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Editorial

Değerli Okuyucular,

Dergimizin yeni bir sayısını acil tıp camiası başta olmak üzere toksikoloji ile ilgilenen tüm bilim dallarının üyelerine ulaştırmaktan büyük bir mutluluk duyuyoruz.

COVID-19 pandemisi tüm hızıyla sürerken, bu durum en çok sağlık çalışanlarını etkilemektedir. Dergimizin her aşamasında çalışan değerli hocalarımız aynı zamanda sahada aktif çalışan birer sağlık çalışanı ve bu süreçte bir yandan yoğun şekilde insanlara sağlık hizmeti sunarken diğer yandan da kendi sağlık problemleri ile uğraşmak durumunda kaldılar. Tüm bu nedenlerden ötürü maalesef birkaç ay önce yayınlamamız gereken sayımız gecikmeye uğradı. Elimizde olmayan sebeplere bağlı olarak yaşanan bu gecikmeden ötürü özürlerimizi sunarız.

Eurasian Journal of Toxicology dergisinin bu sayısını da yine yeni, ilgi çekici ve toksikoloji literatürüne katkı yapacağını düşündüğümüz derleme, orijinal araştırma makalesi ve vaka sunumlarından oluşan bir bütün olarak yayınlıyoruz. Derginin oluşması noktasında desteklerini hiçbir zaman esirgemeyen başta ATUDER Yönetim Kurulu Başkanımız Prof. Dr. Başar Cander ve yönetim kurulu üyelerimize, yine ilk andan itibaren ciddi çabalar harcayan editöryal ekip ve danışma kurullarına, bilimsel yazıları ile dergi gelişimine katkı sunan yazarlarımıza şükranlarımızı sunuyoruz.

Keyifli okumalar dileriz.

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Prof. Dr. Zeynep Gökcan Çakır

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Antiprotozoal İlaçlar ve Toksisite

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Özet

Paraziter hastalıklar sağlık, sosyal ve ekonomik bir etkiye sahiptir ve dünyanın tüm bölgelerinde özel bir sorundur. Bu makale insanlarda önemli protozoon enfeksiyonlarının tedavisi ve ilaç toksisitelerini gözden geçirmektedir.
Bu kısa incelemenin bilim insanlarını ilaç toksisiteleri için gerekli ek bilgileri edinmeye teşvik edeceğini umuyoruz.

Anahtar kelimeler: protozoa, antiprotozoal ilaç, toksisite

Abstract

Antiprotozoal Drugs and Toxicity

Parasitic diseases have a health, social and economic impact and are a particular problem in all of regions of the world. This article reviews the treatment and drug toxicities of the major protozoan infections in humans.

We hope this brief review will stimulate scientists to acquire additional information necessary for drug toxicities.

Key words: protozoa, antiprotozoal drug, toxicity

Antiprotozoal İlaçlar

Parazit dünyasının önemli bileşenlerinden olan Protozoalar, tek hücreli canlılardır. Bu canlılara ait hastalıklar, günümüzde de özellikle sağlık koşulları, hijyenik alışkanlıklar ve vektörlerin kontrolleri yetersiz olan, tropikal-subtropikal bölgeler başta olmak üzere tüm ülkelerde önemli bir sağlık sorunu olmaya devam etmektedir.

En önemli protozoal hastalıklar, Malaria (sıtma), Amebiasis, Leishmaniasis, Trypanosomiasis, Trichomoniasis ve Giardiasis'dir. Protozoal enfeksiyonlar, bakteriyel enfeksiyonlardan daha zor tedavi edilir ve antiprotozoal ilaçlar daha toksiktir. Bu nedenle günümüzde, bu enfeksiyonlara yönelik tedavilerin çoğu toksisiteleri ile sınırlıdır[1-4].

Metranidazol

Bir 5-nitroimidazol türevidir (2-Metil-5-nitroimidazol-1-etanol). Metronidazol, antiprotozoal ve antibakteriyel aktiviteleri olan sentetik bir maddedir. Etki mekanizması tam olarak açıklanmamasına rağmen, iyonize edilmemiş metronidazol, zorunlu anaerobik organizmalar tarafından kolayca alınır ve daha sonra düşük redoks potansiyeli olan elektron taşıma proteinleri ile aktif, ara ürüne indirgenir. Azaltılmış metronidazol, DNA sarmalının kopmasına neden olur, böylelikle DNA sentezini ve bakteriyel hücre büyümesini önler. Direnç gelişimi çok nadirdir[1-3,5].

Oral çok iyi emilir. Dokulara iyi dağılır. Karaciğerde metabolize olur. Bu kimyasal maddeye maruz kalma semptomları sinir veya kılıf yapısal değişiklikleri, titreme, ateş, sarılık ve diğer karaciğerde etkilenmeyi içerebilir. Konvülsif nöbetlere, uyuşukluk, bulantı, kusma, karın ağrısı, ishal, nahoş metalik tat, eritematöz döküntü, kaşıntı, baş dönmesi, senkop, ataksi, tromboflebit, stomatit, geri dönüşümlü trombositopeniye sebep olabilir. Elektrokardiyografik incelemede T dalgasının düzleşmesi görülebilir. Ayrıca sinirlilik, depresyon, uykusuzluk, burun tıkanıklığı, dizüri, sistit, poliüri, idrar kaçırma, pelvik basınç hissi, disparoni, libido azalması, proktit ve eklem ağrılarına neden olabilir. Ciltte kızarıklık ve uyuşukluğa neden olabilir. Diğer maruz kalma semptomları arasında kırıklık, geçici döküntüler, gast-

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rointestinal rahatsızlıklar ve periferik nöropati bulunur. Bu bileşiğe maruz kalan hamile kadınlar prematüre, bebekleri doğurabilir. Bu bileşik yutulduğunda, solunduğunda veya cilt emiliminde zararlıdır. Tahrişe neden olabilir. Alkolle beraber alınırsa disülfiram benzeri etki yapar. Metronidazolün geniş kullanımına rağmen, sadece nadir görülen hepatotoksisite vakaları bildirilmiştir ve büyük vaka serilerinde akut karaciğer yetmezliği ve ilaca bağlı karaciğer hasarı nedenleri arasında metronidazol listelenmemiştir. Parenteral veya aşırı dozda verilen yüksek dozlarda metronidazol serum aminotransferaz seviyelerinde yükselmelere neden olabilir, ancak bunlar genellikle kendi kendini sınırlar ve minimal semptomatiktir

Amebiyazisde 3x500-750 mg/gün 10 gün, Çocuklarda 50 mg/kg/gün 3 bölünmüş dozda 10 gün verilir. Giardiazisde tedavi dozu erişkinlere; 3x250 mg/gün, çocuklara; 5 mg/kg/gün 10 gün şeklindedir.

Fenobarbital, metranidazolun metabolizmasını artırarak, yarı ömür ve plazma konsantrasyonlarında bir azalmaya yol açarak mikrozomal karaciğer enzimlerini uyarabilir. Metronidazolün diğer nörotoksik ilaçlar ile birlikte kullanılması nörotoksisite potansiyelini artırabilir. LD50 = 500 mg / kg / gün (ratlarda oral olarak) dir.

Toksik maruziyeti olan hastalarda havayolunu açıklığını koruyup koma, nöbet, hipotansiyon, anafilaksi ye yönelik tedaviler akılda tutulmalıdır. Gastroenterit kaynaklı sıvı kayıpları intravenöz kristaloidlerle karşılanıp eş zamanlı aktif kömür uygulama protokolu devreye sokulmalıdır. Zorlu diürezin rolü belirsizdir. Hemodiyaliz, belki de böbrek fonksiyon bozukluğu ve yüksek düzeyde toksik ajan alan hastalar dışında genellikle uygulanmaz[5,6].

Ornidazol

Ornidazol (1-kloro-3-(2-metil-5-nitroimidazol-1-il) propan-2-ol 1 ve 2 pozisyonlarındaki hidrojenin sırasıyla 3-kloro-2-hidroksipropil ve metil grupları ile değiştirildiği 5 nitroimidazol olan bir C-nitro bileşiğidir. Duyarlı protozoal enfeksiyonların tedavisinde ve anaerobik bakteriyel enfeksiyonların tedavisinde kullanılır. Antiprotozoal, antiinfektif, antibakteriyel, antitrikonmonal olarak kullanılabilir. Oral iyi emilir ve vücut içinde iyi yayılır. Yan etki olarak baş ağrısı, iştahsızlık ve baş dönmesi olur.

