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Letter to the Editor

Original Articles

Case Reports

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Editorial

Değerli Okuyucular,

2021 yılının 2. sayısı toksikoloji ile ilgilenen tüm okuyucularımıza katkı sağlayacak şekilde hazırlandı. İlgi çekici iki araştırma makalesi, üç vaka sunumu ve bir editöre mektup dergimizin içeriğini oluşturuyor. Dergimize katkıda bulunan değerli yazarlara ve derginin hazırlanmasında emeği geçen tüm paydaşlarımıza, desteklerini esirgemeyen Acil Tıp Uzmanları Derneği (ATUDER) yöne-tim kuruluna ve başkanımız Prof. Dr. Başar Cander'e teşekkür ederiz.

Saygılarımızla.

Eurasian Journal of Toxicology Editörler Kurulu

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Letter to the Editor
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Matthew Lawson Koma Skoru

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Matthew Lawson Koma Skoru

Sayın editör,
Kritik hastanın tespiti ve tedavinin yönetilmesinde pek çok klinik ve laboratuvar parametrelerini de içeren skorlama sistemleri geliştirilmiştir. Bu skorlama sistemlerinden bazıları Glasgow Koma Skalası, Acute Physiology and Chronic Health Evaluation II, Rapid Acute Physiology Score, Rapid Emergency Medicine Score olarak sayılabilir. Günlük pratikte sıklıkla kullanılan skorlama sistemleri acil serviste kritik hastanın tespiti için kullanılabileceği gibi yoğun bakım ünitelerinde hastanın tedaviye yanıtını değerlendirme amacıyla da kullanılabilmektedir.

Acil servis ve yoğun bakım pratiğinde kritik hasta yönetiminde bilinç takibi vital parametrelerle birlikte önemli bir klinik belirteçtir. Bilinç durumunun değerlendirmesinde yaygın olarak kullanılan skorlama sistemi Glasgow Koma Skalasıdır. Bunun yanı sıra Matthew ve Lawson tarafından 1966 yılında önerilen Matthew Lawson Koma Skoru özellikle zehirlenme hastalarında kullanılmaktadır. Matthew ve Lawson 1966 yılında yaptıkları araştırmada skorlama sistemini tanımladılar ve barbiturat intoksikasyonu hastalarında kullanılabileceğini önerdiler[1]. Starmark ve Heath 1988 yılında intihar amaçlı kendini zehirleyen 26 hastanın verilerini incelediği çalışmada Matthew Lawson Koma Skorunun kullanılabileceğini önerdiler[2]. Hultén ve arkadaşları da 1992 yılında yaptıkları çalışmada Matthew Lawson Koma Skorunun trisiklik antidepresan intoksikasyonunda da güçlü bir prediktör olduğunu gösterdiler[3]. Staniszewska ve Bujalska-Zadrożny ise 2016 yılında yayınlanan Varşova'da yaptıkları çalışmada akut valproik asit zehirlenmeli 26 hastanın verilerini analiz ettiler[4]. Staniszewska ve Bujalska-Zadrożny yaptıkları araştırmada serum valproik asit düzeyinin araştırılan parametreler ile arasında ilişki olmadığını ortaya koyarken Matthew Lawson Koma Skorunun hastanede kalış süresi ile ilişkili olduğunu raporladılar[4].

Bilinç düzeyi, Matthew Lawson Koma Skoruna göre 0 ile 4 arasında derecelendirilir ve seviyeler roma rakamları ile gösterilir. Grade 0, tamamen bilinçli, uyanık hali ifade eder. Grade I, uykulu ancak sözlü komuta yanıt verme hali ifade eder. Grade II, bilinçsiz hastayı ifade eder ancak hasta minimal ağrılı uyaranlara yanıt verir ve refleksler bozulmamıştır. Grade III, bilinçsiz hastayı ifade eder ve hasta maksimal ağrılı uyaranlara yanıt verir, yüzeysel reflekslerin yoktur ve derin refleksler hafif alınabilir. Grade IV, ağrılı uyaranlara yanıt vermeyen bilinçsiz hastayı ifade eder, korneal, laringeal, faringeal dahil tüm reflekslerin kaybı söz konusudur. Grade III ve IV şiddetli zehirlenme olarak kabul edilir[1].

Matthew Lawson Koma Skorunun az sayıda örneklemler ile yapılan çalışmalarda özellikle santral sinir sistemini etkileyen ilaç zehirlenmelerinde kullanılabileceği önerilmektedir. Bu skorun geliştirilmesi ve ülkemiz ve dünya literatürüne katkı sağlamak amacıyla zehirlenme alanında geniş örneklemler ile yapılacak çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: koma,toksikoloji,skor

References

1. Matthew H, Lawson A AH. Acute barbiturate poisoning, a review of two years experience. Q J Med 1966; 35: 539–552
2. Starmark JE, Heath A. Severity grading in self-poisoning. Hum Toxicol. 1988 Nov;7(6):551-5. doi: 10.1177/096032718800700606. PMID: 3229764.
3. Hultén BA, Adams R, Askenasi R, et al. Predicting severity of tricyclic antidepressant overdose. Journal of toxicology. Clinical Toxicology. 1992 ;30(2):161-170. DOI: 10.3109/15563659209038628.
4. Staniszewska A, Bujalska-Zadro ny M. Acute Valproic Acid Intoxication: An Attempt at Estimating the Correlation Between Serum Level and Clinical Manifestations. In: Kalinin V editör. Epileptology- The Modern State of Science 2016: 225-235.

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Original Article

Eurasian Journal of Toxicology

Level of Knowledge and Attitude of the Medical Educated People About Medicinal Herbs

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Abstract

Objectives: Lack of existence of traditional medicine based on the academic sciences and lack of a study on the knowledge of the community about the indication and contraindications and drug interactions with herbal remedies, we decided to investigate the attitudes and knowledge of people with medical education.

Materials and Methods: In this cross-sectional study, people from medical, nursing and pharmacy groups were selected randomly. Implicit consent was obtained from individuals. The questionnaire consisted of demographic characteristics and four parts of the questions were as following, the first part consisting of people's attitude, the second part containing questions related to indication, the third part of questions related to contraindication and the last part was about drug interactions.

Results: In this study, 388 participants were enrolled. The mean age of the participants was 29.66 ± 8.37 years .180 were female (46.4%). Most patients (66%) rarely or occasionally recommend herbal remedies. Most participants (68%) occasionally or rarely recommend herbal medicines as an alternative for common medicine. 256 participants (66%) believe that the use of herbal remedies has increased and 112 (28.9%) declare unawareness and 20 (5.2%) believe that Consumption has not increased. The reason for increased use is often that people think these drugs are natural.

Conclusion: Most participants do not have enough information about herbal remedies and medications and often claim that because herbal remedies are natural, cheaper and less risky, the tendency to herbal remedies and medicines has increased but the participants themselves often do not recommend replacing prescription medicine with them.

Keywords: Knowledge, Attitude, Herbal Remedies

Introduction

Much of what is considered today as 'alternative medicine' in developed countries. A large part of the world's population, including many developed countries, consider alternative therapies rather than chemical treatments for most health-related problems[1]. In most cultures, medicinal herbs have been a key component of these alternative therapies for a long time. The historical role of herbal drugs in the treatment and prevention of disease and their role as catalysts in drug development do not guarantee their safety for use by a community without control[1]. Concerns about the current expansion of herbal remedies and uncontrolled use and largely unawareness or misinformation of them were the subject of a recent editorial in the New England J Medical Journal (NEJM)[2] and a series of articles in the Journal of the American Medical Association. (Jama)[3]

The marketing and use of these 'natural' options were greatly facilitated by the approval of the 1994 Diet Supplement Health and Education Act (DSHEA)[4].

According to the Presidential Commission›s estimates of dietary supplements, about 1,500-1,800 herbal products are sold in the United States as dietary supplements or clanship drugs. Estimates of the market value of herbal medicines vary, but all sources agree that this is a multi-billion dollar industry[5]. Thus, considering the tendency of the people of our beloved country and the existence of non-academic Atari (name of job, who offers traditional treatment agents) and traditional medicine at the community, and lake of existence of traditional medicine based on the academic sciences and lack of a study on the knowledge of the community about the indication and contraindications and drug interactions with herbal remedies, we decided to investigate the attitudes and knowledge of people with medical education.

Material and Methods

This is a cross-sectional study, participants were randomly selected and enrolled from medical, nursing and pharmacy departments. Considering the available medical, nursing and pharmacy groups of about 20,000 with Cochran formula, data is about 376 obtained in the field and 388 individuals

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were enrolled to improve the results. Also, those with experience in herbs and related field or Atari pharmacies and doctors with a Ph.D. in traditional medicine were excluded.

The questionnaire consisted of demographic characteristics and four parts of the questions, the first part consisting of people's attitude, the second part containing questions related to indication, the third part of questions related to contraindication and the last part was about drug interactions. It should be noted that this questionnaire is based on common medicinal herbs common among people and common herbal drinks in the market and does not include all medicinal herbs, as there is certainly no sufficient information on non-common medicinal herbs.

Then data including age, gender, individual awareness score and score obtained of each section were entered into SPSS 20.0 statistical software. For inside group analysis, descriptive statistical method and for comparison of quantitative data t-test and qualitative data Chi-square method was used. The level below 0.05 is significant.

