 people answering "yes" o "I took place in an intervention team to an CBRN incident" were

Table 2: The relationship between the occupational of Participants and the answers to the questions

Questions:	**In the region where I worked, I encountered injured people who applied to the hospital due to exposure to a CBRN agent.**				
occupational	**n(%)**	**yes**	**no**	**partly**	**p**
Emergency medical technician	15(14.6)	6	9	0	
Nurse	50(48.5)	1	17	1	
Doctor	19(18.4)	1	41	8	<0.001
Paramedic	9(8.7)	5	4	0	
Other	10(9.7)	1	8	1	
Question	**I have sufficient knowledge about the decontamination process in exposure to a possible CBRN agent and where/how this process will be done**				
occupational	**n(%)**	**yes**	**no**	**partly**	**p**
Emergency medical technician	15(14.6)	10	1	4	
Nurse	50(48.5)	3	13	3	
Doctor	19(18.4)	10	21	19	0.002
Paramedic	9(8.7)	4	1	4	
Other	10(9.7)	3	5	2	
Questions:	**I have sufficient knowledge about the warning and alarm signs (Yellow Warning, Red Alarm, Black Alarm, White Warning) used in a possible CBRN event.**				
occupational	**n(%)**	**yes**	**no**	**partly**	**p**
Emergency medical technician	15(14.6)	8	1	6	
Nurse	50(48.5)	4	13	2	
Doctor	19(18.4)	8	17	25	0.001
Paramedic	9(8.7)	2	2	5	
Other	10(9.7)	4	5	1	

emergency ambulance service personnel. The intergroup differences were statistically significant (p<0.001). (Table 3)

The proportion of participants expressing to have sufficient information about emergency plans and applications for CBRN incidents in the work place increased statistically significantly with increasing working experience (p:0.001). In the same way, 13 out of 14 people expressing to encounter injured people because of CBRN agent exposure in the working region had a working experience of over 15 years which was statistically significant (p:0.001). 10 out of 17 people expressing to have sufficient information about the locations and how to access to the CBRN shelters in the healthcare organization they work were determined to have a working experience of more than 5 years (p:0.02). 28 out of 48 people finding the expression "A worker in an automobile industry being affected by the exhaust gas is not an CBRN incident" had more than 5 years of working experience and it was determined to be statistically significant (p:0.01). 10 out of 12 participants with less than 1 year of working experience answered this expression as "no". (Table 4)

Table 3: The relationship between the department of Participants and the answers to the questions

Questions:	**In the region where I worked, I encountered injured people who applied to the hospital due to exposure to a CBRN agent.**				
departments of Participants	**n(%)**	**yes**	**no**	**partly**	**p**
ambulance	25(24.3)	12	13	0	<0.001
Emergency services	13(12.6)	0	9	4	
Polyclinics	5(4.9)	1	3	1	
Other services	32(31.1)	0	27	5	
Intensive care unit	12(11.7)	1	11	0	
Other	16(15.5)	0	16	0	
Questions:	**Previously, I took part in the response team to the CBRN incident.**				
departments of Participants	**n(%)**	**yes**	**no**	**partly**	**p**
ambulance	25(24.3)	9	16	0	<0.001
Emergency services	13(12.6)	0	13	0	
Polyclinics	5(4.9)	1	3	1	
Other services	32(31.1)	0	31	1	
Intensive care unit	12(11.7)	1	11	0	
Other	16(15.5)	0	16	0	

Table 4: The relationship between the Work experiences of Participants and the answers to the questions

Questions:	**I have sufficient information about the emergency plan and practices for CBRN incidents in the health institution I work for**				
Work experiences (year)	**n(%)**	**yes**	**no**	**partly**	**p**
1≥	19(18.4)	4	14	1	0.01
1-5	34(33)	10	15	9	
5-10	19(18.4)	5	6	8	
10≤	31(30.1)	5	9	17	
Questions:	**I have sufficient information about the emergency plan and practices for CBRN incidents in the health institution I work for.**				
Work experiences (year)	**n(%)**	**yes**	**no**	**partly**	**p**
1≥	19(18.4)	0	17	2	0.001
1-5	34(33)	1	28	5	
5-10	19(18.4)	8	9	2	
10≤	31(30.1)	5	25	1	
Questions:	**I have sufficient information about the location of the CBRN shelters and the access routes to these shelters in the health institution where I work**				
Work experiences (year)	**n(%)**	**yes**	**no**	**partly**	**p**
1≥	19(18.4)	5	12	2	0.02
1-5	34(33)	2	27	5	
5-10	19(18.4)	6	6	7	
10≤	31(30.1)	4	19	8	

Discussion

It should be evaluated as an important lesson that even the most common and equipped healthcare systems were unprepared for COVID19 pandemics therefore preparation process and corporate awareness for CBRN disasters should be started. World Health Organization called all the countries for preparation to the next "unavoidable and possible close" flu pandemics in the middle of 2004[9].

Balicer et al. investigated the perceptions of healthcare professionals of 3 different hospitals to respond an influenza pandemic. According to the results, majority of the employee think that they would work under a serious personal risk, they would have a role without sufficient training about a topic which they do not have sufficient information, and this role would not have a significant effect on the general response of the organization[10]. In our study, perceptions of participants for responding to a possible CBRN disaster were evaluated. We think that positive feedback was obtained in the society of our study in case of a culturally need for help. Moreover, attitude of the healthcare professionals for helping to the disaster victims might change according to the characteristics of the disaster and their perceptions about the subject. For instance, volunteering for medical maintenance activities for the sufferers of an earthquake might not be the same with the volunteering for medical maintenance activitiesfor a biological agent without information of factor and treatment.

Studies around USA resulted that healthcare professionals were found to be unwilling to intervene possible biological epidemic[11,12]. In order to fix this situation, the importance of training for preparation to possible interferences was emphasized[11]. There was no problem for willingness in our study, but there was a serious lack of experience and training.

COVID-19 pandemic caused by Sars Cov-2 virus is a candidate to appear in the debates about CBRN disasters. Kırçiçek et al. emphasized that states should mobilize their resources as if in a war, to quarantine the people with disease symptoms, to keep the non-serious cases separated from the ones suffering from serious illnesses, and to limit the mobility of people for the disease to wipe out itself[13]. Avcı et al. indicated that healthcare professionals were the highest risk group of workers to encounter the virus during the COVID-19 pandemic as they both encountered a high load of virus and they had to work in an insecure environment without sufficient rest due to high amount of working hours[14].

The participants of our study were determined to lack sufficient information and implements about CBRN agents and did not get sufficient training about this topic. We think that the determined training and education requirement of healthcare professionals can be fulfilled with trainings given after the graduation under the law-makers and relevant institutions, and this situation would strengthen the hands of personnel and administrators.

Barış E. investigated the disaster medical training of 248 doctors in his thesis study. Among the doctors, 73% were practitioners, 27% were attending and resident doctors, and 49.6% of these worked in emergency service of the hospital and 50.4% worked in the ambulance service. General evaluation of the research population, 66.5% of them never attended training about disaster medicine15. In our study, the majority of the participants were detected not to have sufficient knowledge and emergency practicum about CBRN agents and incidents.

CBRN incidents are a concept starting to take part in the awareness among healthcare professionals. Medical intervention to such incidents is still not clear in many institutions. Moreover, many personnel join to the institution they work without a prior training about this topic. For this reason, the knowledge and training requirement of healthcare professionals should be fulfilled with platforms named as in-service trainings. In order to provide the active contribution of healthcare professionals to these trainings, the importance of the topic should be adapted well and the attitude of the participants as if the training is useless due to their already intense work load should be changed.

Emergency services of our country helped us to overcome the COVID 19 pandemics process relatively less troubled due to the experience of managing crowded emergency service and fast reflex of health system in obtaining PPE countrywide. However, possible coupling of CBRN with a disaster would increase the impact of destruction due to the affected the healthcare infrastructure and interrupted supply chain. For this reason, attitudes and needs of healthcare professionals who would take basic duties in intervention of CBRN disasters should be determined and redressed, which will contribute to the success of the aimed medical intervention.

Disasters including CBRN incidents acquire a different dimension. The agent in massive accidents might affect a lot of people in a short period via spreading due to possible couplings. Moreover, in case of intervention without being prepared and planned, prognosis of the sufferers would unavoidably be negatively affected as well as the number of sufferers. Okumura et al.indicated that in Tokyo metro attack, most of the PPE were distributed to police and firemen in the crime scene,there were almost no PPE left in medical institutions and that is why the attack caused many secondary exposures in these institutions after the attack. Furthermore, 23% of St. Luke's International Hospital personnel underwent secondary exposure, which led to many important inferences about hospital disaster preparations16. Sapira et al. inspected the willingness of healthcare professionals under the circumstance of a hypothetical rocket attack scenario.A total of 2650 questionnaires were distributed to personnel of 10 hospitals (42%) countrywide. 51% of the personnel responded to the questionnaire and the willingness of healthcare professionals to do their duties increased from 42% to 86% in case they were provided with proper

personal protecting equipment[17]. The thesis study of Sezigen mentioned the importance of organization structure in military hospitals, minimum opportunities and abilities, inside the behavioral model including active intervention of massive injuries resulted from CBRN[3].

Recruitment of PPE forms an additional load to the institutions. Transfer of funds to incidents with low awareness and mostly not experiences, especially like CBRN incidents, might not be accepted as a proper approach by the institutions with limited budget. However, it is the responsibility of all authorities to prepare incidents which are not desired to happen at all but those with a probability all the time.

Yıldırım et al. inspected about PPE in a survey study with 541 pre-hospital healthcare professionals and determined that 61.0% of the participants get personal protection methods training, and 39% did not get it. Also, they emphasized the ability of healthcare professionals to use PPE by indicating that PPE have an important role in intervening to CBRN incidents8. In our study, although, the pre-hospital healthcare professionals are more trained about PPE and CBRN consistently with the literature, most of the participants were seen not to have sufficient information about where and how to decontaminate PPE intended to use in CBRN incidents. We link the reason of this situation to the widened risk perceptions of pre-hospital healthcare professionals to be the first people to be in touch with CBRN incidents, as happens in many other incidents. Healthcare professionals working in the hospitals do not frequently come across with CBRN incidents and therefore have a lower perception of risk for the topic, and are not willing enough to benefit from the in-service trainings. However, it should not be forgotten that healthcare professionals working in the hospitals are under direct risk due to the patients reaching out to the hospitals themselves, and due to secondary contamination in case of CBRN incidents.

Dogan et al. conducted a survey study to measure the requirements of knowledge, training and practice for CBRN incidents. They investigated 425 civil servants working in some public institutions which play a role as a basic solution partner and support solution partner in the disaster intervention plan in a local level in the cities of Gumushane and Trabzon with the criteria they designed. A positively weak and significant correlation betweenpreparation point variable and attitudes of the participants about knowledge, training and practice requirements for CBRN incidents was found. As a result, they indicate that emergency situations with high risk and threats like CBRN incidents require multi-institutional intervention, and public institutions and their partners should consider preparation activities such as training and practices more importantly[4].

In our study, majority of the participants share the opinion that trainings for CBRN incidents were insufficient in their work places. This opinion of the participants is supported with the insufficient knowledge of the participants about decontamination process for equipment and dressing during hospital phase and in decontamination tent, about the usage and planning of isolation and quarantine rooms used for CBRN exposed injured people in the work place.

The thesis of Dönmez mentioned that as a result of an CBRN incident, addition of new and complicated loads to the already chaotic structure of the emergency services would be unavoidable which are the first application place in case of traumatic incidents affecting the society and they investigated the interest and attitude of emergency service personnel towards CBRN incidents. The studyindicated that the hospital has a determined role in the city wide CBRN Incident Management System and the ratio of emergency service clinical chiefs who express that there are protocols between relevant CBRN service managing institutions is 17.2%. Moreover, it was emphasized that emergency service personnel who are cognizant of the importance of preparation for CBRN incidents should be supported by trainings and practices, funding should be provided to the emergency services for CBRN capacity, they should be supported with equipment and diagnostic apparatus, and the coordination of in and inter-institutional CBRN should be increased[18].