Tedavi dozu 2x500mg/gün 5-10 gündür. 1 yaşından küçüklerde erişkin dozun 1/4'ü, 1-6 yaş erişkin dozun 1/2' si, 7-12 yaş erişkin dozun 3/4'ü verilir, Ratlarda LD50 değeri oral alımlarda 1780 mg / kg dir[5-8].

Antimon Bileşikleri

Laymaniasis (leishmaniasis) sağaltımında dünyada ve ülkemizde en yaygın kullanılan ilaçlar beş değerli antimon bileşiklerinden meglumin antimonat ve sodyum stiboglukonattır. Ağır metal yapısındaki bu bileşikler retiküloendotelyal sistem hücrelerinde yoğunlaşmakta, Leishmania amastigotlarında glikolitik enzimleri, yağ asidi oksidasyonunu, DNA ve RNA sentezini inhibe ettikleri düşünülmektedir. Halen kullanılmakta olan bupreparatlarından Glucantim®'in (meglumin antimonat) 85 mg/ml, Pentostam®'ın (sodyum stiboglukonat) ise 100 mg/ml antimon bileşiği içeren 5 ml'lik ampul formları vardır. Oluşabilecek yan etkileri nedeniyle bu ilacın mutlaka hastane koşullarında uygulanması gerekmektedir.

Bu bileşiklerin en sık görülen yan etkileri; karın arısı, bulantı, kusma, halsizlik, başağrısı, karaciğer enzimlerinde artış, nefrotoksisite, miyalji, artralji ve pankreas enzim düzeylerinde yükselmedir. Miyokarditli, pankreatitli, böbrek yetmezlikli ve hepatitli hastalarda kullanımlarının kontrendike olduğu bildirilmiştir.

Kinin

Çinkona alkaloidi olan kinin (4-*N*- (7-klorokinolin-4-il) -1 -*N* 1-*N*-dietilpentan-1,4-diamin), Plasmodium'ların eritrositik safhalarına karşı oldukça etkilidir. İlacın etkinlik mekanizması tam olarak bilinmemekle birlikte, eritrosit içindeki parazitlerin hemoglobin içeren sindirim vezikülleri düzeyinde etki gösterdiği sanılmaktadır. Kinin kardiyak sodyum ve potasyum kanallarını inhibe eder. Sodyum kanal blokajı ile negatif inotropiye, potasyum kanallarının blokajı ile de repolarizasyondaki gecikmeye sebep olur. Bunların dışında işitme kaybı, görme keskinliğinde azalma ve vertigo görülebilir.

Tedavi edici dozlarda, sıklıkla "çinkonizm" görülür. Yaygın özellikleri bulantı, kusma, işitmede azalma, çınlama ve baş ağrısıdır. Taşikardi genellikle vardır. Letal dozu 8 gramdır. Deliryum, koma ve nöbetler genellikle ciddi zehirlenmelerde görülür ve miyokard depresyonu ile birlikte olabilir.

Tanıda İdrar ince tabaka kromatografi kullanılır. İmmunoassay teknikler en güvenilir tekniklerdir. Plazma kinin konsantrasyonu 10 µg/mL nin üzerindeki düzeylerde geçici körlük görülürken 15 µg/mL üzerinde kalıcı görme hasarı, disritmi ve ölüm meydana gelir.

Orogastrik lavaj, aktif kömür (1 g/kg), kardiyak monitörizasyon ve sıvı desteği yapılmalıdır.

Geniş QRS kompleks veya kalp bloğu gelişmesi halinde pH 7.45-7.50 oluncaya kadar hipertonik sodyum bikarbonat verilmelidir. Torsades de pointes gelişirse, magnezyum uygulaması, potasyum desteği verilmelidir.

Sodyum ve/veya potasyum kanallarını bloke edici antiaritmikler kullanılmamalıdırlar. Serum glukozu dekstroz infüzyonu ile desteklenmelidir. Tekrarlayan doz aktif kömür kininin yarı ömrünü belirgin olarak azaltır. Aktif kömür (0.5-1.0 g) ağızdan, her 2-4 saat ara ile toksisite devam ettiği sürece verilmelidir. Hemoperfüzyon, hemodiyaliz ve exchange transfüzyonu rutin olarak önerilmemektedir.

Klorokin, Hidroksiklorokin

4-aminokinolon türevi olan klorokin sıtma sağaltımında kullanılan ana ilaçlardan biridir. Klorokin, aseksüel eritrositik Plasmodium türlerinin besin vakuolünde yüksek seviyelerde birikerek hemin polimerizasyonunu bloke etmektedir. Plasmodium'lar hemoglobinin heme ve globüline ayrılmasıyla ortaya çıkan konak hücrenin globülinini sindirerek kendi besininin büyük bir bölümünü karşılar. Klorokin, zayıf baz yapısındadır ve parazitin asidik yapıdaki besin vakuolünde birikir. Membranda protonlanmasıyla vakuol dışına çıkamayıp birikmeye başlar. Böylece parazitin eritrosit içindeki hemoglobini sindirmesiyle doğal olarak ortaya çıkan ve normal şartlarda yağ yıkıma uğratılan ya da etkisiz hale getirilerek pigment (hemozoin) halini alan toksik hem bileşenleri yıkılamaz ve paraziti etkileyerek öldürür. Kandaki terapötik ilaç düzeyine alımını takiben 2-3 saat içinde ulaırken, karacier ve böbrekler yoluyla vücuttan yava atılır. Vücuttaki yarılanma ömrü dört gündür. 5 gr ve üstü alımlar veya serum konsantrasyonu 5 µg/mLyi aşınca görülür. Etkileri kinine benzer, ancak «çinkonizm" gibi diğer özellikler sık görülmez.

Akut hidroksiklorokin zehirlenmesi klorokin zehirlenmesine benzer bulgular ortaya çıkar. Kardiyovasküler ve santral sinir sistemi depresyonu görülebilir.

Klorokin zehirlenmesinde vazodilatasyon ve miyokard depresyonu için epinefrin ve sedasyon için diazepam kullanılır. Erken entübasyon için dikkatli olunmalıdır.

Orogastrik lavaj ve aktif kömür verilmelidir. Serum potasyum düzeyi sıkı takip edilmeli gerekirse destek tedavisi verilmelidir. Klorokin ve hidroksiklorokin proteine yüksek oranda bağlandığı için atılımı artırma yöntemleri etkili değildir[9-11].

Halofantrin

Zehirlenmelerinde bulantı kusma gibi gastrointestinal sistem bulguları, çarpıntı, hipotansiyon, senkop, QT uzaması, ventrikül fibrilasyonu ve torsades de pointes görülebilir. Birinci derece kalp bloğu sık rastlana bulgudur, aritmiler daha çok aşırı doz durumlarında beklenir.

Çok az hastada nöbet, hafif karaciğer enzim yüksekliği bildirilmiştir.

Halofantrin aşırı doz alımında mide lavajı ve destek tedavisi yapılır. QT uzaması ve aritmiler açısından dikkatli olunmalıdır. QT uzaması ve torsades de pointes tedavisi kinin zehirlenme tedavisi ile aynıdır [11,14].

Meflokin

Dirençli *P. falciparum* türlerine karşı etkili, kinolin metanol türevi bir sıtma ilacıdır. Eritrositer şizontlara etkili olan meflokin, eksoeritrositik safhaya ve gametositlere etkisizdir. Gastrointestinal sistemden iyi absorbe edilir. Plazma proteinlerine yüksek oranda bağlanır En sık görülen etkileri bulantı, kusma ve diyaredir. Aşırı doz Ssmptomları konfüzyon, ajitasyon, ataksi, sersemlik hissi, konuşmada güçlük, yüksek frekanslı duyma kaybı, bulantı, yorgunluk, halsizlik, depresyon, oryantasyon bozukluğu ve parestezidir. Hafif hipotansiyon, seyrek ventriküler erken vuru ile birlikte taşikardi, karaciğer fonksiyon testlerinde çok az yükselme ve protrombin zamanında uzama da bildirilmiştir. Tedavide aktif kömür verilir[11-13].