Ethics: this study was approved by local ethic committee of Tabriz University of medical sciences with no.: IR.TBZMED.REC.1398.835

Results

388 subjects were enrolled in the study, which did not follow the normal distribution according to the Kolmogorov-Smirnov method. (PV≤0.0001)

The mean age of participants (28.83-30.50, 95% CI) was 29.66±8.37 years with a minimum age of 20 years and a maximum of 60 years. The median is 26 years and the mode is 23 years.

Among participants, 104 (26.8%) were pharmacists, 152 (39.2%) were nurses, and 132 (34.0%) were physicians.

356 (91.8%) Of the participants had work experience under 5 years. Sixteen (4.2%) were between 5 and 10 years, and eight (2.1%) were between 10 and 15 years and eight (2.1%) were 30 years. 180 (46.4%) were female and 208 (53.6%) were male.

Most participants obtained information on herbal remedies from university-related courses.

208 participants (53.6%) had prior information on herbal remedies and 180 (46.4%) had no information. 180 (46.4%) had new information on herbal remedies and 208 (53.6%) had no new information added to the previous information.

Most participants (66%) rarely or occasionally recommend herbal remedies (Figure 1).

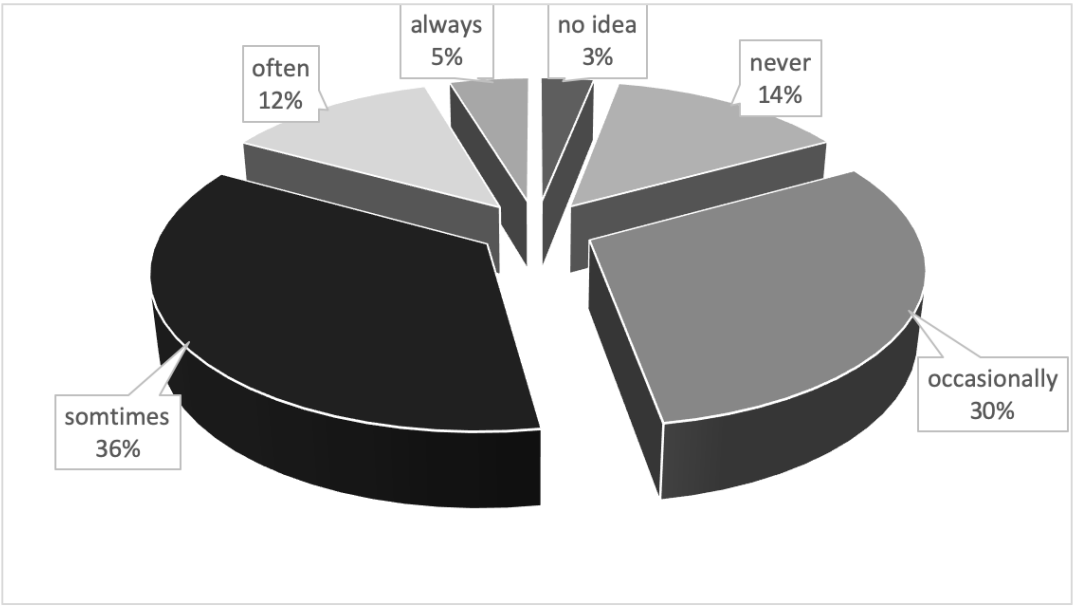
Most participants (68%) occasionally or rarely recommend herbal medicines as an alternative for common medicine.

256 participants (66%) believe that the use of herbal remedies and drinks has increased and 112 (28.9%) declare unawareness and 20 (5.5%) believe that Consumption has not increased.

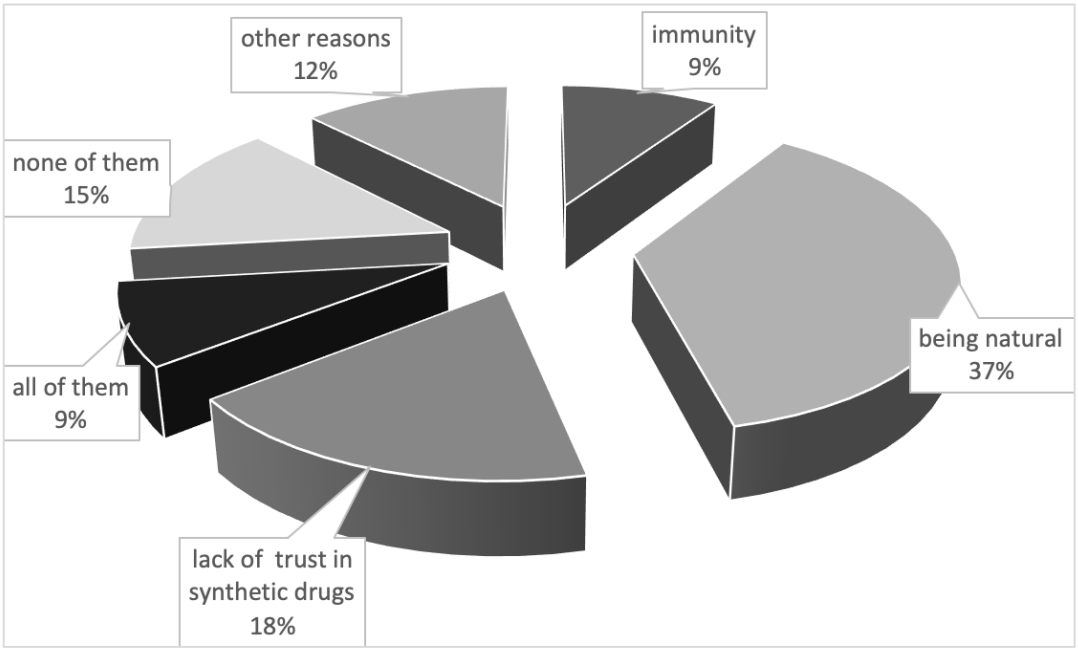
The reason why use has increased is often said that the drugs are natural (Figure 2).

In answer to how they would decide if participants were asked strongly to prescribe herbal medicines, 152 said they would decide by considering the situation and 94 said they will not prescribed under the any condition.

39.6% of participants considered the risk of herbal medicine to be low and 49.1% of participants disagreed and considered it harmful (Figure 3).



Figür 1. Level of participants' recommendation for taking herbal remedies



Figür 2. Frequency of beliefs about the causes of increasing or not increasing the use of herbal medicines

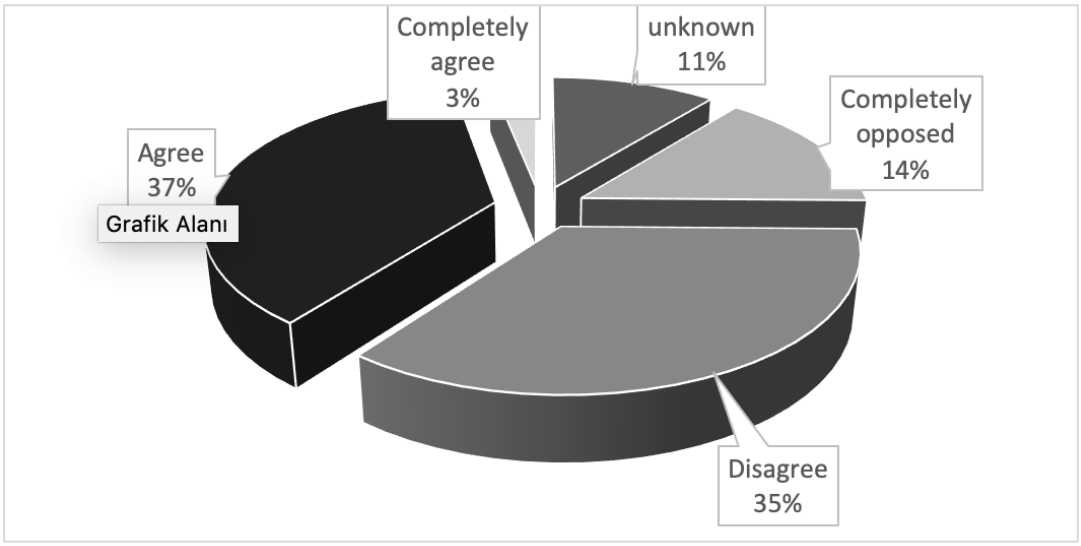
45.9% believe that herbal remedies are cheap for patients but 49.5% disagree. 51% believe that herbal remedies are cheap for health system but 41.3% oppose this. 28.4% of participants believe that herbal remedies are effective in treatment and 53.6% disagree. 59.8% of participants believe that herbal remedies are compatible with people's culture and 29.4% disagree. 43.8% of the participants find it easy to take herbal remedies, but 48.8% disagree.

39.7% believe that complications of using herbal remedies are less common and 54.6% disagree and consider it to be a high (Figure 4).

Discussion

388 volunteers participated in this study. The mean age of participants was 29.66 ±8.37 years with a minimum age of 20 years and a maximum of 60 years. Among participants, 104 (26.8%) were pharmacists, 152 (39.2%) were nurses, and 132 (34.0%) were physicians.