Şahin et al. investigated the attitudes and abilities of the personnel of the public institutions who would take place in the first intervention in case of a CBRN incident. The study revealed thatinstitutions and their personnel included in the CBRN incidents should have a upper-level preparation from the point of their duties and perspectives; firemen, policemen, healthcare professionals and doctors would consider CBRN incidents in different perspectives, the reason of which would be the different experiences and trainings they attended aimed for their duties.The majority of the participants were detected not to be experienced about CBRN and did not attend any relevant practice. Moreover, the importance of organizing frequent in service and inter institutional trainings and providing the attention in a high level in an efficient way in order to provide institution planning efficiencies and to overcome the deficiencies of the institutions was emphasized[19].The results of our study revealed that most of the participants were not experienced about CBRN incidents and there were not enough trainings for them to gain experience. Moreover, they were not sufficiently informed about the contact numbers and institutions in case of a possible CBRN incident. Since there are not frequent massive applications to emergency services, it can be accepted that healthcare professionals do not have enough experience about CBRN cases.This situation can even negatively affect the attitude of the personnel for this topic. It is desired that no CBRN incident would ever happen, but the requirement of experience should be fulfilled with frequent and current trainings and this would be effective in the redress and attention of personnel about this topic.

Limitations

The low number of participants to our study was the most important limitation. Moreover, our study was applied as multi centered because of the scarcity of participants. This situation forms a significant limitation to what extend the obtained data can be generalized or to which region can the data can be accepted as specific.Lack of an equal sampling in the lower categories was another limitation.

Conclusion

As a result, it is obvious that healthcare professionals do not have required level of attention and awareness in allcategories like training, equipment and awareness for preparation of CBRN incidents, however; it is strategically crucial to determine and eliminate the deficiencies in this topic.

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Review

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General Approach to Patients Admitted to The Emergency Department with Poisoning

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Abstract

Poisonings are a group of patients that can cause serious mortality and morbidity and are frequently referred to Emergency Departments. Providing an approach to the poisoning phenomenon with predetermined diagnosis and treatment will increase the success rates in treatment. Diagnosing and evaluating poisoned cases in the emergency department at the earliest stage, early decontamination, elimination, and appropriate antidote treatment are life-saving. In this article, it is aimed to compile the general management of poisoning cases admitted to the Emergency Department in line with the current literature.

Keywords: Poisoning, emergency, drug, toxicology

Özet

Zehirlenmeler ciddi mortalite ve morbiditeye neden olabilen ve Acil Servislere sık başvuran hasta grubudur. Zehirlenme olgusuna yaklaşımın önceden belirlenmiş tanı ve tedavi akışları ile sağlanması tedavideki başarı oranlarını artıracaktır. Zehirlenmiş olguların acil serviste en erken dönemde tanınıp değerlendirilmesi, erken dekontaminasyon ve eliminasyonunun yapılması, varsa uygun antidot tedavisinin verilmesi hayat kurtarıcıdır. Bu makalede Acil Servise başvuran zehirlenme vakalarının genel yönetiminin güncel literatür bilgileri doğrultusunda derlenmesi amaçlandı.

Anahtar Kelimeler: Zehirlenme, acil, ilaç, toksikoloji

Introduction

Intoxication is a public health problem that can cause serious morbidity and death[1]. One of the causes that is increasing the cost of public health worldwide is drug overdose, whether intentional or not[2]. When the poisoned patients seen in the emergency department were examined, it was determined that the majority of them were adults who took an overdose of drugs intentionally. Abuse of illegal drugs, unconscious excessive intake of drugs used for chronic diseases, chronic poisoning, exposure to environmental, industrial and agricultural chemicals and drug interactions are other common causes[3]. When the exposed drugs were examined, the most common were antidepressants (15.2%) and opioids (10.9%)[2]. These constitute the majority of the records created by the calls made to the regional poison control centers of the countries[3].

In our country, the National Poison Information Center (NPIC) is an institution that has been providing 24-hour uninterrupted service since 1988[4]. NPIC records all the information, it collects and contributes to the development of protective measures by publishing a regular report every year. It shares all this evidence-based information with the public and all health personnel free of charge, and contributes to the health economy of our country by preventing ineffective and unnecessary treatment and hospitalizations[5]. It is not possible to give an exact number of poisoning cases in Turkey due to both sociocultural structure and ethnic problems. According to NPIC data, the number of case reports, which was around 15,000 in 2005, was found to be 97,087 in 2009 as a result of new studies. It was determined that the substance or substances that cause poisoning were frequently taken orally (93%) by the patients[4]. Although toxic substances causing poisoning are most commonly by ingestion, inhalation, skin and mucous membranes, and injection[1]. It is important to detect poisoning cases presenting to the emergency department immediately, to recognize and evaluate early, to initiate decontamination, to increase drug elimination, and to plan antidote treatment within indications[3].

In this article, it was aimed to compile the general management of poisoning cases admitted to the Emergency Department in line with the current literature.

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Clinical Features

Toxicological Story and Physical Examination

Since poisoning cases can admitted to the emergency department with a wide variety of complaints and clinical findings, it is very important for physicians to have a systematic and regular approach in the evaluation of these cases and in the management of the emergency department[6].

Generally, patients with poisoning may have altered consciousness or may not be able to adapt during the examination. For this reason, the history may be limited to the information that can be obtained from relatives, family members or witnesses, as well as the information that can be obtained by physical examination in cases where the patient does not cooperate. In poisoned cases, a history should be obtained from all available sources. Substance records, pharmacy records, and medical records checked by authorities are among other sources of reliable and useful information[3]. In the emergency service evaluations, the occupation of the patient, the place where the poisoning occurred, the empty drug boxes around, whether there is a different smell at the crime scene and suicide should be investigated[6]. In case of inhalation poisoning, exposure and poisoning of other persons present at the scene at home or at work should be avoided. In cases of poisoning, it is important to determine the exposed substance correctly, to start treatment and to obtain reliable product information registered about the exposed substance[3].

In general, physical examination of poisoning cases can not be done according to their current clinical features. Therefore, the findings obtained in the physical examination are based on observational findings that do not require patient compliance[3].

In the management of the poisoned patient, airway, respiration, circulation (ABC) should be evaluated in the first evaluation stage in the emergency department, and patient resuscitation and stabilization should be provided when necessary. Vital signs (blood pressure, pulse, fever, saturation), mental status, pupil diameter, skin moisture should be evaluated. Follow-up with pulse oximetry and cardiac monitoring should be provided. Intravenous vascular access should be provided. Fingertip blood sugar should be checked. electrocardiogram (ECG) should be taken. Vital signs monitoring should be repeated at appropriate intervals[6].

Toxidromes

A collection of signs and symptoms that suggest a poisoning is caused by a particular poison are called toxidromas or toxicological syndromes[4].

Sympatomymetic Syndrome

It occurs with toxins (with the release of epinephrine and norepinephrine) that increase sympathetic stimulation. Examples of substances that cause sympathomimetic toxidroma are cocaine and amphetamine[4]. These patients with hypertension, tachycardia, and tachypnea typically have increased vital signs[3]. In patients who are often agitated, dilated pupils are typical. Bowel sounds are active and there is sweating[4]. Seizures may occur[1]. Caused by exposure to amphetamines, cocaine, and cations[3].

Anticholinergic Syndrome

Anticholinergic toxidroma is caused by ingestion of agents that reduce acetylcholine release or inhibit acetylcholine binding at muscarinic and nicotinic receptors[4]. Atropine, antihistamine, antipsychotic drugs cause this group of poisonings[3]. Anticholinergic toxidromas characterized by hypertension, tachycardia and hyperthermia are common in patients with impaired consciousness and delirium. Pupils are mydriatic. There is urinary retention and hypoactivity detected in bowel sounds. Dryness of the skin and mucous membranes is an important finding in differentiating it from sympathomimetic toxidromas[4]. There is no diaphoresis. The definition of "mad like a clown, hot like a rabbit, blind like a bat, red like a beet, dry like a bone" can be used to recall the typical signs and symptoms of anticholinergic toxidromas[3].

Cholinergic Syndrome

Organophosphate and carbamate pesticides, chemical warfare agents (such as sarin gas) cause this intoxication picture[3]. It may be accompanied by fasciculations, seizures, somnolence, fatigue[1]. Caused by exposure to toxic substances such as pesticides. Saliva, tears, urinary incontinence, diarrhea and vomiting are typical findings. Deaths usually occur due to bradycardia, increased bronchial secretion, and bronchospam[4].

Sedative and Hypnotic Syndrome

It is the clinical picture that occurs in patients taking sedative-hypnotic agents (such as ethanol, benzodiazepine, barbiturate group drugs). Hypotension, bradycardia and bradypnea are more common findings. The pupils are isochoric and the patient's state of consciousness tends to sleep[4]. There is a predisposition to hypothermia[1]. Benzodiazepine can have effects such as delirium, psychosis, and transient global amnesia. Barbiturates, on the other hand, can cause hypothermia and skin blisters in high doses[7].

Opioid Syndrome

Opioid toxicity is typically characterized by hypertension, bradycardia, hypothermia, and hypoventilation[4]. Examples are codeine, heroin, morphine poisoning[3].

Serotonin Syndrom

It is a toxidrome defined as a serotonergic excess table due to selective serotonin reuptake inhibitor (SSRI), monoaminoxidase inhibitors (MAO) for examples. In addition, tricyclic antidepressants, amphetamines, fentanyl,

St. John's Wort are examples of this type of poisoning. Altered consciousness, hyperthermia, and agitation, as well as hyperreflexia, clonus, and sweating are common findings[3].

Neuroleptic Malign Syndrome

Alteration of consciousness, hyperthermia, and agitation are common. It differs from the serotonin syndrome in that it tends to rigidity and decreased reflexes rather than clonus and hyperreflexia by peripheral muscle effects. Occurs when exposed to antipsychotic agents[3].

Differential Diagnosis

In a patient presenting to the emergency department due to poisoning, other correctable causes that impair consciousness, such as hypoglycemia, should be excluded. When evaluating the patient, it is important to look at a wide variety of toxicological and non-toxicological causes for differential diagnosis[3].

Diagnostic Tests

In case of undetected overdose or exposure, the use of extensive laboratory testing assists the clinician in identifying possible clinical signs and abnormalities. Routinely requested blood tests are complete blood count, kidney functions, liver function tests, pregnancy test (if patient is female), urinalysis, urine toxicology screening, serum alcohol concentration, serum lactate and fingertip glucose measurement[3]. Blood gas analysis is a very useful test as it can be used in many different differential diagnoses. Determines the type and depth of patient's acidosis or alkalosis, carboxyhemoglobin level and oxygen saturation[4].

Urine toxicological screening tests are not routinely used except for forensic cases. Although urine toxicological screening tests are especially for illicit substance use, false positive and false negative rates are extremely high[4].

If the ingested substance is definitively identified, other tests such as specific serum concentration measurement may be used[3].

ECG should be taken. If the patient is determined to be tachycardic or bradycardic in vital signs, or if there is a history of ingestion of cardiotoxic substances that can prolong the QRS or QT interval, such as cyclic antidepressants and antipsychotic substances, an ECG should be performed, and a control ECG should be performed if necessary[3].

Radiological Imaging

In cases of poisoning, radiological imaging is used to detect some radiopaque substances, lead, heavy metals, enteric-coated tablets and packages containing oral cocaine/heroin. They can be seen radiologically on plain X-ray[4]. However, although it is not seen as a very common clinical picture, radiological imaging may be requested for the evaluation of some rare signs of poisoning (acute lung injury due to salicylate poisoning, pneumomediastinum due to cocaine use, aortic dissection, brain infarction, etc.). Imaging methods such as computed tomography (CT), ultrasonography (USG), transesophageal echocardiography (TEE), magnetic resonance imaging (MRI), positron emulsion tomography (PET) and single photon emission computed tomography (SPECT) should be performed in the appropriate clinic. Conditions in patients exposed to toxins. It can also be used for service evaluation[6].

Poisoned Patient Management

The clinician should have a systematic and consistent assessment management in the management of the poisoned patient[2]. Resuscitation is the first priority in the emergency service evaluation of a poisoned patient. Structured risk assessments are used to determine which of the appropriate antidotes, decontamination, and advanced elimination techniques would benefit the patient stabilized after resuscitation. Airway, respiratory and circulatory stabilization are priority[1]. After the maintenance of the airway and ventilation, which is the basic 'ABC' of resuscitation, the main purpose is to provide the patient's circulation with fluid resuscitation and, if necessary, vasopressor support. Intubation is often the preferred route in patients who are unable to maintain an airway or have insufficient respiratory effort to maintain adequate ventilation. Peripheral and central venous catheters may be preferred for vascular access. There is no suitable antidote for every toxin and therefore supportive care is the mainstay of treatment for the poisoned patient[3].