Primakin

8-aminokinolon türevleri tüm Plasmodium türlerine karşı gametositosidal aktiviteye sahip olan ilaçlardır. Bu grupta yer alan primakin, *Plasmodium vivax* ve *Plasmodium ovale*'nin karaciğerdeki hipnozoit formları üzerine de etkilidir. Yapılan araştırmalarda primakinin hem mitokondrial elektron transport zincirine, hem de pirimidin sentezine karşı etkili olduğu rapor edilmiştir. Oral alındıığnda gastrointestinal sistemden hızla emilir ve metabolize olarak idrar yoluyla atılır. Primakin, glikoz-6-fosfat dehidrogenaz (G6PDH) enzim eksikliği olanlarda kontrendikedir. Yüksek dozlarda methemoglobinemi ve hemoliz meydana gelebilir. Primakin aşırı dozunda bulantı, halüsinasyonlar, sarılık, hepatit görülebilir.

Tedavide aktif kömür verilir. Methemoglobineminin geri döndürülmesi için Metilen mavisi kullanılır.

Proguanil, Primetamin, Sulfadoksin, Dapson ve Atovakuon

Proguanilin profilaksi sırasında yan etkileri bulantı, diyare ve ağız ülserleridir. Ancak zehirlenmeleri ile ilgili yeterli veri bulunmamaktadır. Tek başına primetaminin aşırı doz alımı nadirdir. Bulantı, kusma, nöbet, görme kaybı gelişebilir. Primetamin, sulfadoksin ile nadiren yaşamı tehdit eden eritema multiforme meydana gelebilir. Kronik yüksek doz kullanımında folik asid replasmanı gerektirecek boyutta megaloblastik anemi gelişebilir. Proguanil ve primetamin aşırı dozları sonrası folik asid replasmanı (erişkinde 50 mg, çocuklarda 1 mg/kg) verilmelidir. Destek tedavi yapılır. Ciddi methemoglobinemi metilen mavisi (1 mg/kg) ile tedavi edilmelidir.

Atovakuon gastrointestinal yakınmalar, karaciğer fonksiyon testlerinde yükselme, makülopapüler döküntü, nadiren eritema mutiformeye yol açabilir. Yüksek doz alımında semptomsuz vaka bildirimi olmuştur.

Dapson ve sulfonamidlerin nötropeni, trombositopeni, eozinofilik pnömoni, aplastik anemi, nöropati ve hepatit gibi idiyosinkratik reaksiyonlara yol açtığı bilinmektedir. Dapson bulantı, kusma ve karın ağrısı gibi gastrointestinal sistem bulgularına neden olur. Aşırı dozda dapson alımında methemoglobinemi görülebilir. Hemoliz erken veya geç dönemde

görülebilir. Aşırı doz alımında hepatit ve nöropati bildirilmiştir. Tekrarlayan doz aktif kömür (0.5-1 g/kg, 2-4 saat ara ile) dapsonun atılımını hızlandırır. Simetidin dapsonun toksik metabolitine dönüşmesini engellemede kullanılabilir[1-4,15].

Artemisinin

Biyoyararlanımı kısıtlı ve yarı ömrü çok kısa olduğu için uzun süreli kullanımı gerekmektedir. Genellikle artemisininler meflokin ile birlikte kullanılır. Artemisininin etkinliği ve toksisitesi özellikle hem varlığında trioksan moleküler çekirdeğin hücre içi serbest radikal oluşturma yeteneğine bağlıdır. Hayvanlarda, uzun süre, yüksek doz ve parenteral uygulama sonrası beyin sapı çekirdeklerinde hasar meydana gelir.

Yan etkilerinin insanlarda çok düşük insidansta olduğu görülmüştür. Az sıklıkta görülen yan etkiler bulantı, kusma, karın ağrısı, diyare ve baş dönmesidir. Santral sinir sistemine ait nadir bildirilerde tedavi dozlarında santral sinir sistemi depresyonu, nöbetler, aşırı ilaç alımlarında serebellar semptomlar bildirilmiştir. Asemptomatik QT uzaması ve QRS değişikliği bildirilmiştir.

Aşırı doz alımlarda destek tedavi verilmelidir. Hastalar kardiyovasküler ve santral sinir sistemine yönelik gözlem altına alınmalıdır[1-6,15].

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Original Article

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Spatial Analysis and Evaluation of Carbon Monoxide Poisoning Admitted to A Tertiary Hospital- A Pilot Study

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Abstract

Objectives: In this study we aimed to define a free spatial analysis method that can be used for toxicology patients and contribute to the poisoning data of our country by performing this method on carbon monoxide poisoning cases admitted to emergency department of our hospital.

Materials and Methods: The population of this retrospective study included all adults who were admitted to our clinic with carboxyhemoglobin level above 10%. Two heat maps were created based on address of carbon monoxide poisoning and carboxyhemoglobin values of the persons in this position.

Results: 414 patients were included in the study. 39 patients were excluded from the study. 52.3% of the patients were female and 47.7% were male. Median of carboxyhemoglobin values was 14% (IQR = 13). The number of cases admitted during the winter was found to be higher than the other seasons. Two heat maps were created based on addresses of carbon monoxide poisoning.

Conclusion: Carbon monoxide poisoning is an important health problem in our country. Multicenter studies with Geographical Information Systems may contribute to the measures to be taken for carbon monoxide intoxication.

Key words: carbon monoxide, geographical information systems, spatial analysis

Özet

Amaç: Mekansal analiz yöntemi tanımlamak ve hastanemiz acil tıp kliniğine başvuran karbon monoksit zehirlenmesi olgularının demografik verileri ve karboksihemoglobin düzeyleri ile ilgili mekânsal analizler yaparak zehirlenme verilerine katkıda bulunmayı amaçladık.

Gereç ve Yönetim: Çalışmamız kliniğimize karbon monoksit zehirlenmesi ile başvuran hastalardan karboksihemoglobin düzeyi %10' un üzerinde olanlar dahil edildi. Hastaların demografik verileri değerlendirilerek zehirlenme adresleri kullanılarak vaka yoğunluğu ve karboksihemoglobin değerlerine göre iki ısı haritası oluşturulmuştur.

Bulgular: Çalışmaya 414 hasta dahil edildi. 39 hasta çalışma dışı bırakıldı. Hastaların %52,3'ü kadın, %47,7'si erkekti. Ortalama karboksihemoglobin değerleri %14 idi (IQR = 13). Kış aylarında kabul edilen vaka sayısının diğer mevsimlere göre daha yüksek olduğu bulundu. Karbon monoksit zehirlenmesinin adreslerine dayanarak iki ısı haritası oluşturuldu.

Sonuç: Karbon monoksit zehirlenmesi ülkemizde önemli bir sağlık sorunudur. Coğrafi Bilgi Sistemleri ile çok merkezli çalışmalar karbon monoksit zehirlenmesi için alınması gereken önlemlere katkıda bulunabilir.

Anahtar kelimeler: karbon monoksit, coğrafi bilgi sistemleri, mekânsal analiz

Introduction

With the developing technology, the importance of health applications is increasing rapidly among the fields of application of geographical information systems. These applications help the decision makers in the field of health through maps produced by associating the available data[1].

Carbon monoxide (CO) is a preventable cause of death, often caused by accidents. In our country, it often causes mortality and morbidity after stoves, water heaters and industrial poisonings[2]. CO can cause hypoxia at the tissue level by binding to hemoglobin after inhalation and decreasing the oxygen carrying capacity of the blood. Heart and nervous system, which needs oxygen more than other tissues, is particularly affected and life-threatening changes occur in the tissue[3].

The purpose of the present retrospective pilot study was to define a free spatial analysis method that can be used for toxicology patients and contribute to the poisoning data of our country by performing this method on carbon monoxide poisoning cases admitted to emergency department (ED) of our hospital.

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Materials and Methods

Study design

This retrospective study was conducted at a 672-bed tertiary academic hospital with an annual ED census of 438000. We collected data of the patients who visited our ED with a COHb level above 10% during the date January 1, 2015 and January 1, 2018 retrospectively.

Study population

Our study population was patients who admitted to our ED with a COHb level above 10% during the date January 1, 2015 and January 1, 2018. Patients with missing data on the hospital computer-based data system about address of poisoning especially workplace or hookah cafe were excluded.