356 (91.8%) Of the participants had work experience under 5 years. Sixteen (4.2%) were between 5 and 10 years, and eight (2.1%) were between 10 and 15 years and eight (2.1%) were over 30 years. 180 participants were female and 208 were male, and most of the participants were educated at



Figür 3. Participants' beliefs about the harmlessness of herbal remedies for patients

Tabriz University of Medical Sciences. 124 had a history of working in a pharmacy, often working in a private pharmacy. Most of the participants in this study obtained information on herbal remedies from university-related courses, and 208 participants had prior information on herbal remedies and 180 had no information. Many herbs have preventive or curative effects. Therefore, like any therapeutic agent, they can cause side effects if the drug is overused or misused. The likelihood of producing side effects increases when the production and sales of such goods are largely uncontrolled and the consumer is not aware of its proper use. Recent articles (2 and 3) focus on discussing the importance of the growing use of medicinal herbs in the United States in their editorial at NEJM, Angel, and Kasser. They expressed concern about the potential risks associated with the widespread use of medicinal herbs and their scientifically unproven preparation methods[2].

In our study, 256 participants (66%) believe that the use of herbal remedies and drinks has increased and 112 (28.9%) declare unawareness and 20 (5.5%) believe that Consumption has not increased. The reason why use has increased is often said that the drugs are natural.

In answer to how they would decide if participants were asked strongly to prescribe herbal medicines, 152 said they would decide by considering the situation and 94 said they will not be prescribed under any condition.

39.6% of participants considered the risk of herbal medicine to low and 49.1% of participants disagreed and considered it harmful. 45.9% believe that herbal remedies are cheap for patients but 49.5% disagree. 51% believe that herbal remedies are cheap for the health system but the rest oppose this.

In a study by Angel and colleagues, they noted that although most herbal remedies are probably harmless, some may be quite toxic and the consumer is largely oblivious to its potential side effects[2].

Wayne Jonas, former director of the National Institute for Alternative Drug Medicine Health, tried to evaluate both sides of the issue in his JAMA editorial and emphasized the fact that there is the possibility to replace common medicine in positive and negative aspects[6].

He noted that common medicine has the advantage of confirming the benefits of scientific methods, while traditional and alternative medicine largely depends on informal reports.

He warned that due to lack of standardization in harvesting and processing, the beneficial effects of medicinal herbs may vary. Thus, while acknowledging the beneficial effects of alternative medicines, Jonas calls for increased research to confirm the useful and safe applications and to further investigate the mechanisms that underlie the therapeutic effects of alternative medicines. In our study, 28.4% of participants believe that herbal remedies are effective in the treatment and 53.6% disagree. 59.8% of participants believe that herbal remedies are compatible with people's culture and 29.4% disagree. 43.8% of the participants find it easy to take herbal remedies, but 48.8% disagree.39.7% believe that complications of using herbal remedies are less common and 54.6% disagree and consider it to be high.

61.3% of the participants believe that society has a strong belief in the usefulness of herbal remedies and 32% disagree.

In a study by Fontanarosa and Lundberg, they noted: Although millions of patients are using these methods, the tests and studies that have been accidentally performed on these materials have not been right and regular.

Therefore, consumers spend billions of dollars annually on treatments that may be effective and, in most cases, do not have insurance reimbursement.

Fontanarosa and Lundberg also point out that in some cases, the methods used as alternatives are contraindicated and worsen the condition. The use of medicinal herbs was quite common in the United States in the nineteenth and early twentieth centuries.

Participant awareness

Most participants do not have enough information about herbal remedies and medications and often claim that because herbal remedies are natural, cheaper and less risky, the tendency to herbal remedies and medicines has increased but the participants themselves often do not recommend replacing prescription drugs with them.

Conclusion

Most participants do not have enough information about herbal remedies and medications and often claim that because herbal remedies are natural, cheaper and less risky, the tendency to herbal remedies and medicines has increased but the participants themselves often do not recommend replacing prescription drugs with them.

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Conflict of interest: There is no conflict of interest

References

1. Matthews HB, Lucier GW, Fisher KD. Medicinal herbs in the United States: research needs. Environmental health perspectives 1999 Oct;107(10):773-8.

2. Angell M, Kassirer, JP. Alternative medicine-the risks of untested and unregulated remedies. N EngI J Med 339:839-841 (1998).
3. Journal of the American Medical Association (JAMA) 280 (1998).
4. Bass IS, Young AL. Dietary Supplement Health and Education Act: A Legislative History and Analysis. Washington, DC:The Food and Drug Law Institute, 1996.
5. Commission on Dietary Supplement Labels. Report of the Commission on Dietary Supplement Labels, Report to the President, Congress, and The Secretary of the Department of Health and Human Services. Washington, DC:U.S. Government Printing Office, 1997.
6. NIEHS news: herbal health. Environ Health Perspect 106:A590-A592 (1998).
7. Jonas WB. Alternative medicine-learning from the past, examining the present, advancing to the future. JAMA 280:1616-1618 (1998).
8. Fontanarosa PB, Lundberg GD. Alternative medicine meets science. JAMA 280:1618-1619 (1998).

Original Article

Eurasian Journal of Toxicology

Evaluation of Poisoning Case Followed in Intensive Care Units: Eskisehir Study

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Abstract

Objectives: In this study, we aimed to retrospectively evaluate poisoning cases followed in tertiary care between 2019 and 2020.

Materials and Methods: 2726 cases followed between January 2019 and December 2020 were reviewed retrospectively. 154 (5.65%) of these cases were identified as poisoning cases. Cases under the age of 18 and chronic poisoning cases were not included in the study.

Results: A total of 154 cases, 87 women and 67 men, were retrospectively analyzed. The mean age of the patients was found to be 37.11 ± 15.7 years. 106 cases were recorded as suicide, 42 cases as accidental and 6 cases as poisoning due to overdose.

Conclusion: The highest poisoning agent was found to be drug. The fact that the cause of poisoning is the highest rate of drugs suggests that issues such as educating the public about drug use, reducing the sale of over-the-counter drugs and not keeping drugs within the reach of everyone should be taken into consideration.

Keywords: poisoning, acute intoxication, intensive care, retrospective study.

Introduction

Poisoning is an event that occurs when a substance that enters the body through oral, inhalation and dermal routes disrupts or stops the functioning of any system in the organism. Intensive care may be required after emergency admission and may cause death depending on exposure[1]. Poisoning is an important global public health problem. According to WHO data, an estimated 193460 people worldwide died from unintentional poisoning in 2012. 84% of these deaths occurred in low- and middle-income countries. In the same year, unintentional poisoning caused more than 10.7 million years of loss of healthy life[2]. According to German data, 178425 poisoning cases were treated in 2016.[3]

About one million people die by suicide each year, and chemicals account for a significant portion of these deaths. For example, deliberate ingestion of pesticides is estimated to cause 370,000 deaths each year. The number of these deaths can be reduced by limiting the availability and access of highly toxic pesticides[4].

As in the whole world, poisoning is a public health problem in our country as well. According to the Turkish Statistical Institute (TUIK), 35% of deaths between the ages of 15 and 34 between 2009 and 2019; On the other hand, 8.3% of the deaths between the ages of 35 and 59 were due to external injury or poisoning[5]. According to the 2020 annual report of the National Poison Center (UZEM), there were 123366 case applications[6].

In this study, we aimed to retrospectively evaluate poisoning patients followed in the intensive care unit in 2019 and 2020.

Materials and Method

2726 cases followed up in the intensive care unit of xxxx between January 2019 and December 2020 were retrospectively analyzed. 5.65% (n=154) of these cases were identified as poisoning cases. Cases under the age of 18 and chronic poisoning cases were not included in the study. All the methods in the study were approved by the Ethical Committee of Eskisehir Osmangazi University (Date: 29/06/2021, #2021-213/37). The study was carried out in accordance with the statement of Helsinki Declaration.

The age, gender, cause and purpose of the poisoning, length of stay in the intensive care unit, month of poisoning, and prognosis of the patients were evaluated. SPSS 21 program was used for statistical evaluation. Data are given as mean ± standard deviation, number or %. Chi-square test was used to compare categorical variables. For statistical significance level, $p < 0.05$ was accepted.

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Table 1. Characteristics of cases.

	Number of Patient (n)	Percentage (%)
Sex		
Female	87	56,5
Male	67	43,5
Type of Explosure		
Accidental	42	27,3
Suicid	106	68,8
Intentional	6	3,9
Route of Explosure		
Oral	142	92,2
Inhale	12	7,8
Group of Poison		
Drug	97	63
Chemical	49	31,8
Natural	5	3,3
Alcohol	3	1,9

Results

The ratio of poisoning cases to all intensive care unit cases (n= 2726) was 5.65% (n=154). 56.5% (n=87) of the cases were female, 43.5% (n=67) were male. 68.8% (n=106) of the cases were poisoned by suicide, 27.3% (n=42) accidentally and 3.9% (n=6) as overdose. 92.2% (n=142) of poisonings occurred by oral route, 7.8% (n=12) by inhalation. The characteristics of the cases are given in Table 1.

In the study, the mean age was 37.1 ± 15.7 (min. 18, max. 83). The mean age of female patients was 33.7 ± 14 years; mean age of male patients was 41.5 ± 16.7 years. Age distribution of the cases is given in Table 2.