Treatment

Decontamination

The decontamination process is used to clean the skin surface exposed to the toxic substance. Decontamination should be done in a separate area close to the emergency service, but in a way that does not contaminate the emergency service and other environments. The decontamination process is carried out by the healthcare personnel using appropriate equipment (bone, gloves, eye protection) in international standards, by undressing the patient and washing with plenty of water. Clothing exposed to the toxin is properly packaged and disposed of properly[1].

In addition to contact with the skin, in case of eye contamination, it is provided by washing with plenty of water[3]. Abundant irrigation with crystalloid solutions can be done for eye contamination. Local anesthetic application and valve retractors may be required to facilitate the procedure[1].

Ipecac Syrup

It is not appropriate to use ipecac syrup in patients who apply to the emergency department with a history of poisoning for purpose of vomiting[3].

Gastric Lavage

Gastric lavage is the direct removal of material from the stomach using a 30 Fr or larger orogastric tube, and few data have been found to demonstrate the effectiveness of this treatment[3]. In patients with toxic doses, gastric lavage therapy is recommended within the first hour after ingestion of the substance. However, it is inconvenient to apply if the patient's airway safety cannot be ensured in cases of poisoning, if there is caustic substance intake, if the risk of aspiration is increased, if there is a risk of gastrointestinal bleeding and perforation[6]. Because of the risk of aspiration and esophageal trauma, the American Central Poison Association recommends gastric lavage within the first hour after ingestion of a potentially life-threatening venom that is not absorbed with activated charcoal or has no antidote[3].

Vomiting

In the past, vomiting was used to extract the toxic substance to which it was exposed. However, it is not recommended to induce vomiting in the emergency management of oral toxic substances[1].

Antidote

The correct use of antidotes is important. Required for patient stabilization after exposure to toxic substances[1]. However, there is no suitable antidote for every toxic picture[3].

Activated Carbon

Activated charcoal, which has the ability to bind to many toxins; It binds to these toxins and prevents toxin absorption[6]. Activated charcoal is most effective in the first one to two hours after ingestion of the toxin. It has been reported that a single dose of activated charcoal is not routinely required in every case of poisoning. Activated charcoal may be considered if a potentially toxic amount of poison is present and less than 1 hour has passed[4]. Activated charcoal is not recommended if the ingested poison or drug has low toxicity (eg, ibuprofen, diazepam) or if an effective known and available antidote is available (eg N-acetylcysteine for acetaminophen, digoxin immune-fab for digoxin)[3]. Activated charcoal can be given by giving an oragastic or nasogastric tube in intubated patients. The dose of activated charcoal is 1 gram/kg in children and 50 grams PO in adults. Repeated doses of activated charcoal are usually recommended for overdose. The recommended dose is 50 grams PO followed by 25 grams PO every 2 hours[1].

Repeated Activated Coal Application

A single dose of activated charcoal aims to prevent the absorption of a drug. Repeated dosing of activated charcoal aims to eliminate an absorbed toxin[3]. Repeated doses of activated charcoal increase the elimination of toxins from the enteroenteric, enterohepatic, or enterogastric circulation[1]. However, it accelerates the elimination of toxins with its low volume of distribution, low binding affinity and long elimination half-life. It has been found to be beneficial in poisoning due to exposure to carbamazepine, phenobarbital, theophylline, quinine, aspirin, dapsone[6]. Repeated doses of activated charcoal should not be given if bowel sounds are hypoactive or absent[1]. For toxins whose serum level can be monitored, repeated doses of activated charcoal are discontinued if the serum level is not in the toxic range[3].

The Entire Bowel Lavage

The entire bowel lavage procedure is the administration of an osmotically stable polyethylene glycol solution through a nasogastric tube[6]. Entire bowel irrigation is indicated if extended-release drugs, illicit drug packages, or oral metals (eg, iron and lead) are present. However, it is contraindicated in patients with impaired general condition, intestinal hypoperfusion or intestinal obstruction. Because it has been reported to increase morbidity and mortality in such clinical conditions[3].

Hemodialysis

Toxins are metabolized by hepatic and renal pathways after ingestion and absorption. In overdose exposures, it is appropriate to eliminate some toxins by extracellular mechanisms (eg hemodialysis) and some toxins by mechanisms that increase intracellular elimination (eg urine alkalization and repeated dose activated charcoal). Hemodialysis and similar treatments are the most suitable methods to remove low molecular weight, low protein binding and high water soluble toxins[3]. Hemodialysis can be applied in lactic acidosis triggered by exposure to lithium, phenobarbital, salicylate, valproic acid, methanol/ethylene glycol, potassium salts and theophylline, and in metformin, which is life-threatening poisoning. As complications of hemodialysis, hypotension, infection at the catheter site, and bleeding can be seen[1].

Hemoperfusion

It is a method that allows the absorption of the toxin by passing the whole blood through a cartridge covered with activated charcoal or a non-ionic resin[8,9]. It is a suitable treatment for toxins with high molecular weight and protein binding[2,9]. A higher rate of anticoagulation is required in hemoperfusion[9,10]. It can be applied in theophylline, carbamazepine, thallium, procainamide poisonings[11]. Thrombocytopenia, leukopenia and hypocalcemia are complications different from hemodialysis. As in hemodialysis, hypotension, infection at the catheter site, and bleeding may also occur[1].

Contınuous Hemofiltration and Hemodiafiltration

Hemofiltration and hemodiafiltration can be applied for toxins that can be applied hemodialysis. Unlike hemodialysis, it is also effective in toxins with higher

molecules (approximately 25000 Da)[8,12,13]. Due to the increasing technical need and transportation difficulties, its use in poisoning cases is limited[8,14].

Exchange Transfusion and Plasmapheres

In both methods, it is effective on digoxin, thyroxine, antidigoxin antibodies and high molecular weight immunoglobulins by removing plasma proteins[11]. It is suitable for methemoglobinemia, which occurs with toxins such as xenobiotics, sodium nitrate, dapsone, which are not suitable for hemodialysis[8,15,16]. It is easy to apply in the newborn patient group[11].

Serum Alkalization

Water-soluble substances (such as salicylates, methotrexate, and phenobarbital) can be eliminated by alkalizing the serum by an ion-scavenging mechanism. This is crucial for salicylate poisoning. Because alkalinization prevents salicylates from entering the central nervous system by crossing the blood-brain barrier and ensuring their elimination[3]. In salicylate poisoning, it can reach medium and high concentration values such as 0.3-0.5 lt/kg[17]. The primary indication is medium and high dose salicylate poisoning in which hemodialysis cannot be applied. Serum pH and bicarbonate levels and urine pH values should be monitored in patients undergoing alkalization. Serum pH value should be around 7.5, urine pH value should be around 8.0. Serum potassium value should be closely monitored. One of the reasons that reduce the effectiveness of urine alkalization is hypokalemia[1]. 150 milliequivalents of sodium bicarbonate can be added to 1 liter of 5% dextrose in the alkalization process, and it can be applied at a rate not exceeding 250cc per hour. Potassium (20-40 milliequivalent I.V. in total) can be added to the prepared liquid and given[3].

Intravenous Lipide Emulsion

It was first applied in the treatment of local anesthetics[3]. Intravenous lipid emulsion therapy may be considered in cases where all interventions fail to respond[6]. An exact indication for the application has not been reported. It has been shown that successful resuscitation results are obtained in cases of beta-blocker overdose, calcium channel blockers, cyclic antidepressants, bupropion and cocaine toxicity, except for anesthetic agents treated with intravenous lipid emulsion therapy[3]. The most common complications are pancreatitis, electrolyte disturbance, acute respiratory distress syndrome[6].

Follow-up, Discharge and Admission

In most cases, an observation period of 6 hours is sufficient to exclude serious toxicity to schedule patient discharge from the emergency room[1]. Patients with severe toxicity should be admitted to the intensive care unit. Patients who are asymptomatic on admission to the emergency department, but who have dangerous toxin intake that may cause deterioration in their clinical status, or who use extended-release drugs are suitable for hospitalization and follow-up. Discharge of patients hospitalized or observed in the emergency department should be planned after the first 24 hours after ingestion or after the effect of the poisoning has disappeared[3]. It is appropriate for patients with deliberate overdose to be evaluated by a psychiatrist after their treatment is completed[4].

Conclusion

It is important to develop a systematic and consistent approach in cases of poisoning presenting to the emergency department with very different signs and symptoms for early diagnosis and planning of appropriate treatment. A detailed history should be taken from the patient, patient's relatives and the staff at the scene. Providing information about the case to the national poison information center is a suitable option both to contribute to the national poisoning registry and to determine the treatment management. It can be used for direct toxicity detection for toxins whose serum level can be measured, although it is recommended to schedule a large blood test to reveal the effects of the toxin. There is no suitable antidote for every toxin exposure. But some specific antidote applications can be lifesaving. In case of poisoning, decontamination, gastric lavage, administration of activated charcoal, serum alkalization, whole bowel irrigation, extracorporeal methods, IV. lipid emulsion methods can be preferred according to the toxic substance. Determining systematic and consistent diagnosis and treatment management strategies in emergency service evaluations of poisoning cases will increase the success of patient resuscitation.

Table 1: Toxidromes and differential diagnosis

TOXIDROME	Heart Rate	Respiratory Rate	Fever	Pupil Diameter	Bowel Sounds	Diaphoresis
Anticholinergic	increases	not affected	increases	increases	decreases	decreases
Cholinergic	not affected	not affected	not affected	decreases	increases	increases
Opioids	decreases	decreases	decreases	decreases	decreases	decreases
Sympathomimetic	increases	increases	increases	increases	increases	increases
Sedative and Hypnotic	decreases	decreases	decreases	decreases	decreases	decreases

Table 2: Antidotes and indications[3]

ANTIDOTE	INDICATION
N-Acetylcysteine	Acetaminophen
Fomepizole	Methanol / Ethylene Glycol
Oxygen / Hyperbaric	Carbon Monoxide
Alaxon	Opioids
Physostigmine	Anticholinergic
Atropine / Pralidoxime	Organophosphate
Methylene Blue	Methemoglobinemia
Nitrites / Hydroxycobalamin	Cyanide
Deferoxamine	Ferrous
Succimer	Lead, Mercury
Caedta	Lead
Fab Trailers	Digoxin, Crotalids
Glucagon	Beta Blockers
Sodium Bicarbonate	Salicylates, Tricyclic Antidepressants
Calcium, İnsulin/Glucose	Calcium Channel Antagonists
Dextrose, Glucagon Octreotide, Pyridoxine	Oral Hypoglycemic Agents, İsoniazid
Intravenous Fat Emulsion	Local Anesthetic Systemic Toxicity, Base Oil Soluble Drugs
Dimercaprol (BAL)	Arsenic, Lead

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Review

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Management of Paracetamol (Acetaminophen) Intoxication

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Abstract

Acetaminophen intoxication is one of the most frequent causes of poisoning caused by medical treatment and deaths. Acetaminophen intoxication happens when it is taken in a single high dose or several times above the treatment dose. The approach to the patient with acetaminophen intoxication includes stabilization, decontamination and n-acetyl cysteine (the specific antidot of acetaminophen). In this article, it is aimed to review the approach to patients with paracetamol poisoning in the emergency department with current medical literature.

Keywords: Paracetamol; acetaminophen; intoxication; emergency

Özet

Asetaminofen zehirlenmesi tedaviye bağlı zehirlenmeler ve ölümlerin en sık görülen nedenlerinden biridir. Asetaminofen zehirlenmesi tek doz fazla miktarda alım ya da tedavi dozunun üzerinde tekrarlayan alımlarla gerçekleşmektedir. Asetaminofen zehirlenmesi olan hastaya yaklaşım stabilizasyon, dekontaminasyon ve spesifik antidot olan N-asetilsistein tedavilerini içerir. Bu makalede parasetamol zehirlenmeli hastalara acil serviste yaklaşımın güncel tıbbi literatür bilgileri eşliğinde derlenmesi amaçlandı.