Data collection

Demographic characteristics (age, gender), application seasons and COHb levels of the patients and spatial analysis of the poisonings were performed. The application seasons of patients were defined as spring (March, April, May), summer (June, July, August), autumn (September, October, November), and winter (December, January, February).

Primary outcome was a free spatial analysis method. The secondary outcomes were demographic data and carboxyhemoglobin levels.

Spatial analysis

Address data of poisonings were revised in Microsoft Office Excel 2007 environment due to possible repetition or missing data. Geocoding process was made by geocoding services which provide free services. A heat map was created based on these positions and COHb values of the persons in this position.

Statistical analysis

In the statistical evaluation of the data, IBM Statistics 20.0 (SPSS) statistical package program was used. The baseline patient characteristics are presented as frequencies for categorical variables and as medians and interquartile ranges for continuous variables. Averages were shown with standard deviations. Statistical analysis of categorical variables was done by "chi-square" test and numerical variables were analyzed by Mann Whitney U test and "t test". Spearman correlation was used to evaluate relationships involving ordinal variables. A p value less than 0.05 was regarded as statistically significant.

Ethics

Ethics committee approval required for the study was taken from Ethics Committee (date: 21/03/2018, approval number: B.10.1.TKH.4.34.H.GP.0.01/36). We retrospectively reviewed the secondary data extracted from the electronic medical records. However, the extracted data included clinical data only; it didn't include any personal identifiable information. Therefore, the need for informed consent was waived.

Results

The study included 414 patients with COHb levels above 10% who were admitted to our clinic. 39 patients were excluded from the study because of repetition or missing data. 52.3% (n = 196) of the patients were female and 47.7% (n = 179) were male.

The ages of the patients ranged from 3 to 94 years, and median of age was 36 years (IQR = 37.4). The measured COHb levels of patients ranged from 10-63%, and median of COHb levels was 14% (IQR = 13). No significant difference was found between COHb levels and gender (p=0.652). Cases were classified according to their decades. There was no statistically significant correlation between COHb levels and this decade groups (p=0,115) (Pearson correlation test).

The distribution of patients according to the seasons is evaluated; It was seen, 43.7% (n = 164) in winter, 23.7% (n = 89) in spring, 15.5% (n = 58) in summer, 17.1% (n = 64) in the autumn season. The number of cases admitted during the winter was found to be higher than the number of those admitted in the other seasons with a significant difference (p <0.001)

A heat map was created based on addresses of CO poisoning shown in figure 1. Second heat map was created based on these positions with COHb levels shown in figure 2. The second map shows the poisoning addresses in red circles. The diameters of the red circles were shown to be proportional to the COHb levels.

Discussion

Geographical Information Systems will play an active role in increasing the service quality and satisfaction as a decision support system that provides accurate analysis of spatial data in the areas of policy production, strategic planning and management, especially in the areas of corporate applications[4]. Heat maps are used for georeferencing health data. These maps might link such data geographically to potential sources of environmental exposures, the geodemographic characteristics of populations, and the locations of health resources[5,6]. They can be helpful tools for preventing, understanding, and treating diseases. Spatial analysis and heat maps performed for avian influenza and other topics relating to pandemic influenza by World Health Organization and The Centers for Disease Control and Prevention[7,8]. New live heat maps are preparing for new coronavirus pandemic[9,10].

The identification of spatial patterns of CO poisoning is a critical first step in a more complete understanding of the

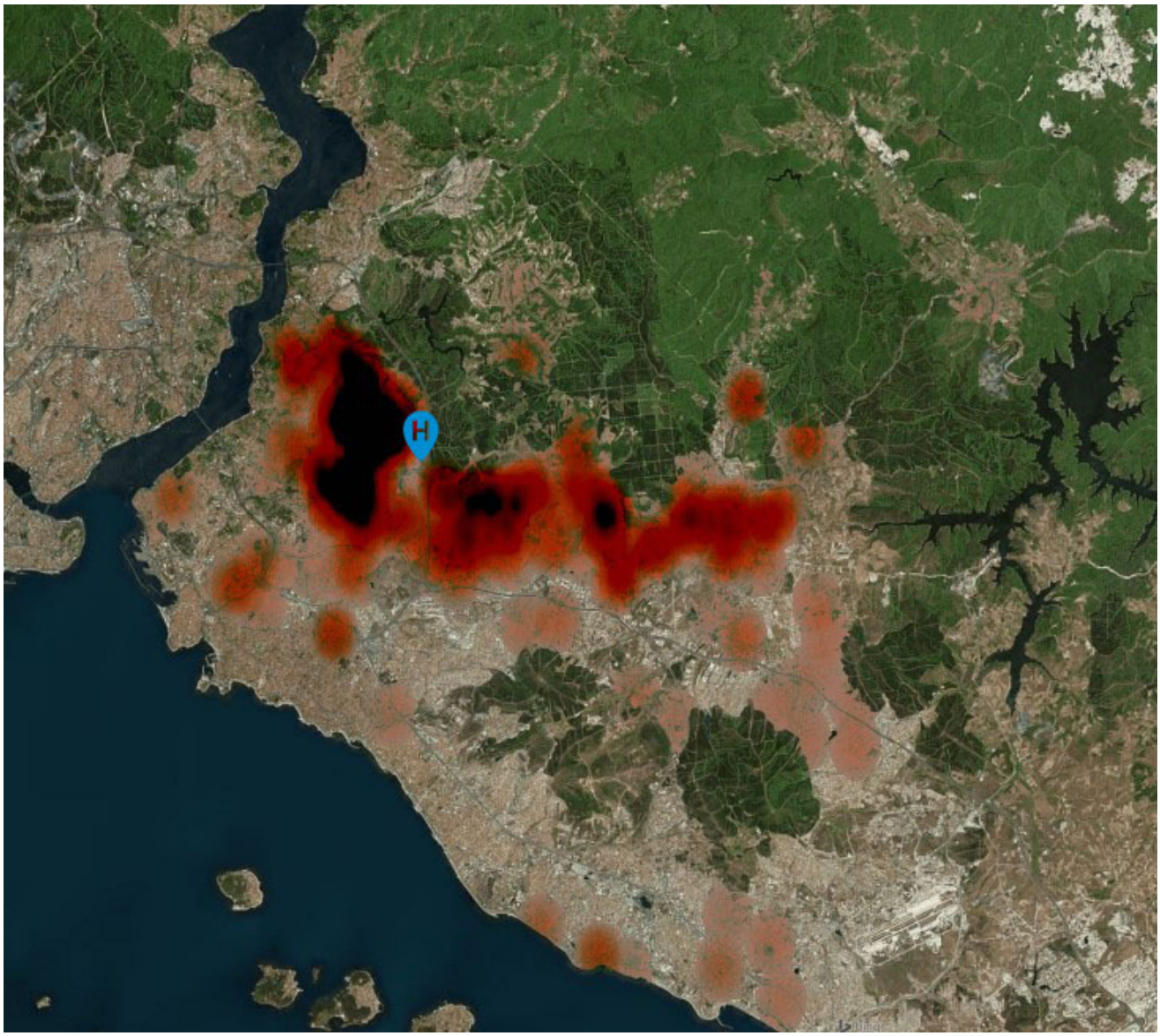

Figure 1. The heat map based on addresses of CO poisoning

epidemiology of this public health challenge and these techniques are instrumental in designing valid observational and analytical studies to more fully study the problem.

Black areas on the first map shows of the most intense of the patients. The fact that this region was close to the hospital where the data was obtained was associated with the single-centered study. We believe that the location of this black region may change in multicenter studies.

In the second map showing COHb levels, the regions with large circles were associated with higher COHb levels. High levels of arterial COHb were associated with increased intensive care mortality[11]. We believe that these regions could be associated with high mortality and morbidity.

In this study we found that the female patient group was more males. Over-exposure of women was consistent with the literature[12-15]. We believe that this is due to the fact that women get time indoor more than men.

The number of cases encountered increases during the winter months because of being in an indoor environment not ventilated enough during the fuel consumption for heating is the most common reason for intoxication[16-19]. We found that during the winter, there were more cases of CO intoxication than during the other seasons.