It was determined that 55.2% of the men (n = 37) and 79.3% of the women (n = 69) were poisoned by suicide. 65.1% (n=69) of the cases of poisoning with suicidal intent were women; 34.9% (n=37) are male. There was no significant difference between gender and poisoning ($p>0.05$), but the rate of females was found to be significantly higher in poisoning due to suicide ($p<0.05$).

Drugs were found to be the most common cause of poisoning (63%), and 41 patients (42.3%) received a single drug from these drugs, and 56 patients (57.7%) took more than one drug. Agents of poisoning are shown in Table 3, and the list of orally used drugs is shown in Table 4.

Table 2. Age distribution of the cases.

Age	Female	Male	Total
18 - 29	43	19	62
30 - 39	20	16	36
40 - 59	16	22	38
60 +	8	10	18

While the most poisoning cases were detected in summer (57%), the lowest rate (27%) was detected in winter. Drugs as the cause of poisoning were detected at the highest rate in all months, the most in March (n=26) and the least in December (n=3). Case distribution according to seasons is given in Table 5. Due to the change in the intensive care patient profile due to the COVID-19 pandemic, no seasonal comparison was made between the dates examined.

Of these cases, 130 patients (84.5%) were discharged from the intensive care unit, 19 patients (12.3%) were transferred to the service and 5 patients (3.2%) died. The mean hospital stay of the patients is 2.3 days (min 1 day, max 11 days).

Table 3. Agents that cause poisoning.

Agent	Number of Patient (n)	Number of Deaths (n)
NSAID	62	0
Paracetamol	41	0
Antidepressant	40	0
Antipsychotic	26	1
Mushroom	5	0
Organophosphate and pesticides	7	2
Alcohol	3	3
CO	12	0
Other Addictive Substances	31	0

Discussion

Poisoning cases are an important group of patients who require intensive care and follow-up, which can occur both from suicide and accident. Studies in Turkey and around the world have also found that poisoning cases are higher in women (7-9). In our study, it was determined that poisoning cases were more common in women (56.5%).

While the average age was 28.1 years in Yeşiler et al.'s study in 2019 and 27.6 years in Dağlı at el.'s study in 2016, the average age in this study was 37.1 years and 62% of the study participants were between the ages of 18 and 29. (8, 9). The difference may be regional, but the age distribution in our study is consistent with the literature. Studies have reported that suicide events constitute the majority of poisoning cases[10, 11]. Similar results were found in this retrospective study.

Although there are regional differences, drugs were found to be the most common poisoning agent in many studies[7, 12]. Likewise, in our study, drugs were found to be the most common cause of poisoning, and this finding was found to be consistent with the literature. Studies have shown that most of the cases of drug poisoning were analgesics and antidepressants[7, 8]. In our study, similar data were found with the literature.

In studies conducted in Turkey with the same poisoning agent, it was found as 4.5% in Yeşiler et al.'s study, 6.9% in Akköse et al.'s study, and 19.2% in Yağan et al.'s study[8,13,14]. In the United States, 16 out of every 100000 emergency admissions were identified as CO poisoning[15]. This difference may

Table 4. Drugs that cause poisoning

Drug	Number of Patient (n)
Paracetamol	41
Diclofenac	21
Dexketoprofen	17
Sertraline	13
Etodolac	14
Various Antibiotics	13
Quetiapine	5
Duloxetine	12
Naproxen	11
Fluoxetine	9
Flurbiprofen	6
Diazepam	4
Venlafaxine	4
Risperidone	3
Olanzapine	3
Alprazolam	3
Carbamazepine	3
Valproic Acid	2
Aripiprazole	2
Metamizole	2
Gabapentin	2
Propranolol	2
Levothyroxine	2
Acetylsalicylic acid	2
Trifluoperazine	2
Pantoprazole	2
Others*	18
Uncertain	4

*Lithium, Bupropion, Pregabalin, Modafinil, Pinaverium, Clonazepam, Lorazepam, Thiocolchicoside, Montelukast, Levocetirizine, Hydroxyzine, Escitalopram, Ibuprofen, Levetiracetam, Isotretinoin, Mirtazapine, Mianserin, Methylphenidate

be related to the socioeconomic status of the poisoning cases.

The unconscious and careless use of pesticides and organophosphate products is also a major problem in our country. In a study conducted in Pakistan in 2020, the ratio of pesticide and organophosphate poisoning to all poisonings was found to be 65.2%[16]. In Turkey, it has been found at various and lower rates such as 3.2%, 2.7% and 1.15%[13,14,17]. Only 7 cases (4.5%) were recorded in this retrospective study. This situation may be related to the seasonal and geographical characteristics and socioeconomic conditions of the place where the study was conducted.

84.5% of the cases examined in our study were discharged with recovery, 12.3% were transferred to the service and 3.2% died. In studies conducted in Turkey, the rates of cure and discharge were recorded as 96.4% and 98.1%[18, 19]. In a study conducted in Australia in 2017, 74% were discharged[11]. The reason for the difference in discharge rates may be the less exposure of the admitted cases or the shorter application period.

TTable 5. Seasonal distribution of cases.

Season	Number of Patient (n)	Percentage (%)
Spring	42	27,3
Summer	57	37,0
Autumn	28	18,2
Winter	27	17,5

Conclusion

In the study, most of the poisoning cases were found to be suicidal. It was determined that drugs were the most common cause of poisoning. The limitation of the study is that the information accessed is limited due to its retrospective nature. In addition, the change in the intensive care patient profile due to the COVID-19 pandemic in the specified date range made data analysis difficult. The fact that the cause of poisoning is the highest rate of drugs suggests that issues such as educating the public about drug use, reducing the sale of over-the-counter drugs and not keeping drugs within the reach of everyone should be taken into consideration.

References

1. Yeşil O, Akoğlu H, Onur Ö, et al. Acil servise başvuran olguların geriye dönük analizi. Marmara Medical Journal 2008; 21(1): 26-32.
2. WHO. Poisoning Prevention and Management. 2016.
3. Zellner T, Prasa D, Färber E, et al. The use of activated charcoal to treat intoxications. Dtsch Arztebl Int 2019; 116: 311–7.
4. Dawson AH, Eddleston M, Senarathna L, et al. Acute human lethal toxicity of agricultural pesticides: a prospective cohort study. PLoS Med 2010;7(10):e1000357.
5. Turkish Statistical Institute. Adult Mortality Due to Extrinsic Injury and Poisoning, Statistics Data Portal. Publication Date: 06/08/2020.
6. Turkish National Poison Center Annual Report. https://hsgm.saglik.gov.tr/depo/kurumsal/yayinlarimiz/Raporlar/Uzem/UZEM_Ayrintili_Faal_Ek_f8b2cc15-f605-4953-95f1-9733b621c662.pdf
7. Köse I, Zinciroğlu Ç, Şenoğlu N, et al. Yoğun bakım ünitemize kabul edilen zehirlenme olgularının bir yıllık geriye dönük incelemesi ve mortaliteyle ilişkili faktörlerin değerlendirilmesi. Tepecik Eğit. ve Araşt. Hast. Dergisi 2015; 25: 28-32.
8. Yeşiler Fİ, Şendur ÜG, Demiroğlu Gİ. Yoğun Bakım Ünitesinde Akut İntoksikasyon Vakalarının İncelenmesi. Aegean J Med Sci 2019; 1:14-18.
9. Dagli R, Kocaoglu N, Bayir H, et al. Yoğun Bakım Servisimizdeki İntoksikasyon Vakalarının İncelenmesi. Medical Journal of Mugla Sitki Kocman University 2016;3(1):17-20.
10. Aydın A. Yoğun Bakım Ünitesinde Takip Edilen Zehirlenme Olgularının Değerlendirilmesi: Retrospektif Çalışma. Firat Med J 2019; 24(3): 129-33.
11. Athavale V, Green C, Lim KZ, et al. Characteristics and outcomes of patients with drug overdose requiring admission to Intensive Care Unit. Australas Psychiatry. 2017;25(5):489-493.

12. Müller D, Desel H. Common causes of poisoning: etiology, diagnosis and treatment. Dtsch Arztebl Int. 2013;110(41):690-700.

13. Akkose S, Bulut M, Armagan E, et al. Acute poisoning in adults in the years 1996-2001 treated in the Uludag University Hospital, Marmara Region, Turkey. Clin Toxicol (Phila). 2005;43(2):105-109.

14. Yağan Ö, Akan B, Erdem D, et al. The retrospective analysis of the acute poisoning cases applying to the emergency unit in one year. Şişli Etfal Hastanesi Tıp Bülteni 2009; 43: 60-4.

15. Rose JJ, Wang L, Xu Q, et al. Carbon Monoxide Poisoning: Pathogenesis, Management, and Future Directions of Therapy. Am J Respir Crit Care Med. 2017;195(5):596-606.

16. Abubaker Z, Nisar M, Jamshed A, et al. A Retrospective Analysis on Poison Related Mortalities in a Tertiary Care Centre in Pakistan. Asia Pacific Journal of Medical Toxicology 2020; 9(3), 85-90.

17. Özayar E, Değerli, Güleç H, et al.. Yoğun Bakıma Kabul Edilen Zehirlenme Olgularının Retrospektif Analizi. Yoğun Bakım Derg 2011; 3: 59-62.