Anahtar Kelimeler: Parasetamol; asetaminofen; zehirlenme; acil

Introduction

Paracetamol is the most widely used analgesic agent because of its reliability, efficacy and inexpensiveness. Paracetamol intoxication is reported frequently, because it is used commonly and accessed easily. Acetaminophen is found solitarily or combined with different medications that produced in tablet, capsule, gel or liquid form. Poisonings often result from either the wrong belief that the drug is very safe, or the poisoned patients not knowing that the drug they are taking contains acetaminophen.

In this article, it is aimed to review the approach to patients with paracetamol poisoning in the emergency department with current medical literature.

Epidemiology

According to the report of the American Association of Poison Control Centers, above 100.000 cases of paracetamol intoxication reported, 50.000 cases admitted to the emergency service and 10.000 patients are hospitalized every year[1]. The number of hepatotoxicity because of overdosing of paracetamol and death rates are rising lately with the increasing frequency of drug use[2]. Paracetamol intoxication causes hepatocellular necrosis and thus responsible for 500 deaths annualy in the United States of America.

Mechanism of Action and Pharmacokinetics

Hepatotoxicty occurs frequently with paracetamol intoxication, however renal failure, metabolic acidosis, coagulopathy, encephalopathy and recurrent gastrointestinal symptoms are also seen. Oral paracetamol is converted to a toxic metabolite, N-acetyl-p-benzoquinonimine (NAB), by cytochrome p450 enzyme system in the liver and detoxified by endogenous glutathione. Glutathione storage is decreased when paracetamol is taken in high doses and hepatotoxicity occurs because of the lack of detoxification of toxic metabolites. N-Acetylcysteine (NAC) is a glutathione precursor. NAC prevents bonding between toxic metabolites and hepatic macro molecules thus renews reduced glutathione storage. NAC also decreases hepatic necrosis by

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antioxidant mechanisms. It is reported that administration of NAC in the first 8 hours of intake greatly prevents toxicity in acute paracetamol intoxication[1-4]. It is recommended that paracetamol be taken 10-15 mg/kg up to 4-6 times per day in children and 650-1000 mg up to 4-6 times per day in adults. The recommended maximum dose is 4 grams in adults and 10-15 mg/kg in children. Paracetamol after the oral intake is well absorped from the gastrointestinal tract and in serum it reaches its peak concentration in 2 hours. The time to reach the peak plasma concentration may last longer in delayed gastric emptying. It may take 4 hours to reach the peak plasma concentration in time-release tablets. The absorption rate depends on the mode of administration. The absorption rate in suppository form does not exceed 40% however the absorption rate is between 60-98% in oral intake. The extent of protein binding is between 10-30%[5].

After oral intake, paracetamol is metabolized by conjugation with sulphate and glucuronide 90% in the liver. Glutathione levels decreased in high dose intake and hepatotoxicity occurs because the metabolites can not be detoxified. Acetaminophen metabolism may vary depending on age thus in elderly patients the likelihood of developing hepatotoxicity is high. . Children under 5 years of age are more resilient to hepatotoxicity than adults. Besides hepatic necrosis, renal tubular necrosis and hypoglycemic coma are the other fatal effects. Conversion to toxic reactive metabolites occur when paracetamol is taken in excessive doses. This substance that excreted in urine is responsible for renal tubular acidosis[6].

Clinical Features

After the acute intake of acetaminophen, patients may be asymptomatic or they might have mild non-specific symptoms like nausea, vomiting, fatigue, sweating and loss of appetite in the early stage. Liver damage becomes significant by the increase of aspartate aminotransferase (AST) after 8-36 hours. Right upper quadrant pain (or tenderness), nausea and jaundice may develop once the liver damage starts. AST levels continue to rise rapidly and reaches the peak level in 2 to 4 days. Alanine aminotransferase (ALT), prothrombin time (PT) and bilirubin levels begin to rise typically and AST reaches the point within hours after those. All the AST, ALT and PT levels may rise within 24 hours with severe toxicity[7].

With maximum liver damage, signs and symptoms consistent with fulminant hepatic failure that includes metabolic acidosis, coagulopathy and hepatic encephalopathy may develop in patients. Death may occur due to hemorrhage, adult respiratory distress syndrome, sepsis, multiple organ failure or cerebral edema. Risk of renal damage (Hepato-renal syndrome) increases with the level of liver damage is seen less than 2% of patients with no hepatotoxicity and 25% of patients with severe hepatotoxicity. The aminotransferases get back to normal in 5-7 days during the recovery period however complete histological healing in liver might take months. Once histological recovery is made, long term hepatic sequelae is not seen in patients[7].

Four Stages of Acetaminophen Intoxication

The clinical presentation acetaminophen intoxication in humans can be examined in 4 phases. Patients may be asymptomatic or they may show minimal toxicity symptoms like loss of appetite, nausea, vomiting and fatigue or non-specific symptoms in the first 24 hours (Stage 1) of exposure. The symptoms seen in stage 1 resolve on the second and third days but hepatotoxicity findings including right upper quadrant pain and tenderness with the increase of serum transaminases might occur. Patients who have mild to moderate hepatotoxicity recover fully with no sequelae even without any treatment. However some patients progress to fulminant hepatic failure on the third and fourth day (Stage 3)[8,9]. Characteristic stage 3 features include metabolic acidosis, coagulopathy, renal failure, encephalopathy and recurrent gastrointestinal symptoms. Patients who survive the complications of fulminant hepatic failure begin to improve in 2 weeks (Stage 4) and by the end of 1-3 weeks, hepatic dysfunction completely disappears. Acetaminophen also causes acute, extrahepatic toxic effects. It's because the presence of CYP450 or similar enzymes (e.g. prostaglandin H synthase) in other organs. Isolated renal damage, cardiac toxicity and pancreatitis can be rarely observed in isolated cases[10,11].

Diagnosis

The diagnosis of paracetamol intoxication starts with clinical suspicion in the emergency room. Therefore serum paracetamol level should be measured in patients suspected of having intoxication to determine the correct and early diagnosis and treatment. The amount of medication, the purpose and the form of use, dosage time and the other medications taken together should be questioned in all patients with suspected paracetamol intoxication. Serum levels should be viewed again 4 hours later after taking the drug acutely. BUN and creatinine, serum total bilirubin level, INR, AST, ALT, amylase, urinalysis, prothrombin time and blood gas test may be ordered. Blood and urine tox screen should be performed in patients with a history of suicide and deliberate attempt[6].

Goals of patient evaluation after acetaminophen intake: determining the risk of patients, diagnostic testing and treating with the antidote, NAC when appropriate.

Acetaminophen exposure can be classified as an acute or a chronic exposure and all types of exposure require various tests and risk assessment. Acute intake is generally thought to be a single intake or self-administered drug intake within

an 8-hour period. Taking supratherapeutic doses accidentally and taking self-administered drugs longer than 8 hours are considered to be chronic intake[7].

Risk Assessment in Acute Acetaminophen Intake

First, patient's risk of acute acetaminophen exposure should be determined. Laboratory risk classification is required in patients with acute intentional intake of acetaminophen regardless of the amount told by the patient. More than 10 grams or 150 mg/kg or 25 tablets of 500 mg should be taken acutely for hepatotoxicity to occur in adult patients. Serum acetaminophen levels should be assessed in patients admitted with acetaminophen intake or in intentional overdose patients who has access to acetaminophen even if the patient denies taking it. Acetaminophen has been found in the blood of 8% of the patients who refuse taking medication. Unidentified acetaminophen toxicity prevalence (18%) is high in patients who admitted with liver failure with no apparent cause.

It should be determined whether there is a need for antidote treatment by measuring the serum acetaminophen level in the 4th hour after intake or Rumack-Matthew nomogram. If the serum acetaminophen level is at or above the treatment line, this indicates the treatment indication of NAC. If the serum acetaminophen level is below the treatment line and the strongest possible scenario for the time of intake is taken, the patient does not need an antidote[7].

Rumack-Matthew Nomogram

The measured acetaminophen level is evaluated by marking on the Rumack-Matthew nomogram (Figure 1). This nomogram was derived from retrospective analyzes of patients who overdose acetaminophen and their outcome. The original nomogram line separating possible toxicity from non-toxic one is based on being 200 micrograms/ml of acetaminophen in the 4th hour, however the acetaminophen level in the 4th hour was changed to 150 micrograms/mL in order to increase the safety of treatment decisions afterwards.

The nomogram can be applied to the acetaminophen level obtained after a single intake only, or to acetaminophen levels between 4 hours and 24 hours after ingestion of the drug. This nomogram is not used to predict patient outcome in acetaminophen levels measured outside of this window or in chronic conditions or recurrent exposures. In the absence of hepatotoxicity, more than one measurement of acetaminophen is rarely required in acute poisonings[7].

Considering the data obtained before the widespread use of antidote therapy, the risk of hepatotoxicity in patients with serum acetaminophen levels above the original threshold value was found to be 60%, renal failure risk 1% and mortality risk 5%. In addition, patients with extremely high serum acetaminophen levels have a 90% risk of developing hepatotoxicity. It has been confirmed that acetaminophen level below 150 microgram/mL in the 4th hour after drug intake predicts good outcome in patients not receiving antidote therapy. According to the nomogram, patients with acetaminophen levels below this value have a 1% risk of hepatotoxicity and these patients recover without complications[12,13].

Treatment

The basis of the treatment is the correction of vital signs, removal of the poisoning agent from the body and administration of a specific antidote, N-acetylcysteine (NAC). Antidotes used in paracetamol intoxication are NAC, cystamine, dimercaprol and methionine[6].

Decontamination

In paracetamol poisonings, absorption should be prevented primarily, and supportive treatment should be started as soon as possible by following the levels showing the clinical course. Gastric lavage and activated charcoal can be applied to prevent absorption within the first 4 hours after ingestion of high-dose paracetamol. Activated charcoal binds to paracetamol in the intestinal lumen and prevents its absorption. Oral administration of 1 g/kg (maximum dose 50 grams) is recommended[6].

Increased Elimination

Dialysis is not routinely applied in cases of excessive intake of acetaminophen, as there is a highly effective antidote with good clinical results when given within 8 hours of ingestion. However, hemodialysis may be beneficial if the load of absorbed acetaminophen is high enough to cause hepatotoxicity despite normal doses of NAC. Consultation with a poison control center or a medical toxicologist is recommended for the initiation of hemodialysis in patients with high acetaminophen levels, hepatorenal syndrome, metabolic acidosis, encephalopathy and high lactate levels within 4 hours after acute massive ingestion. There is no conclusive evidence for the effectiveness of hemodialysis, but removing excess acetaminophen can prevent toxicity by allowing NAC to deal effectively with the reduced toxin load[7].

Antidote Treatment

When indicated, NAC should be administered as soon as possible. Delay of NAC for more than 8 hours after ingestion increases the risk of hepatotoxicity. When administered early (<8 hours), NAC's main role is to prevent hepatotoxicity by detoxifying NAPQI and reducing NAPQI production. In patients treated with NAC within 8 hours, the risk of liver damage is less than 4% and the death rate approaches zero. Although they can not tolerate the oral formulation due to vomiting and hepatic encephalopathy, both po and iv formulations of NAC are equally effective in patients admitted 8-24 hours after ingestion.

Once hepatic failure has occurred, NAC is only given intravenously. In acetaminophen-related liver failure, iv

NAC reduces the risk of hypotension, cerebral edema and death. Oral NAC should only be used if iv NAC is not available. The loading dose of oral NAC is 140 mg/kg. The maintenance dose consists of 70 mg/kg every 4 hours for a total of 72 hours of treatment.

The standard regimen of intravenous acetylcysteine is a 21-hour treatment protocol consisting of a 150 mg/kg loading dose for 1 hour, followed by an initial maintenance treatment at 50 mg/kg for 4 hours, and a second maintenance treatment at 100 mg/kg for 16 hours. IV Acetylcysteine is available as a 20% commercial solution and must be diluted to a 2% solution for administration through a peripheral vein. For this, 5% dextrose or 0.45% NaCl can be used. Due to the volume and hypotonicity of the required fluid, children and adults <40 kg should be monitored closely during the treatment to prevent fluid overload and hyponatremia[14,15].

Treatment guidelines according to the time of admission to the emergency department

Admissions within the first 4 hours after intake; Treatment begins with gastrointestinal contamination and acetaminophen level is monitored in the blood 4 hours after taking the drug. The result is placed on the nomogram. If acetaminophen level cannot be determined within 8 hours after intake, empirical acetylcysteine treatment is started without waiting for the result[16,17].