There are several limitations to our study. Firstly, in some cases, incomplete files or incorrect addresses were noticed. Therefore, we could not evaluate all the patients with CO poisoning. Also, we could not reach the mortality and morbidity data of the patients because of our study was designed retrospectively. Secondly, a usual pitfall of these analyses is that the maps must be corrected by the number of inhabitants in the various areas. Here, as we do not have the spatial repartition of the population, we cannot be sure the increased number of CO poisoning is not simply due to a high number of people living in those areas. Thirdly, the low

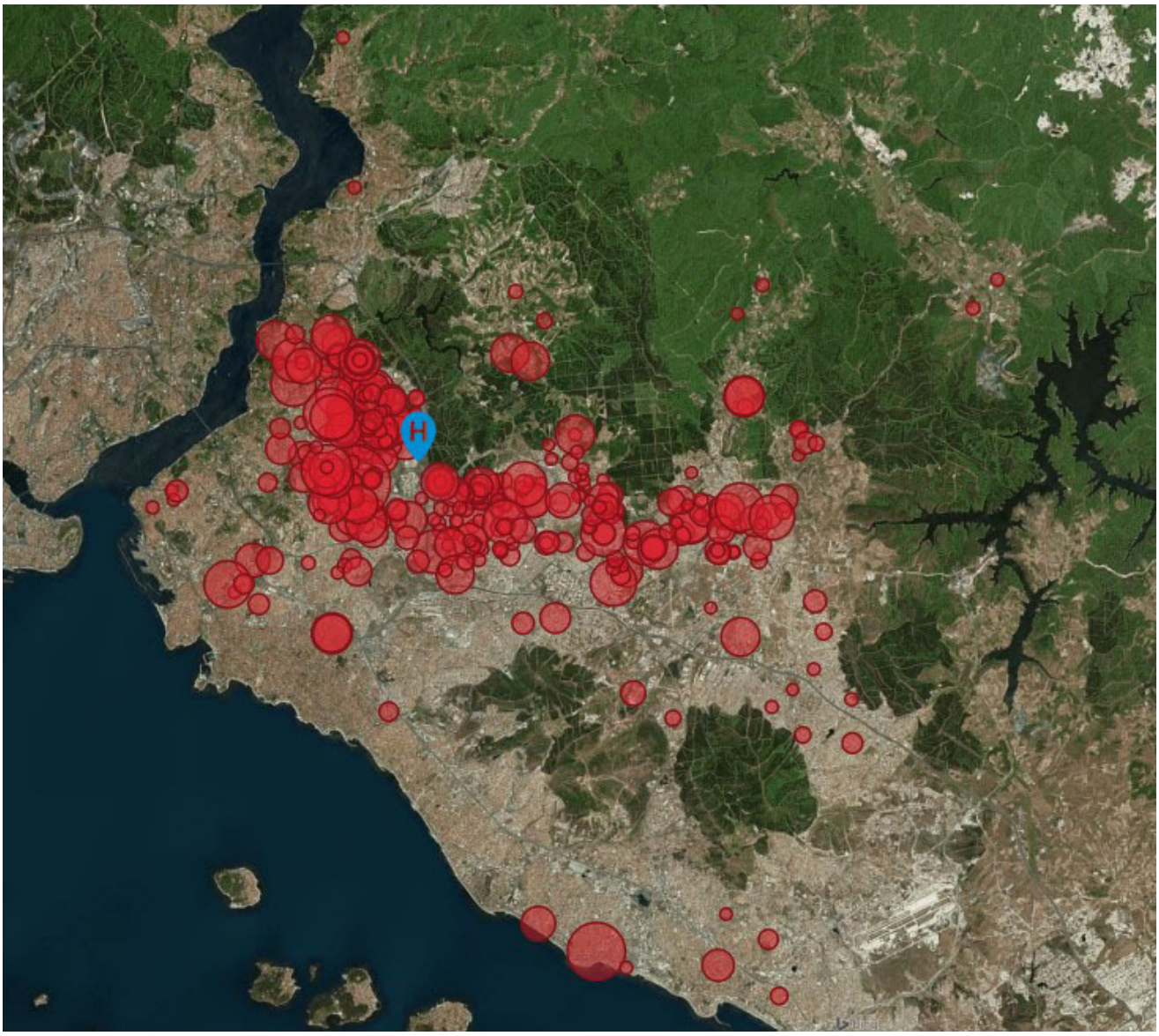

Figure 2. The heat map based on addresses of CO poisoning with COHb levels

number of cases in our study means that the results are limited in terms of generalization and wide applicability. Lastly, this is a single-center study and only shows the patients with CO poisoning coming to a single hospital and only one part of city. Consequently, multi-center studies are needed.

In conclusion, geographical analysis used to explore the possible links between accidents and geographical particularities. In CO poisoning, it may be used to detect the influence of certain area, social categories. Although the spatial analysis and evaluation of a local area has been conducted in our study, extensive studies and analyzes are needed. Multicenter studies with Geographical Information Systems may contribute to the measures to be taken for CO intoxication.

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Original Article

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Retrospective Evaluation of Snake Bites in Eastern Black Sea Region

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Abstract

Objectives: The aim of this study is to review snake bites, which are rarely encountered and thus regionally neglected in Eastern Black Sea Region but which cause potentially serious clinical pictures, in order to provide a better patient management.

Material and Method: In this study, 27 cases who referred to tertiary emergency service due to snake bite were analysed retrospectively.

Results: Of the 27 cases, 70.4%(n=19) were female and average age was found as 46.77±16.11. Referrals were in the month of July when tea and hazelnut farming was frequently done regionally. However, two patients developed syncope and hypotension after admission. The most common complaints of referral were pain (96.3%,n=26), ecchymosis and swelling (88.9%,n=24) due to bite in the lower extremity dorsum of the foot (96.3%,n=26). While 18.5% were referred to our hospital after they were applied antivenom therapy in another health institution, antivenom therapy was applied to 2 patients(7.4%) due to their clinical picture at admission. 29.6% of the patients who referred to the emergency service were followed and treated by being hospitalized. None of the patients admitted with snake bite died. Elevated INR was the most common serious complication with 11.1%(n=3).

Conclusion: Snake bite is a rare situation in Eastern Black Sea region. In cases in the region which is the natural habitat of Vipera kaznakovi, depending on the feature of the venom, hematotoxic complications can occur, local lesions caused by other Viperia species being at the forefront. Appropriate follow-up and treatment should be based on the existing clinical picture.

Key words: snake bite, eastern black sea region, emergency service visit

Özet

Amaç; Doğu Karadeniz Bölgesinde nadir olarak karşılaşılan ancak potansiyel ciddi klinik tablolara neden olan bu durum karşısında daha iyi bir hasta yönetimi sağlanabilmesi için bölgesel olarak ihmal edilen bu durumun gözden geçirilmesini sağlamaktır.

Gereç ve Yöntem: Bu çalışma üçüncü basamak acil servise yılan ısırması nedeniyle başvuran 27 olgu retrospektif olarak incelendi.

Bulgular: Toplam 27 olgunun %70.4'ü (n=19) kadındı ve yaş ortalaması 46.77±16.11 olarak tespit edildi. Başvuru, bölgesel olarak çay ve fındık tarımının sıklıkla yapıldığı Temmuz ayındaydı. Hastaların hepsinin başvuru esnasında genel durumları iyi ve vital bulguları stabildi. Ancak 2 hastada başvuru sonrasında senkop ve hipotansiyon gelişti. En sık başvuru şikayeti alt ekstermite ayak dorsumundaki ısırık nedeniyle (%96.3, n= 26) ağrı (%96.3, n=26), ekimoz ve şişlik (%88.9, n=24) di. Downey ve arkadaşlarının sistemine göre yılan ısırığın ciddiyeti en sık %51.9 (n=14) ile grade 0 olarak değerlendirildi. Olguların %18.5'i başka bir sağlık kuruluşuna başvuru sonrası antivenom tedavi uygulanarak hastanemize yönlendirilmişken 2 hastaya (%7.4) ise başvuru sırasında mevcut klinik tabloları nedeniyle antivenom tedavi uygulanmış. Acil servise başvuran hastaların %29.6'sı yatırılarak takip ve tedavisi düzenlendi. Yılan ısırığı nedeniyle başvuran hastalarda ölümle sonlanım olmamıştır. INR yüksekliği %11.1 (n=3) ile en sık görülen ciddi komplikasyondu.