18. Destegül D, Çapar A. Kayseri Eğitim ve Araştırma Hastanesi anestezi yoğun bakım ünitesinde takip edilen akut zehirlenme vakalarının değerlendirilmesi. Türkiye Klinikleri J Anest Reanim 2018; 16: 8-13.

19. Demir G, Eren GA, Hergünsel O, et al. Yoğun bakım ünitemizde 2003-2007 yılları arasında takip edilen zehirlenme olgularının geriye dönük analizi. Bakırköy Tıp Dergisi 2008; 4: 139-43.

Case Report
Eurasian Journal of Toxicology

Colchicine Intoxication In A Patient With Unilateral Renal Agenesis

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Abstract

Colchicine is an alkaloid used in the treatment of acute gout attacks, Familial Mediterranean Fever, Behçet's Disease and inflammatory bowel diseases. Depending on the dose taken, the clinic occurs in various ways. Gastrointestinal manifestations are common in colchicine intoxication, but multi-organ failure is a more rare and more serious problem. As the blood level of colchicine is determined by the kidney and the liver, toxicity may progress more rapidly in dysfunction of these organs. In this case report, we aimed to remind that colchicine intoxications may be more mortal in patients with renal insufficiency.

Keywords: renal failure, renal agenesis, colchicine intoxication

Introduction

Colchicine is an lipid-soluble alkaloid obtained from the plant 'Colchicum autumnale'[1]. It is rapidly absorbed from the gastrointestinal tract between thirty minutes and two hours after oral administration and reaches peak concentration. After absorption, approximately 50% is transported by binding to plasma proteins, so it is not possible to eliminate it by hemofiltration[2].

Colchicine is used in the treatment of acute gout attacks, Familial Mediterranean Fever (FMF), Behçet's Disease and inflammatory bowel diseases. The therapeutic dose and the toxic dose of colchicine are very close to each other and the signs of toxicity occur in acute, subacute and chronic periods[3].

In this article, we present a patient with unilateral renal agenesis who showed all periods of toxicity after high dose colchicine ingestion for suicidal purpose and showed rapid progression.

Case Report

A 21-year-old, 45 kg female patient who has been using colchicine for FMF for 5 years has took 40 colchicine dragees (Colchicine Dispert 0.5 mg) for suicide purpose.

Considering that the patient would need intensive care, she was referred to the Süleyman Demirel Medical Faculty Emergency Department four hours after taking the drug. The patient was taken to the Anesthesiology and Reanimation intensive care unit for follow-up and treatment.

From her history we learned that she had FMF, had been using colchicine for five years, and that her single kidney was agenetic. On physical examination, GKS was 15, pulse was 110 bpm and BP was 100/90 mmHg. Intestinal sounds were hyperactive, other than that physical examination findings were normal. Laboratory findings were WBC: 5800 mm3, Hb: 12.9 g/dL, Plt: 140000 mm3, BUN: 47.2 mg/dL, Kre: 3.23 mg/dL. ALT, AST and serum electrolyte values were normal. The patient was administered 1 mg/kg activated charcoal four times a day with a nasogastric tube.

6 hours after hospitalization; the patient's urine output decreased so hemodialysis was performed. On control blood samples after hemodialysis; Hb: 9.3 g/dL WBC: 2000 mm3, Plt: 76000 mm3, AST: 163 U/L, ALT: 37 U/L, creatinine: 1.98 mg / dL, BUN: 37.4 mg / dL and serum electrolytes were normal. Blood gas was pH: 7.4, pCO2: 30.6 mmHg, pO2: 78.9 mmHg, HCO3: 1 9.5. In her follow-up, hemoglobin dropped to 7 g/dL and erythrocyte suspension replacement treatment was performed. Whether there was a bleeding source was investigated and no source was detected.

24 hours after hospitalization; her condition deteriorated. Her consciousness disappeared and the pupils became anisocoric. GKS was calculated as 8. The patient was intubated. Conjunctival hemorrhage occurred. Brain CT was filmed. No pathology was detected. Since there was a hematoma in the femoral region where the dialysis catheter was present, USG was performed. It was observed that there

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were about 1.5 units of bleeding. In follow-up, hemoglobin value dropped to 4.8 g/dL despite erythrocyte suspension replacement. No area compatible with bleeding was found in the whole body CT. Urine output stopped completely. ALT and AST rose. Laboratory results were evaluated as compatible with pancytopenia; WBC: 2100 mm3, Hb: 4.8 g/dL, Plt: 57000 mm3. Necessary transfusions were made.

36 hours after hospitalization; distention developed in the abdomen. On physical examination, she had defence in the abdomen and there was no intestinal sounds by listening. Air-fluid levels were observed on the lateral decubitus radiograph. It was diagnosed as ileus related to colchicine. Hemodynamics remained stable. Urine output stopped. Hemofiltration was performed to the patient whose laboratory values were BUN: 34 mg/dL, Creatinine: 2.46 mg/dL, blood gas pH: 7.31, pCO2: 37.8 mmHg, pO2: 36.6 mmHg, HCO3: 18.7.

48 hours after hospitalization; AST and ALT increased to 2803 U/L and 1534 U/L respectively. D-dimer was 1468 mg/dL and Fibrinogen was 220 mg/dL. Disseminated intravascular coagulation (DIC) was considered. Inotropic support therapy was started for the patient who developed multiple organ failure. Thrombopheresis was applied. The patient's fever was also high so cultures was sent considering neutropenic fever. Empiric antibiotic treatment was started. Except for ionized calcium, electrolyte follow-ups were observed at normal levels.

On the third day; the patient who developed septicemia, had resistant deep metabolic acidosis and did not respond to inotropics died. Staphylococcus Aureus growth was reported in the blood cultures after the patient died.

Discussion

Colchicine intoxication shows progression by dose. When colchicine is taken at doses below 0.5 mg/kg minor toxicity develops and there is 100% improvement, when taken at doses between 0.5-0.8 mg/kg major toxicity develops and %10 mortality is observed, and when taken at doses above 0.8 mg/kg it has been reported that patients are lost as a result of cardiogenic shock within 72 hours. However, the risk of toxicity in acute intake of these doses is higher than the risk of toxicity in patients using it chronically[4-5]. Although the degree of toxicity is evaluated according to the dose range, there are cases that reported death at low doses and improvement at high doses[6]. In our case, although the patient had been using for colchicine five years with the diagnosis of FMF and who ingested colchicine at a dose of 0.5 mg/kg for suicidal purpose, so no significant toxicity was expected, she died.

Colchicine is metabolized in the liver within 48 hours of being absorbed from the gastrointestinal tract. Their metabolites are excreted in urine and faeces. It enters enterohepatic recirculation before its excretion. The application of activated charcoal in the first 48 hours and in repeated doses is important in this respect[7]. We applied activated charcoal to the patient at a dose of 1 mg/kg, 4 times a day.

The main effect of colchicine is observed in tissues where mitosis is rapid. One of the places where these tissues are found most is the gastrointestinal tract. As a result of this, ileus can occur in colchicine intoxications. In the acute period of intoxication, nausea vomiting becomes abdominal pain. In the following stages, erosive hemorrhagic gastritis, dehydration, electrolyte disorders and paralytic ileus may develop[8-9]. In our case, severe abdominal pain, abdominal distention and ileus was observed on the second day of hospitalization.

One of the tissues where the cell cycle is fast is bone marrow. It causes pancytopenia by causing hypoplasia in the bone marrow, and as a result septicemia can occur. These septicemias are quite mortal[8]. In this case, neutropenic fever was caused by leukopenia. There was no growth from the first set of cultures. Staphylococcus Aureus growth occurred in blood cultures taken on the third day.

Colchicine toxicity is divided into three periods. First period; begins hours after taking the drug. It is characterized by symptoms of the gastrointestinal tract, such as nausea, vomiting, abdominal pain and diarrhea. There is peripheral leukocytosis. The second period is seen 24 to 72 hours after drug intake. Multiple organ failure, leukopenia, thrombocytopenia, anemia, liver failure, electrolyte imbalance is observed. The third period is seen after the 10th day following toxic intake. In this period, patients may develop septicemia and alopecia may be observed. (10) Similar periods were observed in our case. However, the progression was much faster. The patient, who spent the acute period with gastrointestinal system symptoms, had pancytopenia within hours. Ileus developed afterwards. The patient entered multiple organ failure within 2 days. Then, blood pressure dropped and inotropic support was initiated. Septicemia that is normally expected after the tenth day occurred on the third day. The patient who developed cardiac collapse did not respond to inotropics and died.

References

1. Gilman AG, Goodman LS, Rall TW, et al. Goodman and Gilman's The Pharmacological Basis of Therapeutics, 8th ed. New York, Macmillan 1990;674-6.
2. Amanova A, Kendi Celebi Z, Bakar F, Caglayan MG, Keven K. Colchicine levels in chronic kidney diseases and kidney transplant recipients using tacrolimus. Clin Transplant. 2014 Aug 14. doi: 10.1111/ctr.12448. [Epub ahead of print]
3. Kaplan MM, DeLellis RA, Wolfe HJ. Sustained biochemical and histologic remission of primary biliary cirrhosis in response to medical treatment. Ann Intern Med. 1997;126:682–688
4. Bismuth C, Baud F, Dally S. Standardized prognosis evalua-

tion in acute toxicology: Its benefit in colchicine, paraquat and digitalis poisonings. J Toxicol Clin Exp 1986; 6:33-38.