Admissions <4 hours and >24 hours after intake; The serum acetaminophen level should be determined as soon as possible. Especially if additional drug intake is suspected, GI decontamination can be applied, but its effectiveness may be limited due to the delay in admission. The need for acetylcysteine treatment should be determined by placing the acetaminophen level on the nomogram. Otherwise, empirical acetylcysteine treatment is started[11].

Admissions >24 hours or unknown time of intake; Serum acetaminophen level, transaminase, bilirubin and prothrombin time tests should be determined for patients with clinical findings suggestive of acetaminophen poisoning and whose time of intake is unknown. Acetylcysteine treatment should be started as soon as possible while the results are awaited. A detectable acetaminophen level (>10 micrograms/mL or >66 micromol/L) suggests that the patient is at risk of developing hepatotoxicity. Increased serum transaminases are markers of ongoing hepatic toxicity. Continuation of acetylcysteine therapy is required. If serum acetaminophen level is <10 microgram/mL or <66 micromol/L, and serum transaminases are not high, acetylcysteine treatment can be discontinued[16,17].

Other treatments

Cimetidine: Many studies have shown that some drugs show additional benefit in preventing acetaminophen-induced liver damage. The most important of these is cimetidine, which plays an inhibitory role in the metabolism of acetaminophen[18-20]. This treatment was found to be beneficial in animal studies, but it was observed that it did not provide additional benefits in patients treated with N-acetylcysteine[18,21]. Earlier studies investigated the benefits of methionine, dimercaprol, and cysteamine, but these studies were terminated due to side effects[18,22].

Dialysis: Although acetaminophen can be removed by dialysis, it is not included in the standard treatment protocol due to the safety and efficacy of N-acetylcysteine. Extracorporeal removal can be used to lower serum acetaminophen in patients unsuitable for N-acetylcysteine, but there are no systematic studies of the efficacy of this treatment[18,23]. Hemodialysis should not be considered as an alternative to N-acetylcysteine therapy.

Discharge

Asymptomatic patients who meet the treatment criteria should be treated with NAC. This treatment can be applied in the medical inpatient unit or the emergency room observation unit. The motivation behind any intake should be evaluated and psychiatric consultation should be ordered when necessary. Patients showing signs of severe hepatotoxicity and those at risk of fulminant hepatic failure should be hospitalized in a monitorized bed or intensive care unit. Frequent neurological checks, monitoring of vital signs, and repeated laboratory studies are required in these patients. If patients present with significant hepatotoxicity, transfer to a 3rd level care center, which specialized in the management of patients with liver failure and liver transplantation, is recommended[7].

Conclusion

1. As in all poisonings, the basic approach in paracetamol intoxication is to check the airway, respiration and circulation first.
2. Patients who admitted in the first 24 hours after an acute ingestion of paracetamol poisoning generally have no complaints or symptoms. Patients admitting later show signs of hepatic and renal damage. Signs and symptoms that may be caused by liver damage or failure such as nausea, vomiting, weakness, abdominal pain, renal damage, coagulopathy (eg, gastrointestinal bleeding), hepaticencephalopathy, cerebral edema or hypotension may be found in patients admitting late.
3. There are no early signs of toxicity and severity of intoxication in acute ingestion can be measured by showing the serum paracetamol level on the Rumack-Matthew nomogram. It is potentially serious if the dose taken is greater than 150 mg/kg.

Table 1: Acetylcysteine dosing regimens[17].

	PO	Adults iv	Children iv (21-40 kg)	Children iv (5-20 kg)
Preparation	Available in 10% and 20% solutions. Dilute to 5% solution for PO application	Available in 20% solutions. Dilution is required.	Available in 20% solutions. Dilution is required.	Available in 20% solutions. Dilution is required.
Loading dose	140 miligram/kg	150 mg/kg infused in 200 milliliters of 5% dextrose in 60 minutes	150 mg/kg infused in 100 milliliters of 5% dextrose in 60 minutes	150 mg/kg infusion in 60 minutes in 3 ml/kg 5% dextrose
Maintenance dose	17 doses of 70 milligrams/ kg every 4 hours	50 mg/kg in 500 ml 5% dextrose followed by infusion in 4 hours 100 mg/kg infusion in 16 hours in 1000 ml 5% dextrose	50 mg/kg infusion in 4 hours in 250 ml 5% dextrose 100 mg/kg infusion in 16 hours in 500 ml 5% dextrose	Following infusion in 4 hours in 50 mg/kg, 7 ml/kg 5% dextrose 100 mg/kg, 14 ml/kg infusion in 16 hours in 5% dextrose
Treatment time	72 hours	21 hours	21 hours	21 hours
Recommendations	Dilute with powdered drink mix, juice or soda	Monitor for drug-related side effects or anaphylactoid reactions	Monitor for drug-related side effects or anaphylactoid reactions	Monitor for drug-related side effects or anaphylactoid reactions

4. After ingestion of a potentially toxic dose of paracetamol (single dose >7.5 grams), patients benefit from gastrointestinal decontamination and oral activated charcoal is recommended within the first 4 hours after ingestion.
5. Treatment includes stabilization, decontamination and application of the specific antidote, acetylcysteine.
6. There are 2 treatment protocols for acetylcysteine administration, 21-hour intravenous and 72-hour oral.
7. The 21-hour IV protocol includes a 150 mg/kg IV 15-60 minute loading dose followed by a 4-hour IV infusion of 12.5 mg/kg/h and a 16-hour 6.25 mg/kg/h IV infusion.
8. The 72-hour oral protocol includes a loading dose of 140 mg/kg po, followed by a total of 17 doses of 70 mg/kg acetylcysteine every 4 hours.

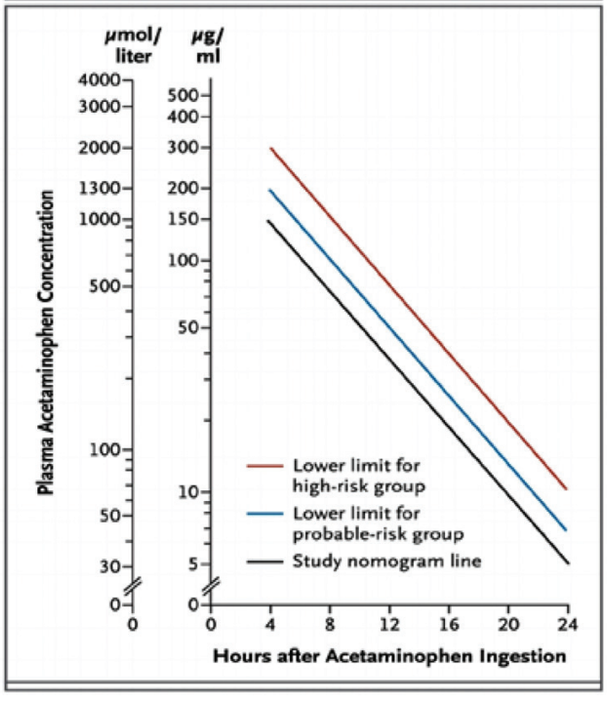

Figure 1: Rumack-Matthew nomogram

9. During the treatment, INR, plasma creatinine and ALT levels should be monitored. If there is any test abnormality at the end of the treatment or if the patient is symptomatic, further monitoring is required and additional treatment methods are investigated. Acetylcysteine treatment is continued.

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Case Report

Eurasian Journal of Toxicology

Two Ischemic Stroke Cases Accuring Despite High INR Levels

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Abstract

Warfarin is a vitamin K antagonist commonly used in the treatment and prevention of thromboembolic cases worldwide. Its therapeutic range is narrow and is followed by the international normalized ratio (INR). Ischemic conditions are observed at low INR levels whereas bleeding is seen at higher INR levels. A 45-year-old woman and a 79-year-old man using warfarin were admitted to the emergency department with a neurological deficit. Ischemic stroke was revealed via radiological imaging in both patients. However, INR levels were significantly higher in laboratory tests (11.44 and 12.37 kU/L).Ischemic stroke occurred although bleeding is normally expected at such high INR levels. Contrary to many studies published in the literature, this case report revealed interesting information in terms of its conclusions.

Keywords: İschemic stroke, high INR levels, warfarin overdose, emergency medicine

Özet

Warfarin, dünya çapında tromboembolik vakaların tedavisinde ve önlenmesinde yaygın olarak kullanılan bir K vitamini antagonistidir. Terapötik aralığı dardır ve bunu uluslararası normalleştirilmiş oran (INR) ile takip edilir. Düşük INR seviyelerinde iskemik durumlar gözlenirken, daha yüksek INR seviyelerinde kanama görülür. Varfarin kullanan 45 yaşında kadın ve 79 yaşında erkek hasta nörolojik defisit ile acil servise başvurdu. Her iki hastada da radyolojik görüntüleme ile iskemik inme saptandı. Ancak INR düzeyleri laboratuvar testlerinde (11.44 ve 12.37 kU/L) anlamlı olarak daha yüksekti. Bu kadar yüksek INR seviyelerinde normal olarak kanama beklenmesine rağmen iskemik inme meydana geldi. Literatürde yayınlanan birçok çalışmanın aksine bu olgu sunumu sonuçları açısından ilginç bilgiler ortaya koymuştur.

Anahtar Kelimeler: İskemik inme, yüksek INR seviyeleri, warfarin doz aşımı, acil tıp

Introduction

Warfarin is a vitamin K antagonist commonly used in the treatment and prophylaxis of thromboembolic diseases. It is extensively used in diseases such as prosthetic heart valve diseases, dilated cardiomyopathy, atrial fibrillation (AF), deep vein thrombosis (DVT), and pulmonary embolism (PE)[1]. In particular, anticoagulation, which is well controlled with warfarin, can prevent more than half of the strokes associated with AF and heart valve replacements[2]. The therapeutic index of warfarin is narrow, followed by the international normalized ratio (INR). INR provides a standard scale for monitoring patients receiving oral anticoagulant therapy. The rate of prothrombin time (PT) of the patient is calculated as its rate to the control PT obtained using a thromboplastin reagent, an international reference developed by the World Health Organization (WHO)[3]. In this case report, we will present two stroke cases occurring despite high INR levels, which is not encountered in the literature.

Case 1

A 45-year-old woman was admitted to the emergency department with complaints of, dizziness, nausea, and numbness in the left arm. We learned that she had been taking 5 mg of warfarin daily for her previous occlusive cerebrovascular disease. The patient was conscious. Her general state was good, Glasgow Coma Scale (GCS) was 15, and vital signs were stable. Her neurological examination showed dysarthria and 4/5 muscle strength hemiparesis in her left upper and lower extremities.The patient had no stiffness and no additional pathological reflexes. In the blood sampling, Hemoglobin was found as 9.7 g / dl, WBC was 15.070 and PLT was 272.000. His electrocardiogram (ECG) showed sinus rhythm. No electrolyte imbalance was detected in the biochemical analysis. INR was found as 11.44 kU / L (studied twice). In the cranial imaging of the patient, computerized brain tomography (CBT) showed chronic ischemic changes, while magnetic resonance imaging (MRI) showed a 10 mm diameter diffusion restriction on the left

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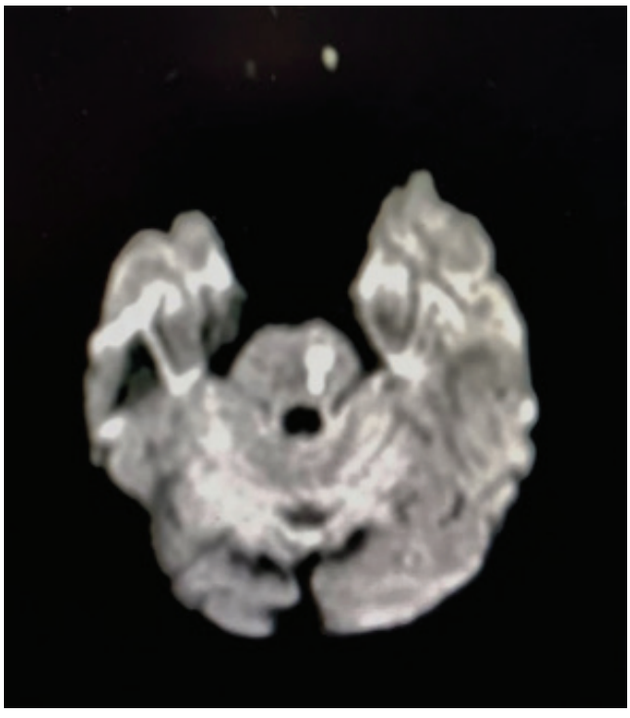