Sonuç: Doğu Karadeniz Bölgesin de yılan ısırığı nadir bir durumdur. Vipera kaznakovinin doğal yaşam alanı olan bölgedeki vakalarda venomun özelliğine göre diğer Vipera türlerinin neden olduğu lokal lezyonlar ön planda olmak üzere hemototoksik komplikasyonlara da neden olabilir. Uygun takip ve tedavi mevcut klinik tabloya göre düzenlenmelidir.

Anahtar kelimeler: yılan ısırığı, doğu karadeniz bölgesi, acil servis başvuruları

Introduction

In many regions of the world, particularly in subtropical and tropical countries, poisoning from snake bite is an important public health problem[1]. There are more than 600 species of venomous snakes in the world and most of them belong to Elapidae and Viperidae families[2, 3]. In our country, almost all of the poisoning cases belong to Viperidae family (viper snake) and the sub-types show regional differences. For the Eastern Black Sea region, Vipera kaznakovi (Caucasian viper) has been identified as a dangerous sub-type. Especially the structure of the Eastern Black Sea Region has favourable conditions for the life of this species[4].

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Vipera kaznakovi venom is a cocktail rich in protein and peptide toxins with specificity for a wide variety of tissue receptors. With the entry of venom into the body, the clinical picture changes according to the characteristics of the toxin and the local or systemic response of the person to the toxin[5].

The aim of this study is to review snake bites, which are rarely encountered and thus regionally neglected in Eastern Black Sea Region but which cause potentially serious clinical pictures, in order to provide a better patient management.

Materials and Methods

27 patients who referred to Recep Tayyip Erdoğan University Training and Research Hospital Emergency Clinic due to snake bite between 2010 and 2018 were included in this study. The data were collected retrospectively from the hospital data system.

Findings of poisoning were evaluated in all patients. The severity of the reaction was made according to the classification described by Downey et al.[6]. According to this system, stage 0: no local or systemic findings of poisoning, but <2.5 cm swelling and erythema around the tooth marks; stage 1: no systemic findings of poisoning, but swelling and erythema between 2.5-15 cm; stage 2: mild systemic findings with swelling and erythema between 15-40 cm; stage 3: systemic findings with swelling and erythema over >40 cm; stage 4: serious systemic findings accompanied with coma and shock. Demographic and epidemiological characteristics, clinical symptoms and findings, laboratory results, treatment and results were analysed.

The data were analysed by using SPSS for Windows version 17 (SPSS, Chicago, IL, United States). Descriptive statistics were given as average ± standard deviation for metric discrete variables, while they were given as case and percentage for categorical variables.

Results

Demographic and Epidemiological Features: 40.7% (n=11) of the 27 patients who referred due to snake bite between 2010 and 2018 referred in the month of July. The snakes which caused bite were not brought to hospital. However, the snakes were seen and according to the description made, it was estimated that the snakes were Vipera kaznakovi, also called Caucasian viper, located in the region. 40.7% of the patients referred within the first hour after the incident during tea collection procedure in settlements of the city centre in Rize (Table 1).

Anatomical region of the bites was lower extremity dorsum of the foot with a rate of 96.3% (n=26). According to the system of Downey et al. the most common snake bite severity was evaluated as grade 0 with 51.9% (n=14) (Table 2).

Table 1. Demographic Features (n=27)

Gender	Female	19 (70.4%)
	Male	8 (29.6%)
Age	46.77 ± 16.11 (min: 14, max: 87)	
Occupation	Worker	26 (96.3%)
	Student	1 (3.7%)
Place of residence	Rize, City centre	11 (40.7%)
	Artvin, Hopa	6 (22.2%)
	Rize, Kalkandere	2 (7.4%)
Referral to hospital after the incident	Within the first hour	14 (51.9%)
	(min: 1 hour, max: 168 hours)	

Minimum-Maximum (Mean ±Standard Deviation).

Table 2. Severity of the snake bite according to Downey et al.'s system

Stage 0	14 (51.9%)
Stage 1	8 (29.6%)
Stage 2	5 (18.5%)

Symptoms, Clinical Findings and Laboratory Tests: The patients referred to the emergency service most commonly with the complaint of pain (n= 26, 96.3%). Tables 3 and Table 4 show the patients' clinical symptoms, findings, complications and laboratory findings. 59.3% (n=16) of the follow-ups after referral were made in the emergency service of the health institutions the cases referred to. Follow-up period in the hospital varied between 1 and 11 days and the average time was found as 2.77 ± 2.66. 44.4% (n=12) of the patients were followed for one day, 22.2% (n=6) were followed for two days and 3.7% (n=1) patient was followed for 11 days.

Table 3. Clinical Symptoms and Findings

Local	
Tooth mark	22 (81.5%)
Pain	26 (96.3%)
Ecchymosis	24 (88.9%)
Swelling	24 (88.9%)
Paraesthesia	1 (3.7%)
Regional swelling in lymph nodes	9 (33.3%)
Allergic reaction	1 (3.7%)
Systemic	
Nausea	2 (7.4%)
Vomiting	1 (3.7%)
Hypotension	2 (7.4%)
Syncope	2 (7.4%)

Table 4. Complications and Findings Related to Snake Bite

Complications	n (%)
Wound infection	7 (25.9%)
Thrombophlebitis	1 (3.7%)
Compartment syndrome	1 (3.7%)
Laboratory findings	n (%)
Leucocytosis	20 (74.1%)
Thrombocytopenia	1 (3.7%)
Elevated PT/APTT/INR	3 (11.1%)
Elevated urea	5 (18.5%)
Elevated creatinine	2 (7.4%)
Elevated CPK	14 (51.9%)
Elevated SGOT/SGPT	2 (7.4%)
Elevated LDH	17 (63%)
Haematuria/proteinuria	3 (11.1%)

APTT, Activated partial thromboplastin time; CPK, Creatine phosphokinase; INR, International Normalized Ratio; LDH, Lactate dehydrogenase; SGOT, Serum glutamic-oxaloacetic transaminase; SGPT, Serum glutamic-pyruvic transaminase; PT, Prothrombin time

Treatment and Outcome: After the patients were admitted to the emergency service, they were followed in terms of vitals, local, systemic and delayed findings. The wounded extremity was immobilized and rested. The patients were evaluated in terms of tetanus immunization and tetanus prophylaxis was performed on patients if necessary. Depending on the presence of symptom, analgesic, antiemetic, antiallergic and antibiotherapy were applied by taking fluid electrolyte balance and urine output into consideration. Dialysis was not required in any of the patients who were found to have elevated urea and creatinine. No serious coagulation disorder was found.

18.5% of the cases had been referred to out hospital after having been given antivenom therapy in another health institution. Two patients (7.4%) received antivenom therapy at admission due to their existing clinical picture. 29.6% of the patients who referred to the emergency service were followed and treated by being hospitalized. None of the patients admitted with snake bite died.

Discussion

Snake bite is included in the "Neglected Tropical Diseases" which require intervention by the World Health Organization[7]. This situation is not only limited to tropical regions; it is also valid in the Eastern Black Sea Region of our country. When the literature was reviewed, no case series related to snake bites of the region were found.

Geographical structure of Eastern Black Sea Region and the growing areas of main sources of livelihood such as tea and hazelnut create a natural habitat for Vipera kaznakovi. Although snake bites are not very common especially regionally, lack of adequate protective measures in July, which is the period with the highest temperature in tea or hazelnut collection periods, increased exposure. We think that this situation can be evaluated as a professional exposure for the region. In a study Al et al. evaluated snake bites in adults in Southeast Anatolia Region in 2010, snake bites were found to be a professional risk in middle aged individuals[8]. This result is similar to our results.

It was found that 70.4% of the exposed individuals were female. This is due to the fact that female workforce is at the forefront in the agricultural areas which are the main source of income regionally. In studies conducted worldwide, victims were found to be generally adult males[9]. We think that this situation results from the regional differences within the country as well as difference between countries. Although snake bites are seen in all age groups, it was found that average age was 46.77 ± 16.11 (min: 14, max: 87) with a wide range. It is noteworthy that the wide age range in this study is due to the differences between the communities in which other studies are conducted.