5. Weakley-Jones B, Gerber JE, Biggs G. Colchicine poisoning: Case report of two homicides. Am J Forensic Med Pathol 2001;22:203-206.

6. Jarvie D, Park J, Stewart MJ. Estimation of colchicine in a poisoned patient by using high performance liquid chromatography. Clin Toxicol 1979; 14: 375-381.

7. Jayaprakash V, Ansell G, Galler D. Colchicine overdose: the devil is in the detail. N Z M J. 2007;120:1248.

8. Biçer S, Soysal DD, Çıtak A, Uçsel R, Karaböcüoğlu M, Uzel N. Acute colchicine intoxication in a child: a case report. Pediatr Emer Care. 2007;23: 314–317.

9. Milne ST, Meek PD. Fatal colchicine overdose: report of a case and review of the literature. Am J Emerg Med 1998; 16:603-608.

10. Stapczynski JS, Rothstein RJ, Gaye WA, Niemann JT. Colchicine overdose: report of two cases and review of the literature. Ann Emerg Med 1981; 10: 364-369.

Case Report

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Digoxin's Interactions with Various Drugs and A Case Report

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Abstract

Digoxin is a drug commonly used to achieve rate control in heart failure and atrial fibrillation with some form of arrhythmia. It shows a positive inotropic effect by inhibiting the Na+/K+ ATPase pump in the myocardial cell membrane. Since digoxin is a drug with a narrow therapeutic range, the therapeutic dose range should be monitored and the individual dose regimen should be established, taking care of plasma concentrations. Factors such as patient's age, renal dysfunction, abnormal electrolyte values, drug-drug or drug-plant interactions increase the risk of intoxication. Patients may present with nausea and vomiting in digoxin intoxication and may present with ventricular arrhythmias with fatal rhythm disorders. Although digoxin should be discontinued as treatment, accompanying electrolyte imbalances should be treated. In patients with malignant arrhythmias, digoxin-specific antibodies should be considered in treatment. In this study, various drug-drug interactions that are frequently observed and easily prevented in patients taking digoxin are discussed with a case report.

Keywords: digoxin, toxicity, drug interactions.

Introduction

Digoxin is basically a cardiac glycoside used in chronic congestive heart failure and treatment of some arrhythmias, characterized by a decrease in cardiac output, and characterized by systolic dysfunction of the ventricles[1]. However, since the therapeutic / toxic dose range (0.8-2.0 ng/mL) is narrow, digoxin poisoning can easily develop. When digoxin plasma concentration exceeds 2 ng/mL, it causes toxic symptoms such as headache, gastrointestinal complaints (nausea, vomiting, etc.), visual dysfunction, irregular heartbeat, and diarrhea[2-4].

Case Report

A 59-year-old woman with a history of diabetes mellitus, hypertension, hyperlipidemia, ischemic dilated cardiomyopathy, atrial fibrillation, and chronic obstructive pulmonary disease; She came to our hospital with the complaints of nausea-vomiting and general condition disorder. Her vitals were as following systolic blood pressure of 120 mmHg and diastolic blood pressure of 80 mmHg, the respiratory rate of 18 breaths per minute, the pulse rate 50 beats / min, the fever 36.7 degrees Celsius, and oxygen saturation of 89%. It was learned from the anamnesis of the patient that she used carvedilol 2x12.5 mg, ramipril 1x5 mg, spironolactone 1x25 mg, rosuvastatin 1x20 mg, and digoxin 1x0.125 mg. The creatinine observed at the time of admission was 2.1 mg/dl and the serum digoxin level was 6.56 ng / mL. The patient was considered digoxin intoxication accompanied by acute renal failure and digoxin was discontinued. Digoxin-specific antibodies were not considered in therapy, since the patient's hemodynamia was stable. The general condition of the patient with a Glasgow coma score of 12, blood gas and some respiratory parameters were pH:7.33, PaO_2:33.9 mmHg, $PaCO_2$:40.5 mmHg, PaO_2/FiO_2 < 200 mmHg. In the follow-up, the patient was given bronchodilator nebula treatment with a mechanical ventilator to improve his existing chronic respiratory disorders and general condition. The patient was treated with positive airway pressure from time to time. System examination: Cardiovascular system: S1 and S2 +, no additional sound, no murmur. Respiratory System: Both hemi thorax participate equally to breathing, basal ral +, no roncus. Gastrointestinal System: abdominal relaxed, no defensive rebound, no sensitivity. Other system examinations were normal. The patient was treated symptomatically, taking into account the results of biochemical and clinical research. On the 5th day of hospitalization, serum digoxin level was measured as 1.91 ng/mL and the patient left the mechanical ventilator due to the physical examination, blood gases and normal signs of life. The patient was discharged with cure on the 7th day of his application by organizing medical treatment of the patient, whose general

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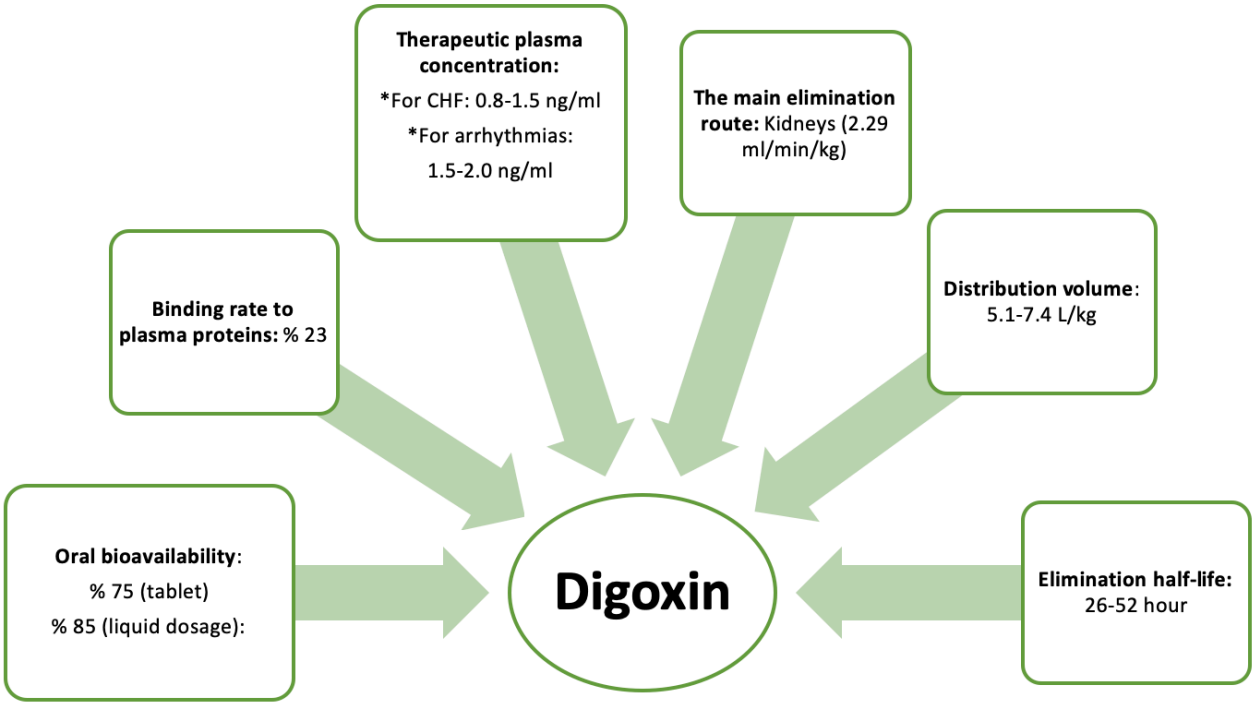

Figure 1: Pharmacokinetic properties of Digoxin (CHF: Congestive heart failure).

condition was good in the follow-up and his kidney functions decreased to normal.

Discussion

Although new treatment methods have been developed, the use of digoxin is a common agent that increases the contractile power of the heart. Na +, which is located on the myocardial cell membrane, reversibly inhibits K + dependent ATPase pump and increases intracellular calcium level. In addition to its inotropic effect, it is distinguished from other inotropic agents and maintains its superiority with its slowing down heart rate and its recently revealed sympathetic feature. However, since the therapeutic / toxic dose range is narrow, digoxin intoxication can easily develop[2-4].

Since digoxin has a narrow therapeutic range, serum levels; body weight, age, kidney function, liver failure, and changes in concomitant drug administration. A disrupted volume of digoxin distribution due to low renal function (digoxin is mainly excreted by the kidneys) or congestive heart failure may be one of the causes of digoxin toxicity[5]. Therefore, the pharmacokinetic properties given in Figure 1 should be considered when adding digoxin to treatment[6].