Figure 1: Magnetic resonance imaging of Case 1

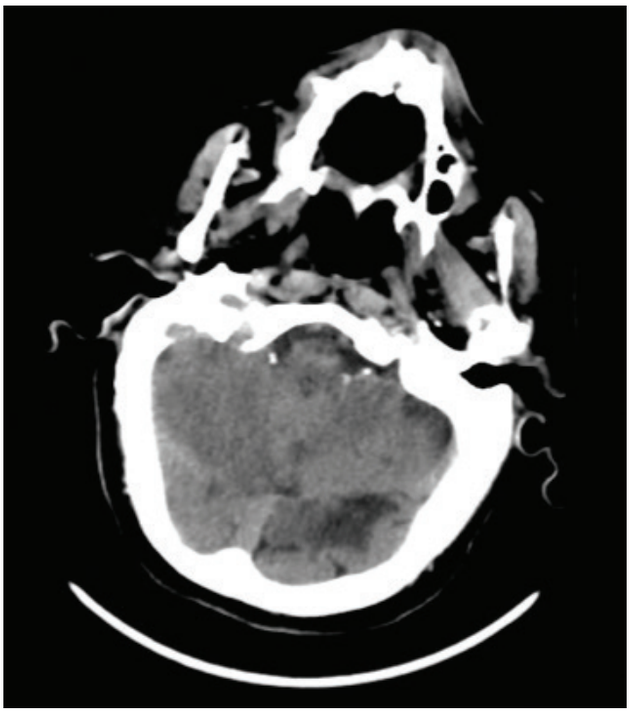

Figure 2: Computerized brain tomography of Case 2

side of the brain stem (Figure 1). The patient was admitted to the intensive care unit for follow-up by consulting with the neurology clinic. In the subsequent examination of the patient, antiphospholipid antibodies (APS), anticardiolipin antibodies (ACA) and antinuclear antibodies (ANA) were found to be negative.

Case 2

A 79-year-old male patient was admitted to the emergency department with dysarthria and blurred consciousness. The patient had a history of hypertension, AF, and chronic kidney disease. He had confusion, his orientation and cooperation were impaired and his GCS was 10.His vital signs were stable,blood glucose level was found as 128 mg / dl, BUN was 34.02 mg / dl, creatinine was 1.94 mg / dl, and INR was 12.37 kU / L (studied twice). We learned that the patient had been using 5 and 2.5 mg of warfarin every other day. Computerized brain tomography revealed periventricular white matter density and diffuse diminution, and heterogeneous hypodense lesion area in the occipital lobe on the left side (Figure 2). Subsequent MRI revealed diffusion in both cerebellar hemispheres at the occipital lobe of the left central subcortical area. In the hyperintense ADC map of the images, signal limitation areas which were compatible with hypointense acute ischemia in the millimeter size in the thalamus on the left and in the periventricular white matter on the right were observed (Figure 3). The patient was admitted to the intensive care unit in consultation with the neurology clinic.

Discussion

Warfarin inhibits the synthesis of vitamin K-dependent coagulation factors, including factor II, VII, IX and X and anticoagulant proteins C and S[4]. The therapeutic range of warfarin is narrow.In particular, it is difficult to use as it is influenced by many factors such as dose adjustment, genetic factors, drug interactions, and diet. The targeted INR value is usually 2 to 3 in patients with AF, DVT / PE, and occlusive cerebrovascular disease. The targeted INR value in patients with prosthetic heart valve disease is 2.5-3.5[5]. The most common side effect is bleeding[6-7]. Especially in cases whose INR values exceed 4.5, the risk of major bleeding increases[2]. Intracranial hemorrhage (ICH) is considered as the most dangerous bleeding complication of anticoagulant therapy. In warfarin-dependent ICHs, the mortality rate is high and a large proportion of these patients die within 30 day[8]. In most of the bleeding, INR values are high.Many side effects have been reported in the literature due to warfarin use. Most of the rare side effects have been reported in case reports. In those reports, acute kidney injury, skin lesions, hepatoxicity, and penile gangrene despite the normal INR level have been reported[9-11]. In another study, nonhaemorrhagic arthritis findings independent from INR values have been reported in 61 patients using vitamin K antagonist[12]. The risk of thromboembolism

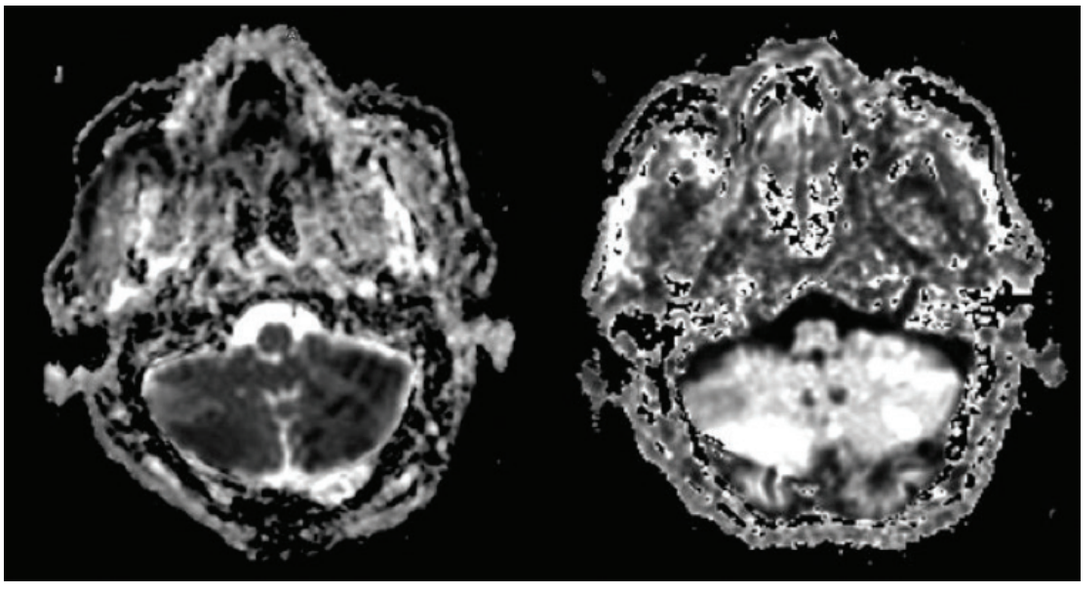

Figure 3: Magnetic resonance imaging of Case 2

increases dramatically in lower INR values, especially below 1.9-2.0 [13]. Bleeding is observed in higher INR values. In our cases, INR values were significantly higher than the therapeutic range (11.44 and 12.37). Normally, bleeding was expected to be with those INR levels. However, ischemic stroke developed in those two patients. In the first case, a history of previous ischemic stroke and a relatively young age strengthened the possibility of a genetic predisposing factor in the foreground. Although APS, ACA, and ANA were negative in this case, protein C, protein S and factor V Leiden mutation could not be investigated due to technical deficiency.In the second case, the risk factor for thromboembolic events is AF and partly advanced age. However, the likelihood of developing ischemic stroke at such high INR levels is unexpected in both cases, regardless of the underlying condition.

Conclusion

As a result, unlike many studies published in the literature, this case report revealed interesting information. More detailed studies on this issue may be reported to support our findings.

Declarations: We previously presented our case report as an oral presentation in XVII. Ulusal Acil Tıp Kongresi & 8. Intercontinental Emergency Medicine ve 8. International Critical Care Congress in 2021 in Antalya.

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Case Report

Eurasian Journal of Toxicology

Alüminyum Fosfit Zehirlenmesi

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Abstract

Phosphine used in barn and grains praying is highly toxic. It is used as an insecticide in mouse-like species. It is especially used in Asian countries. It is quite toxic and easy to reach. In our country, the rare preparations in the form of phosphine tablets impregnated with clay. It has nospecific antidote. Death is common in poisoning. We present a case report with Aluminum Phosphide poisoning. A 21-year-old hypotensive female patient with Glasgow Coma Scale (GCS) 10 was brought by ambulance. Bradycardia and hypotension developed during follow-up. The patient with arrest was intubated and cardiopulmonary resuscitation was started. The patient died after 13 hours during follow-up.

Keywords: Aluminum phosphide, death, symptomatic treatment

Özet

Ambar ve tahıl ilaçlamasında kullanılan fosfin oldukça zehirlidir. Fare benzeri türlerde insektisit olarak kullanılır. Özellikle Asya ülkelerinde sık kullanılır. Oldukça zehirli ve ulaşması kolaydır. Ülkemizde kile emdirilmiş fosfin tabletleri halinde preparatlar vardır. Kendine özgü bir antidotu yoktur. Zehirlenmelerinde ölüm sık gözlenir. Alüminyum Fosfit zehirlenmesi olan bir olgu sunduk. Glaskow Koma Skoru (GKS) 10 olan 21 yaşında hipotansif kadın hasta ambulans ile getirildi. Takiplerinde bradikardi ve hipotansiyon gelişti. Arrest olan hasta entübe edilip kardiopulmoner resüsitasyona başlandı. Hasta takiplerinde 13 saat sonra eksitus oldu.

Anahtar Kelimeler: Alüminyum fosfit, ölüm, semptomatik tedavi

Giriş

Alüminyum fosfit kile emdirilmiş alüminyum fosfit tabletler olarak piyasada bulunmaktadır. Fosfin gazı ürünlerde kalıntı bırakmaması ve organizmayı her dönemde öldürebilmesi nedeni ile oldukça sık kullanılan bir üründür. Alüminyum fosfitin ağızdan alımlarında mide sıvısı ile temas ettiğinde açığa çıkan fosfin gazı nedeni ile sarımsak kokusu oluşur ve asıl zehirli etken fosfin gazıdır. Özgün bir antidotu yoktur. Zehirlenmelerinde ölüm oranları alınan doza bağlı % 30 - 100 arasında değişmektedir. Ülkemizde alüminyum fosfit zehirlenmesi sık görülmesine rağmen satışında herhangi bir sınırlandırma yoktur[1]. Özellikle Orta Asya ülkeleri, Hindistan ve İran gibi ülkelerde öz kıyım amaçlı oldukça sık kullanılmaktadır[2].

Olgu Sunumu

Hasta tarım ilacı içtiği söylenen 21 yaşında bir kadın idi. Hastanın yakını yoktu ve ilacın ne zaman alındığı net olarak bilinmemekte idi. Ambulans ile Suriye'den getirilen hastanın yaklaşık 4 saat önce alüminyum fosfit içtiği bilgisine ulaşıldı. Geldiğinde genel durumu kötü, bilinci konfüze, GKS: 10 (E:3 M:4 V:3), tansiyon arteriyel 120/60 mm Hg, nabız: 80/dakika ve solunum 22/dakia idi. Diğer fizik muayene bulguları normal idi. Hastanın kan tetkiklerinde; beyaz kan hücre sayısı 26000 /µL, hemoglobin 10,3 g/dL, PT-INR 1,82, Troponin I 1,71 ng/mL, kreatinin 1,88 mg/dL, glukoz 227 mg/dL idi. Kan gazında pH: 7,12, PaCO2: 27,8 mmHg, PaO2: 267 mmHg, HCO3: 14 mmol/L, SpO2: %98, metabolik asidozu mevcut idi. Diğer laboratuvar değerleri normal olan hasta izole edildi. Takiplerinde tansiyon arteriyel 90/40 mmHg, nabız: 60/dakika, solunum sayısı 26/dakika olan hastanın kontrol elektrokardiyografisinde sinüs aritmisi gelişti. Semptomatik medikal tedavi olarak 1000 mL izotonik sıvı i.v. bolus verildi ve hipotansif olduğundan pozitif inotropik tedavi amaçlı dopamin 10 mikrogram/kg/dk dozunda başlandı. Takiplerinde aritmi nedeni ile 2 gr magnezyum sülfat 100 cc %5 dekstroz içerisinde 1 saatte verildi. Hastaya mide lavajı yapıldı ve aktif kömür verildi. Hastanın takipler-

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inde hipoksi meydana geldi. Elektrokardiyografisinde sinüs aritmisi ve ventriküler ekstrasistoller izlendi. Hastanın oksijenizasyonu bozuldu. Hipoksi gelişen hasta entübe edildi. Takibinin 6. saatinde kardiyak arrest olan hastada kardiyopulmoner resüsitasyona başlandı. Resüsitasyona cevap veren hasta yoğun bakıma yatırıldı. Yoğun bakım takibinde alınan kan tetkiklerinde beyaz kan hücre sayısı 36200/µL, hemoglobin 9,8 g/dL, PT-INR 3,28, Troponin I 4,2ng/mL, kreatinin 3,28 mg/dL, glukoz 178 mg/dL, kan gazında pH: 7,05, PaCO2: 50,8 mmHg, PaO2: 92 mmHg, HCO3: 14 mmol L-1, SpO2: % 67 ve miks asidozu mevcut idi. Yoğun bakımda takiplerinde ardışık arrest olan olgu yatışının 13. saatinde eksitus oldu.