Snake venom is a cocktail rich in protein and peptide toxins that are specific for a wide variety of tissue receptors that can cause local and systemic findings[10, 11]. This feature varies according to the type of snake and thus causes the emergence of different clinical pictures. As in other Viperid species, Vipera kaznakovi, which lives in the Eastern Black Sea Region, often causes local reactions such as pain, bruising and swelling and tissue necrosis, coagulopathy, haemorrhage, Rhabdomyolysis and/or acute kidney damage[20]. In the present study, it was found that the patients referred to emergency service within the first hour most frequently with the complaints of pain as a result of bite in lower extremity foot dorsum with a rate of 96.3%. In parallel with the literature[12, 13], in the present series, it was found that all patients were conscious upon admission, while 7.4% of the patients were found to have a tension artery lower than 90/60 mmHg and their vitals were not stable. This is seen as the effect of a protein suppressing the myocardial functions in the venom of some Viperia species[14]. In addition, as an indicator of consumption coagulopathy caused by venom, it was found that INR, PT, APTT values were high in 3 patients and thrombocytopenia was found to develop in one patient. According to the system of Downey et al.[6], the severity of snake bites was evaluated most frequently as grade 0 with a rate of 51.9%. The results found showed similarity with other case series of Viperia species snake bites in terms of both local effects and systemic findings. Although the risk of an individual's being bitten by a snake is low, death rate is high. Traditional treatments such as sucking and cutting are used especially in snake bites in rural areas and most of the time,

these cases die before they reach the hospital. In the present series, 96.3% of the cases occurred during tea collecting in the rural area. However, only 40.7% referred to emergency service from their settlement within the first hour and they received tourniquet, which is a traditional method. Following their admission to the emergency service, the patients were followed in terms of vitals, local, systemic and delayed findings and the affected extremity was immobilized, tetanus prophylaxis was performed to patients who needed tetanus prophylaxis and depending on the presence of symptoms and paying attention to fluid electrolyte balance and urinary output, fluid, analgesic, antiemetic, antiallergic and antibiotherapy were applied. 25.9% of the patients received antivenom therapy in parallel with the literature due to their existing clinical state[15,16]. Antivenom therapy is thought to be unnecessary for all snake bites, and it was applied only on cases when necessary in the present study[17]. Depending on the snake bite, it can cause myonecrosis compartment syndrome which occurs under the influence of venom. Although this is not an actual compartment syndrome, in cases with typical findings, it is necessary to measure the pressure between compartments and to request surgical consultation in case of increase[18, 19]. In this series, compartment syndrome developed only in one case and fasciotomy was applied.

Various complications resulting from systemic involvement and delayed treatment or incorrect applications can cause death[20]. However, none of the patients followed and treated in this series (n= 27) died and all of them were discharged in healthy conditions.

As a conclusion, snake bite can be defined as a rare and neglected situation for Eastern Black Sea region. For this reason, our study was conducted with limited number of cases. In cases in Vipera kaznakovi's natural habitat, systemic complications such as hemototoxic and cytotoxic complications can occur, local lesions caused by other Viperia species being at the forefront. Appropriate follow-up and treatment should be arranged according to the existing clinical picture. We think that this approach can prevent or decrease complications.

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Original Article

Eurasian Journal of Toxicology

Clinics Following Patients' Suicide Attempt, Consultations Performed, and the Role of the Emergency Departments

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Abstract

Objectives: Intervention of patients after suicide attempt requires a multidisciplinary approach. Today, the treatment and follow-up of this patient group is mostly carried out in emergency departments and intensive care units. In this study, it was aimed to evaluate the consultations and follow-up clinics of the patients with suicide attempt.

Materials and Methods: Patients over 16 years of age who applied to our emergency department between January 2014 and January 2017 due to suicide attempt were examined prospectively.

Results: A total of 426 patients were included in this study. 285 (66.9%) of the patients included in the study were hospitalized and followed up in the emergency room. Psychiatric consultation was requested for 404 patients (94.8%) who were conscious and did not need urgent operation.

Conclusion: Emergency departments, psychiatry clinics, and surgical clinics, especially in patients requiring traumatic intervention, played an important role in the treatment of patients presenting with suicide attempt. Therefore, we think that developing and preparing the relevant clinics for the management of this patient group will increase the quality of care.

Keywords: emergency department; consultations; suicide attempt

Özet

Amaç: İntihar girişimi olan hastaların bakımı multidisipliner bir yaklaşım gerektirir. Günümüzde bu hasta grubunun tedavi ve takipleri büyük bir oranda acil servislerde ve yoğun bakım ünitelerinde yapılmaktadır. Biz bu çalışmamızda intihar girişimi ile hastanemiz acil servisine başvuran hastaların takip ve tedavilerinin hangi kliniklerde yapıldığını, acil serviste yapılan konsultasyonlarını incelemeyi amaçladık.

Gereç ve Yöntem: Acil servisimize Ocak 2014 - Ocak 2017 tarihleri arasında intihar girişimi sonrası başvuran 16 yaşından büyük hastalar prospektif olarak incelendi.

Bulgular: Toplam 426 hasta çalışmaya dahil edildi. Hastaların 285'i (%66,9) acil serviste gözlem odasında yatırılıp takip edildi. Şuuru açık ve acil operasyon ihtiyacı olmayan 404 hastaya (%94.8) psikiyatri konsültasyonu yapıldı.

Sonuç: İntihar girişimi ile başvuran hastaların tedavisinde acil servislerin, psikiyatri kliniğinin ve özellikle travmatik girişim varsa cerrahi servislerin önemli rol oynadığı görüldü. Bu nedenle ilgili kliniklerin bu hasta grubunun yönetimi için geliştirilmesinin ve hazır hale getirilmesinin bakım kalitesini arttıracağını düşünmekteyiz.

Anahtar kelimeler: acil servis; konsultasyonlar; intihar girişimi.

Introduction

Suicide is an important public health problem[1]. According to the data of the World Health Organization, one of the ten leading causes of death in developed countries is suicide attempts[2]. Patients with suicide attempt are a group of patients that require a multidisciplinary approach. Today, their treatments and follow-ups are mostly done in emergency departments and intensive care units[3]. Considering that most of the patients were taken to the hospital with the need for urgent care, it is understood how important this situation is for the emergency services[4].

Suicide attempts are an important problem for emergency services. Suicide, defined as the voluntary ending of a person's life. It accounts for about 95% of all cases of poisoning. Suicides are one of the most important causes of death in psychiatric illness[5,6].

Apart from the emergency room, there is a need for surgical clinics, psychiatry clinics and intensive care units. In suicide attempts with traumatic methods, surgical services are needed especially for patients in cases such as hanging, self-mutilation by cutting-piercing tools, jumping from high places and firearm suicide, and intensive care units are

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needed for cases of high risk of life[7]. These clinics are activated bye the emergency room physicians with a consultation request. And also these clinics play a major role in the interventions of patients presenting with a suicide attempt. The beginning of psychiatric services is also performed in emergency departments in patients who are conscious and do not require urgent surgical intervention[8,9].

In this study, we aimed to investigate in which clinics the follow-up and treatment of patients who applied to the emergency department of our hospital with suicide attempt. We also aimed to evaluate consultations that were requested from the emergency room for these patients.

Materials and Methods

Patients over the age of 16 who were admitted to our emergency department between January 2014 and January 2017 after a suicide attempt were evaluated prospectively. Consultations and follow-up clinics were examined. Patients age, consulted clinics and outcome data about hospitalization status are recorded.

Patients were also asked for consultation in the emergency room such as psychiatry, general surgery, neurosurgery, thoracic surgery, cardiovascular surgery, internal medicine, cardiology, orthopedics, gynecology, anesthesia intensive care, and neurology. Patients hospitalized in these units were taken as "lay out of emergency"in our study. The follow-up and treatment of patients in the emergency room was carried out after the first inspection in the observation room with monitor.

Statistical Package for Social Sciences (SPSS.20) package program was used for statistical analysis. Paired-sample t test was used to compare dependent variables with normal distribution. For other analyzes, chi-square test wasused. All data wereexpressed as mean ± standard deviation and p <0.05 value was considered statistically significant.

Results

A total of 450 patients applied to the emergency department with a suicide attempt. 24 patients were excluded from the study (10 patients are under 16 years old, 14 patients have missing data). A total of 426 patients were included in the study. The number of patients followed in the emergency room observation unit is 285 (66.9%), and the number of patients hospitalized and followed in the lay out of emergency are 141 (33.1%).