ACE inhibitors, angiotensin receptor blockers, calcium channel blockers, antibiotics (erythromycin, tetracyclines, etc.), antiarrhythmias, β-blockers (carvedilol etc.), statins (rosuvastatine etc.), diuretics, antifungals, proton pump inhibitors, anticholinergic drugs, some psychiatric drugs, ivabradine, cyclosporine, diclofenac, ibuprofen, indomethacin, metformin, and acute renal failure increase serum digoxin concentration. If used with these drugs, the dose of digoxin should be reduced or the frequency of dosing changed[7]. In addition, hypokalemia greatly increases the tendency to digoxin intoxication; Thus, in a patient with severe hypokalemia, intoxication may occur at relatively low serum concentrations. For this reason, although the diagnosis can be supported by measurement of serum concentrations in many cases, the diagnosis of digoxin intoxication is largely made according to the clinic[8]. In addition, *Eleutherococcus senticosus, Ginkgo biloba* and *Hypericum perforatum* there is also interaction with plants[9].

Drugs such as albuterol, antacids, cholestyramine, cholestipol, extenatide, kaolin-pectin, metoclopramide, miglitol, neomycin, penicillin, phenytoin, rifampin, sulfasalazine also reduce serum digoxin level[7].

As mentioned above, kidney function, electrolyte values and medications of patients may be prone to digoxin intoxication. In our case, the patient applied to the emergency room with nausea and vomiting, and acute renal failure and the use of ramipril, carvedilol and spironolactone increased the susceptibility to digoxin intoxication with the interaction mechanisms given in Figure 2. In addition, the rates of increasing these drugs Serum Digoxin Concentration (SDC) are as follows: perindopril (58%), metoprolol (16%), spironolactone (25%) and rosuvastatin (22%)[7].

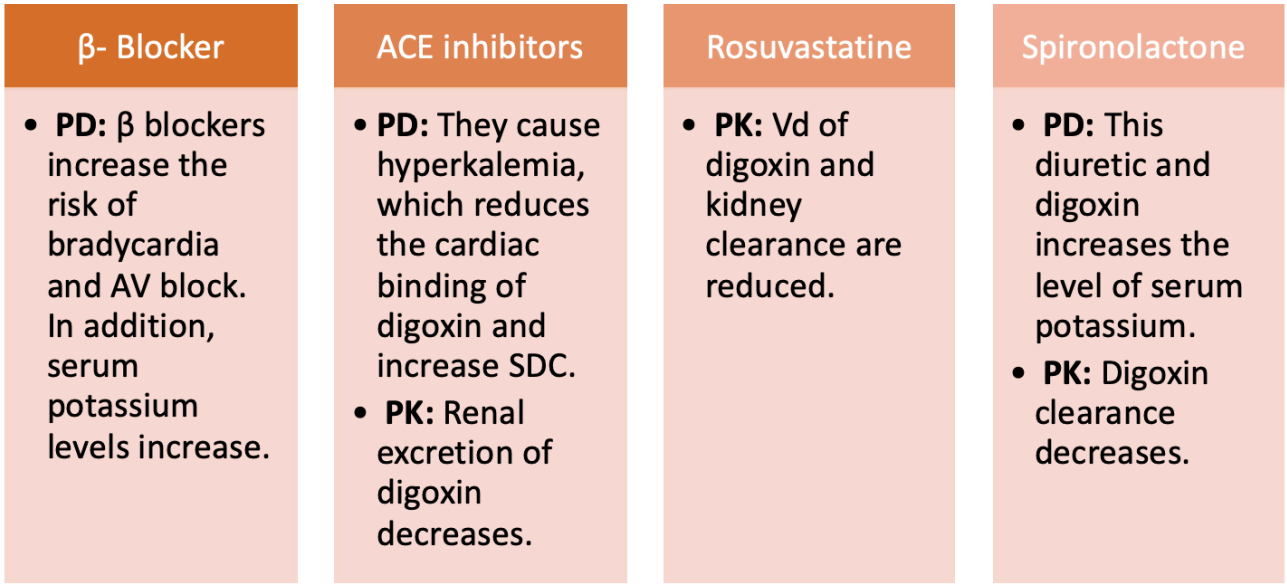

Figure 2: Pharmacodynamic / pharmacokinetic interaction table of drugs that increase Serum Digoxin Concentration (Vd = Volume of distribution, PD: Pharmacodynamic interaction and PK: Pharmacokinetic interaction).

Among the major symptoms of acute digoxin intoxications, cardiac rhythm abnormalities, as well as frequent headaches, nausea-vomiting (possibly due to the direct effect of digoxin on the area post-medema in the medulla), visual function disorders, mental disorders, irregular heartbeat, low blood pressure and ventricular rhythm disturbances[8,10]. Patients can apply with nausea and vomiting in digoxin intoxication, as well as ventricular arrhythmias with fatal rhythm disorders. In our case, headache, visual disturbances, and low coma scale could not be evaluated due to intoxication findings. Nausea-vomiting, hypotension and severe ventricular arrhythmias were observed.

The findings following poisoning are directly proportional to the plasma concentration of digoxin. While the therapeutic dose of digoxin is 0.8 ng / mL, when the plasma concentration is above 2 ng/mL, signs of intoxication appear[2]. After the acceptance of the case, the level of digoxin was measured as 6.56 ng / mL in the first serum sample taken. As the level of digoxin in the blood increases, Purkinje increases in automaticity. Accordingly, the foci that cause abnormal nerve stimuli gain efficiency and abnormal beats occur in the ventricular. The appearance of abnormal pulses is one of the first signs that digoxin plasma concentration has reached the toxic level by leaving the safety range[3].

In digoxin intoxication, firstly, digoxin should be discontinued as a treatment in patients, but the accompanying electrolyte imbalances should be treated. If patients have malignant arrhythmias, digoxin-specific antibodies should be considered in treatment.

Bradyarrhythmias should be treated initially with atropine; If it is not successful, transvenous pacing or Fab antibody treatment should be started. If antiarrhythmic drug therapy is required, phenytoin and lidocaine are sometimes effective in suppressing digoxin-induced ectopic stimuli. If rhythm disturbances have occurred in the presence of hypokalemia, the potassium deficit should be carefully closed[8,11]. Potassium is administered orally or intravenously, according to the blood level.1 In the first controls performed on the patient, the K + level was measured as 5.35 mmol / L and potassium treatment was not performed since there was no critical decrease. Then, measured K + levels were observed normally.

Digoxine specific antibodies (Digibind) can be used as a powerful antidote in the presence of serious life-threatening arrhythmias. After the Fab fragments are administered intravenously, they bind specifically to the circulating digoxin molecules, forming the digoxin Fab antibody complex and inactivating them, allowing the signs of toxicity to regress rapidly[12].

Digoxin-specific antibodies were not considered in therapy, since the patient's hemodynamia was stable.

Conclusion

As a result, digoxin and other digitalis glycosides are frequently used in the treatment of chronic heart failure and various arrhythmias. For this reason, patients should be informed about drug and food interactions that can lead to digoxin intoxication. For example, since hypokalemia greatly increases the tendency to digoxin intoxication, the patient should be warned to consume foods with high potassium content, while in the case of hypercalcemia, myocardium should be warned to restrict calcium consumption as it will increase sensitivity to digital. In patients using digoxin, which is a narrow therapeutic index drug, diseases such as hyperten-

sion and hyperlipidemia are frequently observed, especially when prescribing, potential drug interactions should be paid attention and the patient should be periodically monitored for side effects and toxicity. Therapeutic drug monitoring will play an important role in reducing drug treatment problems, and patients will be able to use their medicines safely.

References

1. Şahinoğlu AH. Yoğun Bakım Sorunları ve Tedavileri. 3rd ed. İstanbul:Nobel Tıp Kitapevleri;2011.
2. Tekelioglu UY, Ayhan SS, Demirhan A, Ozturk S, Akkaya A, Yildiz I, et al. Digoxin Intoxication:A Case Report. Journal of Cardio-Vascular-Thoracic Anaesthesia and Intensive Care Society 2012;17(3):74-76.
3. Kayaalp SO. Rasyonel Tedavi Yönünden Tıbbi Farmakoloji. 10th ed. Ankara:Hacettepe Taş; 2002.
4. Adalet K. Klinik Kardiyoloji Tanı ve Tedavi. 2nd ed. İstanbul:İstanbul Tıp Kitabevi;2013.
5. Punniyakotti S, N BB. A Case Report on Digoxin Intoxication in a Clinical Pharmacist's Perspective. Asian J Pharm Clin Res. 2018;11(4):1-3.
6. Wu AHB. Tıetz Clinical Guide to Laboratuary Tests. 4th ed. USA:Elsevier;2006.
7. Lanoxin Tablets [Internet]. [Access date: 10 May 2019] https://www.rxlist.com/lanoxin-tablets-drug.htm#interactions .
8. Hisar İ. Kardiyolojide Klinik Problemler El Kitabı - Özetlenmiş Anahtar Referanslar ile. 5th ed. Ankara:Bilimsel Tıp Yayınevi;1995.
9. Hu Z, Yang X, Ho PCL, Chan SY, Heng PWS, Chan E, et al. Herb-drug interactions. Drugs. 2005;65(9):1239-1282.
10. Pita-Fernandez S, Lombardia-Cortina M, Orozco-Veltran D, Gil-Guillen V. Clinical manifestations of elderly patients with digitalis intoxication in the emergency department. Arch Gerontol Geriatr. 2011;53(2):106-10.
11. Çiftçi E, Aydın S. Toxicological Evaluation of Digital Glycosides in Congestive Heart Failure. Fabad Journal of Pharmaceutical Sciences 2018;43(3):263-77.
12. Chan, BSH, Buckley NA. Digoxin-specific antibody fragments in the treatment of digoxin toxicity. Clin Toxicol. 2014;52(8):824-836.