Tartışma

Alüminyum fosfit nem ya da midede hidroklorik asitle birleştiğinde ölümcül fosfin gazı açığa çıkar[3].Bu nedenle biyoterör etmeni olarak da bilinir. Doğal halde kokusuz ve renksizdir. Yapısındaki maddeler nedeni ile sarımsak ya da çürümüş balık kokusuna neden olur[4]. Tarımın yaygın olduğu toplumlarda organofosfat zehirlenmesinden sonra ikinci sıklıkta alüminyum fosfit zehirlenmesi görülür. Literatürde kesin bir toksik doz olmasa da 0,15-0,50 gram üzerindeki alımlarda mortalite ve morbiditenin yüksek olduğu bildirilmiştir[5]. Genellikle 1,5 gram üzeri zehirlenmelerde yaşam oranı çok düşüktür ancak 9 gram ve üzeri alımlarda nadiren hayatta kalan vakalar bildirilmiştir[3,4]. Hindistan'da 25 yıllık zehirlenme olgularının değerlendirildiği bir çalışmada 1982 yılına kadar organofosfat zehirlenmeleri ön planda iken 1982 yılından sonra alüminyum fosfit ile olan zehirlenmeler % 65 oranda en sık görülen etken haline gelmiştir[6]. Avrupa ülkelerinde bu oran daha düşük olarak bildirilmiştir[3,7]. Ülkemizde de bu konu ile ilgili kesin sayıları belirten kaynak bulunmamaktadır.

Alüminyum fosfitin özkıyım amaçlı kullanımı oldukça yaygındır. Bazı ülkelerde satışına sınırlandırma getirilse de kaçak kullanımı nedeni ile zehirlenmeler sık gözlenir[4,7]. Ülkemizde satış sınırlaması olmamasına rağmen bildirilen vaka sayısı oldukça azdır. Zehirlenmeler genellikle ağız ya da solunum yolu ile olmaktadır. Deri ile bulaş gözlenmemiştir. Gastrointestinal sistem, solunum sistemi, kalp ve böbrekler etkilenebilir[3-5]. Bulantı, kusma, huzursuzluk, karın ağrısı, çarpıntı, şok, kardiyak aritmiler, pulmoner ödem, nefes darlığı, siyanoz ve duyusal değişiklikler, alımından sonra bir kaç saatte gelişebilir. Bizim olgumuzun takiplerinde karaciğer böbrek ve kalp yetmezliği gelişti.

Alüminyum fosfitin metaboliti olan fosfin gazının bilinen bir antidotu yoktur. Tedavide erken mide yıkama, aktif kömür uygulaması ve destekleyici bakım yer almaktadır. Nadir kaynaklarda magnezyum sülfat ve hindistan cevizi yağı da önerilmektedir. Erken dönemde mide yıkama ve aktif kömür uygulama sağ kalım açısından oldukça önemlidir. Bizim olgumuzda gelişinin 1. saatinde semptomatik medikal tedavi başlanmasına rağmen klinik düzelme sağlanamadı.

Sonuç

Alüminyum fosfit oldukça toksik bir zehirdir ve ön tanı olarak akla getirilmesi ile erken müdahale hayat kurtarıcıdır. Tanıda şüphe ve sarımsak kokusu ile çürümüş balık kokusu önemlidir. Hastadan salınan fosfin gazı zehirlidir bu nedenle hasta izolasyonu ve koruyucu ekipmanlar ile müdahale gerekir.

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Case Report

Eurasian Journal of Toxicology

Spontaneous Resolution of Arrhythmia in Propafenone Intoxication: A Rare Case Report

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Abstract

Propafenone toxicity is rare but poses a life-threatening condition due to malignant arrhythmias. However, there is currently no recommended standard specific treatment or antidote. In our case, we presented a young patient with transient cardiac toxicity and spontaneous recovery in her follow up after taking high-dose propafenone for suicide attempt. Electrocardiography showed sinus rhythm with prolongation of PR interval with 240 ms, QRS width 160 ms, and corrected QT interval QTc with 498 ms; Terminal R wave observed in leads V1 and aVR and metabolic acidosis was also observed at the time of admission. In patient's follow up, sodium bicarbonate and lipid emulsion treatment was planned but did not applied due to the resolution of cardiotoxic arrhythmia in 30 minutes after her admission, and metabolic acidemia was observed to regress with supportive treatment. In conclusion, propofenone intoxication, like other class 1C antiarrhythmics, is a life-threatening, rarely reported toxicity that complicates clinical decisions. It is critical to be aware that propofenone overdose can be fatal, and is also essential to remember that, despite the lack of an antidote, total recovery can be accomplished with constant monitoring and supportive treatment.

Keywords: Propafenone, intoxication, arrythmia, sodiumbicarbonate

Özet

Propafenon toksisitesi nadirdir ancak malign aritmiler nedeniyle yaşamı tehdit eden bir tablo oluşturur. Bununla birlikte, spesifik bir tedavi veya panzehir bulunmamaktadır. Olgumuzda, özkıyım amacı ile yüksek doz propafenon alımı sonrası geç başvuruda geçici kardiyak toksitite gözlenen ve spontan iyileşme görülen genç bir hastayı sunduk. Başvuru sırasında elektrokardiyografide PR intervalinin 240 ms ile , QRS genişliğinin 160 ms ile ve düzeltilmiş QT intervalinin 498 ms ile uzamış olduğu bir sinüs ritmi görüldü. V1 ve aVR'de terminal R dalgası mevcuttu ve metabolik asidoz gözlendi. Hastanın takibinde sodyum bikarbonat ve lipid emülsiyon tedavisi planlandı. Ancak başvurudan 30 dakika sonra kardiyotoksik aritmi düzeldiği için uygulanmadı ve destek tedavisi ile metabolik asidozun gerilediği gözlendi. Sonuç olarak propofenon intoksikasyonu, diğer sınıf 1C antiaritmikler gibi, yaşamı tehdit eden, nadiren bildirilen ve klinik kararları zorlaştıran bir toksisitedir. Bu nedenle mortal seyredebileceği bilinmeli, antidotu olmasa da yakın izlem ve destek tedavi ile tam iyileşme sağlanabileceği unutulmamalıdır.

Anahtar Kelimeler: Propafenon, intoksikasyon, aritmi, sodyum bikarbonat

Introduction

Propafenone is a class 1C antiarrhythmic agent used for the treatment of ventricular, supraventricular tachycardia and atrial fibrillation. Although propafenone intoxication is rare, survival is usually very low due to malignant arrhythmias[1]. Supportive therapy is the mainstay of treatment, and when no response is obtained, treatments such as sodium bicarbonate, buffering with insulin-dextrose, glucagon, calcium, intravenous lipid emulsion and pacemaker have been reported to be beneficial in a limited number of cases[2-4]. However, there is currently no recommended specific treatment or antidote[3]. In our case, we presented a young patient with transient cardiac toxicity and spontaneous recovery in her follow up after taking high-dose propafenone for suicide and aimed to emphasize the importance of supportive treatment in intoxication.

Case Report

A 19-year-old female patient admitted to the emergency department with complains of nausea and vomiting started approximately 18 hours after oral intake of 30 (total 4500mg) propafenone tablets for suicid attempt. Her anamnesis revealed that she had no chronic disease and regularly used medication, and that propefonone belonged to her parents. On examination, patient was well oriented and cooperative, and her glasgow coma scale was evaluated as 15. Vital signs were observed as; SpO2 in room air: 99%, heart

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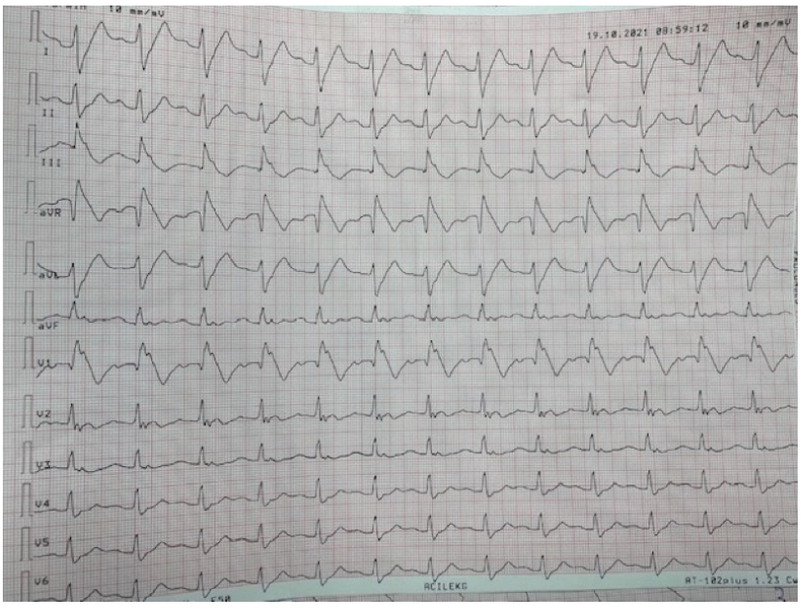

Figure 1: The patient's ECG at admission shows sinus rhythm with PR prolongation up to 240 ms, QRS width 160 ms, and QTc 498 ms in lead II, and terminal R wave in leads V1 and aVR

rate: 99 beats per minute, blood pressure 108/71 mmHg, respiratory rate 18/minute, fever 36.1 °C. Her skin perfusion was normal, pupillary isochoric light reflex was normal bilaterally, and no pathological finding was detected in other systemic examination. Electrocardiography (ECG) showed sinus rhythm with prolongation of PR interval with 240 ms, QRS width 160 ms, and corrected QT interval QTc with 498 ms; Terminal R wave observed in leads V1 and aVR (Figure 1). The patient was followed up with close monitoring and symptomatic treatment was started; 1gr/kg activated charcoal was administered every 6 hours, and hydration was provided with intravenous 0.9 % NaCl isotonic bolus doses. Metabolic acidosis was observed as pH: 7.081, pCO2: 25.3, HCO3: 15, lactate: 9 in the arterial blood gas sampled at the time of admission, however all other laboratory parameters of the patient were within the normal range. Sodium bicarbonate treatment was planned for the patient with stable hemodynamics, due to QRS enlargement in the ECG, but sodium bicarbonate treatment was not given due to the dramatic improvement in the ECG (Figure 2), which was repeated at the 30th minute of admission after symptomatic treatment. The patient, whose metabolic acidosis regressed gradually, did not have additional cardiotoxicity and was transferred to the intensive care unit for follow-up. After a 24-hour intensive care follow-up, the patient was discharged, with full recovery.