Case Report

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Second-Degree Atrioventricular Block in An Adult with An Acute Dermal and Inhalational Amitraz Intoxication

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Abstract

Amitraz is a drug which is used against the external parasites of domestic animals such as lice, fleas, tick species, and scabies agents. There are no indications for use in humans. In this case report, we presented the findings related to intoxication due to the intake of amitraz via dermal and inhalation route. We tried to explain the possible complications and treatment options. Oral ingestion intoxication cases due to the amitraz use have been reported in humans. In addition, several animal experiments have been conducted, but there exists very few publications in the literature related to the amitraz intake via dermal or inhalation routein humans. Here we present a case of a second-degree AV block in an adult with an acute dermal and inhalational amitraz intoxication.

Keywords: cyclosporine, seizure, malignancy.

Introduction

Amitraz, which was first introduced to the market in 1974, is an insecticide derived from formamide. It is usually formulated in an organic solvent such as xylene and therefore also associated with solvent-associated risks. It also has an inhibitory effect on the synthesis of the monoaminoxidase enzyme and prostaglandin E2 [1-3].

Amitraz is easily absorbed by both the oral and dermal routes. Findings of kinetic studies have been mostly obtained from animal experiments. Amitraz is rapidly metabolized and excreted, mainly in the urine. Metabolism of amitraz is similar among many species by hydrolysis to N-(2,4-dimethylphenyl)-N'-methyl formamide and 2,4-dimethyl formanilide, leading to the production of 4-amino-3-methylbenzoic acid. This metabolite is rapidly conjugated and excreted[4].

Amitraz is an α2-adrenergic receptor agonist, its clinical effects occur rapidly through this mechanism[5-8]. α2 adrenergic receptors have pre and postsynaptic localization. Stimulation of presynaptic receptors inhibits noradrenaline discharge, whereas stimulation of postsynaptic receptors has a similar effect to α1 stimulation.

By stimulation of α2 receptors, symptoms such as sedation, convulsions, unconsciousness, coma, myositis with presynaptic effect, mydriasis with postsynaptic effect, bradycardia with inhibition of presynaptic noradrenalin, nonspecific ST changes, respiratory depression with direct effect on respiratory center, decreased salivation and gastric acid secretion, nausea, decreased gastrointestinal intolerance and intestinal distension, hyperglycemia due to the inhibition of insulin secretion, hypothermia or fever, and polyuria are seen[2, 4, 5, 7-9].

Amitraz poisoning is rarely reported in humans, and the majority of the cases are in the infantile age group and accidental. There are no adult dermal and inhalation cases due to amitraz poisoning in the literature and it is thought that the presented case will contribute to the literature.

Case Report

A 55-year-old male patient was admitted to the emergency department with complaints of drowsiness and fatigue after applying the drug [Kenaz^{R}], which has amitraz as its active ingredient, to the entire body. When questioned, the patient stated that he had been scratching his entire body for 6 months. He said that he went to all polyclinics that could be related to itching and the cause could not be found. He also stated that he used a wide variety of drugs during this period, but saw no benefit at all. On the recommendation of a friend, he used a drug called Kenaz^{R} which is used to treat scabies in animals by diluting to approximately 1/10. He applied the medicine to all over his body and slept till the morning. When he woke up in the morning, he felt too weak. He took a bath with the help of his wife. They ventilated the room and changed the linens. Howev-

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er, no change in his condition occurred and the patient was brought to the emergency department at 2:30 p.m. by her relatives. When the patient came, he fell asleep, his blood pressure was 123 / 73 mm / Hg, pulse was 44 beat / min, blood glucose was 115g / dl. ECG showed sinus bradycardia. He was followed-up and hypotension (97 / 50 mmHg) developed during the follow-up. The period between the two blood pressure measurements was 3 hours. When the case was discussed with the poison consultation center, it was stated that central nervous system depression, hypotension, bradycardia, hyperglycemia, myosis, hypothermia, acidosis, liver enzymes elevation and torsades de pointes could develop. The patient was monitored for 24 hours, including serial ECG, mental status, and liver enzymes. No pathology was found in the laboratory values during follow-up. However, bradycardia of the patient transformed into the mobitz type 2 block at the 18th hour of his hospitalization [Figure 1]. The patient's pulse rate was 40/min, blood pressure was 90/50 mmHg, and there was a change in his mental status. 0.9% saline was administered intravenously. Additionally, Atropine 1 mg was given intravenously and responded. The patient's pulse rate increased 56/min, blood pressure became 105/58 mmHg, and his mental status improved. At the end of 36 hours after admission to the hospital, the patient was discharged with suggestions after feeling better and having a stable pulse at 64 / min.

Discussion

Amitraz is a pesticide that is widely used as acaricide and insecticide in both animals and some plants. Although amitraz is widely used, it has been reported that the low number of reported intoxication cases associated with amitraz use may be related to the accidental diagnosis of organophosphate or carbamate poisoning[10]. Reported intoxication cases are mostly seen in children. The majority of these are accidental oral poisoning. Inhalation and dermal poisoning cases have rarely been reported [2, 5, 6, 11]. Our patient is one of the rare cases. He was exposed to the pesticide both by the dermal and inhalation routes. Fortunately, the symptoms are more moderate in dermal exposure and the recovery is earlier than oral poisonings[7, 11]. Especially respiratory, cardiac and central nervous system monitoring and evaluation should be given importance. Supportive treatment should include oxygen, blood pressure support, and giving fluid. The use of atropine in amitraz poisoning is controversial. However, in most studies, atropine has been used for myosis and bradycardia. Atropine is the first treatment for bradycardia and atrioventricular block resulting from vagal stimulation. Central α-2 adrenergic agonist drugs may cause bradycardia by stimulating the dorsal motor nucleus of the vagus. Hsu et al. showed that amitraz-induced bradycardia in animals improved with atropine at 0.045 mg / kg.[12]. Our patient had drowsiness, hypotension, and bradycardia. During the follow-up, mobitz type 2 A.V.block developed, but it was stable as responding to atropine. Cardiac, ECG, mental status, blood glucose, and liver enzymes were followed up for 24 hours. As there is a specific antidote for very few of the causative agents of acute poisoning, general treatment approaches and symptomatic therapies are essential. Amitraz does not have a specific antidote and oxygen therapy, gastric lavage, activated charcoal, and supportive symptomatic treatment are applied[3, 5, 7, 8]. As our patient had dermal and inhalation poisoning, oxygen therapy and fluid treatment were applied. Gastric lavage and active charcoal were not administered as there was no oral intake. The physician should also consider the possibility of amitraz poisoning from clinical findings and statements of the patients and the relatives, and should direct the treatment accordingly.

In conclusion, a basic approach to a patient with amitraz poisoning consists of initial stabilization, reduction of absorption and elimination of toxin. Despite the life-threatening clinical picture, amitraz poisoning in people carries low mortality when appropriate supportive therapy is given. It should be noted that severe rhythm disorders such as the Mobitz type II block may develop in the late period. Recovery usually occurs within 12 to 48 hours and patients are discharged without any organ dysfunction.

References

1. Shannon MW, Borron SW and Burns M. Haddad and Winchester's clinical management of poisoning and drug overdose. System 2007; 133.
2. Yilmaz HL and Yildizdas D. Amitraz poisoning, an emerging problem: epidemiology, clinical features, management, and preventive strategies. Archives of disease in childhood 2003; 88: 130-134.
3. Aydin K, Per H, Kurtoglu S, et al. Amitraz poisoning in children. European journal of pediatrics 2002; 161: 349-350.
4. Klasco R. POISINDEX® System. Thomson Reuters. Greenwood Village, Colorado, 2010.
5. Ertekin V, Alp H, Selimoğlu M, et al. Amitraz poisoning in children: retrospective analysis of 21 cases. Journal of international medical research 2002; 30: 203-205.
6. Kim J, Shin J, Yang Y, et al. Evaluation of developmental toxicity of amitraz in Sprague-Dawley rats. Archives of environmental contamination and toxicology 2007; 52: 137-144.
7. Atabek ME, Aydin K and Erkul I. Different clinical features of amitraz poisoning in children. Human & experimental toxicology 2002; 21: 13-16.
8. Doganay Z, Aygun D, Altintop L, et al. Basic toxicological approach has been effective in two poisoned patients with amitraz ingestion. Human & experimental

toxicology 2002; 21: 55-57.

9. Gursoy S, Kunt N, Kaygusuz K, et al. Intravenous amitraz poisoning. Clinical Toxicology 2005; 43: 113-116.

10. Elinav E, Shapira Y, Ofran Y, et al. Near fatal amitraz intoxication: The overlooked pesticide. Basic & clinical pharmacology & toxicology 2005; 97: 185-187.

11. Kalyoncu M, Dilber E and Ökten A. Amitraz intoxication in children in the rural Black Sea region: analysis of forty-three patients. Human & experimental toxicology 2002; 21: 269-272.

12. Hsu WH, Lu Z-X and Hembrough FB. Effect of amitraz on heart rate and aortic blood pressure in conscious dogs: influence of atropine, prazosin, tolazoline, and yohimbine. Toxicology and applied pharmacology 1986; 84: 418-422.