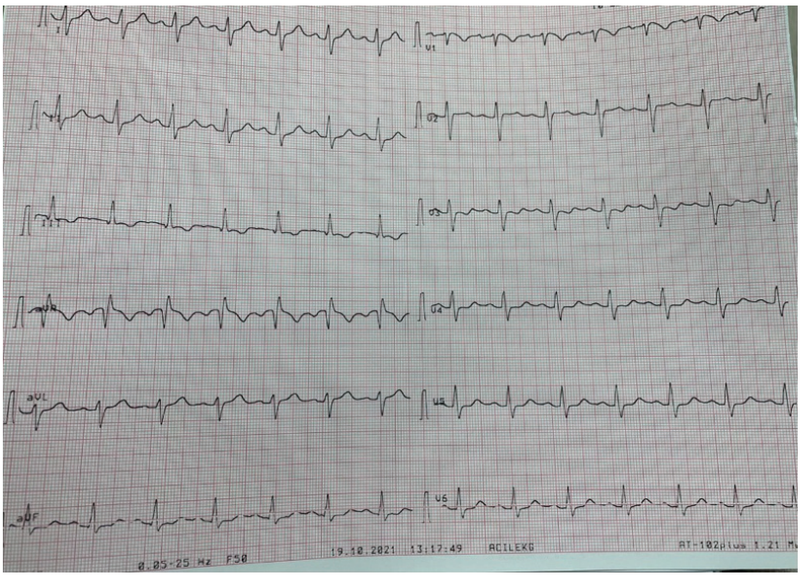

Figure 2: Normal sinus rhythm is seen in the ECG of the patient taken 30 minutes after admission

Discussion

Propafenone exerts its effect by inhibiting action potentials in cardiac sodium channels. It also inhibits β-adrenergic receptors and calcium receptors and has a negative inotropic effect. Although being a proarrhythmic agent, propafenone may cause cardiac and other adverse effects, even at therapeutic doses (300-900 mg/day)[1]. Propafenone toxicity is rare but poses a life-threatening condition. Coma, seizure, cardiac arrest, bradycardia, conduction abnormalities (sinoatrial, atrioventricular, and intraventricular blocks) or tachycardia (ventricular tachycardia), PR prolongation, QRS and QT interval widening, and Brugada phenocopy may occur[3-5]. In our case, PR prolongation, QRS and QT interval widening were observed, and no hemodynamic instability was observed.

Following oral administration, propafenone is nearly completely absorbed (% 90). However, because of a first-pass hepatic elimination effect, its bioavailability is unpredictable[3,6]. Propafenone is metabolized into two major metabolites: 5-hydroxypropafenone and norpropafenone, a process genetically determined by the CYP2D6 enzyme system. The propafenone elimination half-time varies depending on whether the patient is a poor or an extensive metabolizer[3,6].

Although the half-life is short at 5-7 hours, it has been reported that elimination may take up to 17-24 hours in 10% of patients who are genetically poor metabolisers[5]. Therefore, close 24-hour monitoring may be required. We thought that the spontaneous recovery of cardiotoxicity during follow-up in our case may be due to drug elimination due to late admission. Propafenone intoxication is associated with doses between 1800 and 9000 mg, and serum concentrations as high as 12,000 ng/mL have been reported[6]. Although a total intake of 4500 mg propafenone was detected in our case, the serum concentration at the time of admission is not known since the blood level could not be studied in our center.

The treatment of propafenone intoxication is controversial and there is no consensus on the actual treatment.Therefore, it is essential to focus on hemodynamic support after poisoning. Activated charcoal administration, intravenous glucagon, sodium bicarbonate, hypertonic saline, insulin and lipid emulsion therapy are beneficial[5]. Theoretically, sodium bicarbonate is effective in sodium channel blocking agent toxicity, but in a study with class 1C antiarrhythmics, bicarbonate alone was not effective in reversing ECG effects at therapeutic doses[7]. Again, in an animal research study comparing the efficacy of insulin and sodium bicarbonate therapy in acute propafenone toxicity, insulin therapy was found to be more effective[8]. In our case, sodium bicarbonate and lipid emulsion treatment was not applied due to the resolution of cardiotoxic arrhythmia in a very short time after her admission, and metabolic acidemia was observed to regress with supportive treatment.

Conclusion

Inconclusion, propofenone intoxication, like other class 1C antiarrhythmics, is a life-threatening, rarely reported toxicity that complicates clinical decisions. It is critical to be aware that propofenone overdose can be fatal, and is also essential to remember that, despite the lack of an antidote, total recovery can be accomplished with constant monitoring and supportive treatment.

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Case Report

Eurasian Journal of Toxicology

Rare Inferior Myocardial Infarction Triggered by Carbon Monoxide Poisoning

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Abstract

Carbon monoxide (CO) poisoning is one of the most common causes of death due to poisoning in the world. Cardiovascular complications of CO poisoning includes myocardial infarction, left ventricular dysfunction, cardiogenic shock, and various arrhythmias. Carboxyhemoglobin (COHb) levels do not always correlate with severity of symptoms. In this article, We present a patient who developed a rare ST elevated acute myocardial infarction triggered by CO poisoning and was treated with coronary angiography.

Keywords: CO poisoning, inferior myocardial infarction, ST elevation

Özet

Karbonmonoksit (CO) zehirlenmesi sık karşılaşılan dünyada zehirlenmeye bağlı ölümlerin en yaygın sebeplerindendir. CO zehirlenmesinin kardiyovasküler komplikasyonları miyokard enfarktüsü, sol ventrikül disfonksiyonu, kardiyojenik şok ve çeşitli aritmileri içerir. Semptomların şiddeti ile karboksihemoglobin (COHb) seviyeleri her zaman korele değildir. Bu yazıda, CO zehirlenmesinin tetiklediği ST elevasyonlu akut miyokart enfarktüsü gelişen ve koroner anjiografi ile tedavi edilen bir hastayı sunuyoruz.

Anahtar Kelimeler: CO intoksikasyonu, inferior miyokard enfarktüsü, ST elevasyonu

Introduction

Carbon monoxide (CO); since it is a tasteless, odorless and colorless gas, patients may apply to the emergency service in the late period in cases of poisoning. CO shows 200-250 times higher affinity for binding to hemoglobin than oxygen[1]. The symptoms, signs and prognosis of acute CO poisoning correlate poorly with the level of carboxyhemoglobin (COHb)[2].

Since CO binds to cardiac myoglobin with higher affinity than hemoglobin, myocardial depression and hypotension develop; may further exacerbate tissue hypoxia, leading to myocardial infarction[3]. Even 5-10% increases in COHb levels in people with previous coronary artery disease (CAD) may trigger exercise angina. High levels of COHb may affect the myocardium even in young and healthy individuals[4]. The occurrence of ST elevated myocardial infarction (STEMI) is rare.

In this case report, we aimed to present a rare case of STEMI after acute CO poisoning in a patient without coronary artery disease.

Case

An 87-year-old male patient was brought to the hospital by 112 ambulance service with complaints of headache, nausea and vomiting. He had no history of diabetes mellitus, hypertension, coronary artery disease, and was paraplegic after previous surgery. In the detailed anamnesis, it was learned that they lived in a house with a stove. His blood pressure was 90/70 mmHg, his heart rate was 94/minute, and his respiratory rate was 22/minute. Heart beats were dysrhythmic in cardiovascular system examination. No additional sound or murmur was heard. Pulmonary and other system examinations were normal. ST elevation was detected in DII, DIII,

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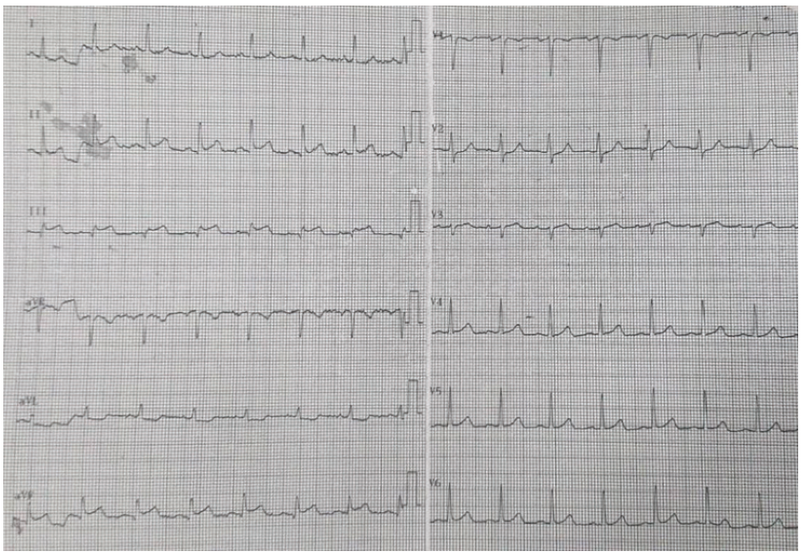

Figure 1: ST elevation in DII, DIII and aVF

aVF in his electrocardiography (ECG) (Figure 1). It was evaluated as acute STEMI. No abnormality was observed except for COHb 22.8%, WBC 19.600/U, glucose: 172mg/dl, creatinine:1.4mg/dl in the first laboratory tests, but cardiac markers were elevated in the follow-up. Troponin I: 41.6 ng/L, CK-MB: 5.7 ng/mL. He was given 10lt/minute O_2 treatment with a reservoir mask and 300 mg tb acetylsalicylic acid. The patient was given 180 mg of ticagrelor. The patient was admitted to the coronary intensive care unit. Coronary artery angiography of the patient revealed complete occlusion in the posterior branch of the right main coronary. The patient was taken to the ward from the intensive care unit on the third day after angiography. The patient recovered clinically and symptomatically and was discharged on the 5th day with full recovery.

Discussion

Early diagnosis is life-saving in CO poisoning. However, the most important factor in the diagnosis is doubt. Detailed anamnesis is important in patients presenting with nonspecific findings. It can present with symptoms ranging from flu-like symptoms to coma and death. The most common symptom is seen in the central nervous system and cardiovascular system, where oxygen use is most intense. The affinity of CO to hemoglobin; it can cause deep tissue hypoxia because it is 200–250 times more than oxygen. At the same time, it directly affects cellular respiration, as it binds to cytochrome oxidase[5].

COHb can be used in the diagnosis and follow-up. Patients with suspected CO poisoning should be given high-flow oxygen, regardless of peripheral oxygen saturation[6]. Our patient also presented with nonspecific findings such as headache, nausea and vomiting, but when the anamnesis was deepened, it was learned that he lived in a house with a stove. The patient was immediately started on oxygen at 10 lt/min with a reservoir mask. The COHb level in the blood gas was found to be high.

While myocardial damage and fibrosis are observed at low dose exposures, it has been reported that fatal arrhythmias can be seen at high dose exposures. It is known that cardiotoxicity in CO poisoning is not only related to hypoxia, but also that CO gas has a direct toxic effect by inhibiting cytochrome oxidase in myocyte mitochondria[7].

Cardiac findings after moderate-severe CO poisoning were examined in a study conducted by Satran et al. It was found that 30% of the patients had ischemic ECG changes, and 35% had myocardial damage in cardiac markers. The mortality of the patients was found to be 5%. With these results, it was suggested that cardiac sequelae are common after CO poisoning and that patients should be followed up with ECG and serial cardiac markers[8].

Dziewierz et al. found inferior STEMI in their patients with a COHb level of 22% in their case report. They reported that acute occlusion of the distal left anterior descending coronary artery was detected in the patient's coronary angiography, and that symptoms regressed after angioplasty[9]. Kim et al. reported complete occlusion in the right main coronary posterior branch in the angiography of the patient in whom they detected STEMI after CO poisoning. They stated that this obstruction disappeared in control angiography after anti-thrombotic therapy[10]. In our patient, although there was no history of coronary artery disease, we detected inferior STEMI. In his angiography, 50-60% occlusion was detected in the right main coronary artery branch. In

patients without coronary artery disease, CO is the mechanism blamed in the pathogenesis of both increasing platelet aggregation and causing vasospasm as a result of its direct effect on the coronary arteries. STEMI is the result of vasospasm[11].

Altay et al. reported a case with previous coronary artery disease in which CO exposure triggered the development of infarction. Çelik et al. also reported that a newly developed left bundle branch block was detected after CO poisoning in a patient known to have coronary artery disease[12,13].

Despite various clinical trials, the best treatment for carbon monoxide poisoning is still a matter of debate. In some patients, the use of 100% oxygen and/or hyperbaric oxygen is preferred according to the symptoms, accompanying diseases and COHb level[12,14]. Our patient was at risk of coronary artery disease because he was old, male and bedridden. We think that CO poisoning also increases cardiac injury. Detection of cardiac injury is among the indications for HBO therapy in CO poisoning patients[15]. However, HBO treatment was not applied since our patient was relieved clinically and symptomatically after angiography after he was admitted to the intensive care unit. He was discharged without any problems during his follow-ups.

Conclusion

Myocardial ischemia is an expected condition in CO poisoning, but STEMI is a rare condition. Even if the patients do not have chest pain or coronary artery disease in their history, ECG and cardiac enzyme follow-up should be performed in the first hour.

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