The patients were classified according to the hospitals and consultations. While the number of patients who applied with nontraumatic methods (drug drinking and gas inhalation) as a suicide method was 408, and the number of patients who applied with traumatic methods (hanging, self-mutilation by cutting-piercing tools, jumping from high places and firearm suicide) was evaluated as 18.

Considering the services that patients who applied with suicide attempt were generally hospitalized or treated, it was seen that more than half of them were followed up in the emergency department. The clinics of patients admitted with suicide attempt are shown in Table 1.

Table 1. Clinics where patients admitted with suicide attempt

	Patient number	Percentage (%)
Clinics		
Emergency Medicine	285	66,9
Internal Medicine	74	17,4
Intensive Care	9	2,1
Psychiatry	19	4,5
Other	13	3,1
Cardiology	3	0,7
Thoracic Surgery	2	0,5
Neurosurgery	2	0,5
General Surgery	8	1,9
Gynecology	2	0,5
Anesthesia	2	0,5
Orthopedics	5	1,2
Cardiovascular Surgery	1	0,2
Total	426	100

The hospitalization status to the emergency clinics was statistically significant compared to other departments (p <0.05). Psychiatric consultation was performed on 397 of the patients. There are 29 patients who can not have psychiatric consultations. Psychiatry consultation could not be done because these patients were unconscious and had a general condition or had an emergency operation. As 24 of the patients were pregnant and an obstetrics and gynecology clinic consultation was performed. Suicide attempt with traumatic methods is the priority of consultation of surgical clinics to patients. Consultations in emergency departments are summarized in Table-2.

Table 2. Consultations made in emergency departments

Consultation Clinics	Number of Consultations
Internal Medicine	100
Intensive Care	22
Psychiatry	397
Cardiology	9
Thoracic Surgery	13
Neurosurgery	24
General Surgery	13
Gynecology	24
Anesthesia	5
Orthopedics	16
Cardiovascular Surgery	8
Neurology	9

Discussion

In our study, it is seen that emergency services have an important role in the follow-up and treatment of patients who applied with suicide attempt. In cases of suicide attempt with traumatic methods, surgical clinics have an important place. A total of 66.9% (n = 285) of the patients were treated in the emergency department.

In our hospital, it was observed that most of the patients were followed up in emergency departments, and patients who attempted suicide by trauma went to surgical clinics. Most of the patients were conscious and their general condition was moderate. It is seen that patients who are admitted with suicide attempt are followed up and especially emergency services play an important role in the follow-up of these patients besides diagnosis and first intervention. Physicians working in the emergency units have sufficient theoretical and practical equipment. This may explain the reason for the high rate of hospitalization in our study.

The most common method of suicide is drug intake[10]. In our study, the number of patients who admitted to drug use and gas inhalation with non-traumatic methods as a suicide method was 408, and the number of patients who presented with traumatic methods, injuries, firearms and cutting tools, and jumping from a high place is 18. The majority of patients who attempted suicide by traumatic methods were hospitalized in non-emergency departments 33.1% (n = 141).

Assessment of risk factors of patients coming with suicide attempt by emergency doctors are important in reducing recurrent interventions[11]. It is important for patients who are admitted to the intensive care units and other clinics to be consulted with psychiatry after medical and surgical treatments after the first intervention performed in the emergency department. Mental disorders rank first among risk factors that increase suicide attempt.Whether or not suicide attempt results in death, it causes serious psychological problems[12].

Emergency medicine systems should be analyzed well in order to provide the most effective and efficient presentation of emergency services. Keeping the records in digital and shareable systems will lead to future studies and increase the quality of emergency medical services[13].

Conclusions

It was observed that emergency services, psychiatry and especially surgical services played an important role in the treatment of patients presenting with suicide attempt. Therefore, we think that the development of these departments related to this patient group and a good psychiatric follow-up will increase the quality of care. It was seen that emergency departments had more role than expected in the follow-up and treatment of these patients. Since suicide attempts and especially intoxications related to drug use are always a medical problem, emergency services should have sufficient knowledge and equipment.

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Case Report
Eurasian Journal of Toxicology

Varfarin Doz Aşımına Bağlı Kanamalarda Hızlı ve Etkin Bir Tedavi Yöntemi: Plazma Kompleks Konsantresi

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Abstract

A 81 years old female presented with weakness, anorexia and black colored defecating. She uses warfarin for 5 years because of prosthetic heart valve. On clinical examination she had hypotension and melena. Blood tests revealed Hemoglobin: 5,14 g/dl and INR:12,08. Vitamin K, Prothrombin complex concentrate and Proton pomp inhibitor was given as treatment in emergency service. The patient hospitalised in intensive care unit for further examination and treatment. Next day blood tests revealed Hemoglobin: 8,84 g/dl and INR:3,83. The patient with no active bleeding focus on gastroscopy and with no decrease in hemoglobin tests discharged from hospital on 2nd day of hospitalization. Low-molecular-weight heparin treatment started.
Warfarin is a drug that still needed for treatment of atrial fibrillation, mechanical heart valves, protein c-s deficiency and antiphospholipid antibody disease. Common pathology of these diseases is predisposition to embolism and thrombus formation. In the emergency services, we need to make decisions according to the patient while treating patients who have warfarin overdose bleeding. On the one hand to stop the bleeding to ensure the patient's hemodynamics, on the other hand, the risk of thromboembolism caused by the use of warfarin should not be ignored. Therefore, it is necessary to reduce the current INR level to the targeted INR level as quickly and safely as possible. In conclusion, we suggest that a timely and protocol-based approach to treat coagulapathy in patients with trauma and drug-induced coagulapathy may improve patients' prognosis.

Key words: acute bleeding, emergency service, warfarin overdose

Özet

81 yaşında kadın hasta halsizlik, iştahsızlık, siyah renkte dışkılama şikâyeti ile acil servise başvurdu. Protez kalp kapağı nedeniylede 5 yıldır varfarin kullandığı öğrenildi. Hipotansif olan hastanın rektal tuşesinde melena vardı. Hastanın kan tetkiklerinde Hgb: 5.14g/dl, INR: 12.08 tespit edildi. Hastaya acil serviste tedavi olarak K vitamini, plazma kompleks konsantresi, ve proton pompa inhibitörü uygulandı. İleri tetkik ve tedavi amacıyla yoğun bakıma yatırılan hastanın ertesi günkü kan tetkiklerinde Hgb: 8.84g/dl, INR: 3,83 tespit edildi. Gastroskopisinde aktif kanama odağı tespit edilmeyen ve hemoglobin değerinde düşme olmayan hasta hastaneye yatışının 2. gününde düşük molekül ağırlıklı heparin tedavisine başlanarak taburcu edildi. Varfarin; atrial fibrilasyon, mekanik kalp kapağı kullanımı, protein C-S eksikliği ve antifosfolipid antibody hastalığı gibi durumlarda halen kullanımına ihtiyaç duyulan bir ilaçtır. Endike olduğu durumların ortak patolojisi trombüs oluşumuna ve embolilere aşırı yatkınlıktır.
Acil servislerde varfarin doz aşımına bağlı kanaması olan hastalara müdahale ederken hastaya ve ihtiyaçlarına göre karar vermek gerekir. Bir taraftan hastanın hemodinamisini sağlamak için kanamayı durdurmak diğer taraftan da varfarin kullanımına neden olan altta yatan nedene bağlı tromboemboli riskini göz ardı etmemek gerekir. Bu nedenle mevcut INR seviyesini hedeflenen INR seviyesine mümkün olan en hızlı ve en güvenli şekilde indirmek gerekmektedir. Sonuç olarak travma ve ilaca bağlı koagülopatili hastalarda bu durumu düzeltmek için zamanında ve protokollü yaklaşımın hastaların prognozlarını iyileştirebileceğini düşünmekteyiz.

Anahtar kelimeler: acil servis, akut kanama, varfarin dozaşımı

Giriş

Varfarin, yaygın şekilde kullanılan bir antikoagülandır. K vitaminine bağlı faktörleri inhibe ederek etkiyen varfarinin güvenlik aralığı oldukça dardır. Uygun doz takibi için uluslararası normalize oran (INR) kullanılır ve doz aşımına bağlı en sık karşılaşılan komplikasyonu kanamadır. Varfarin doz aşımına bağlı kanamalar erken ve doğru müdahale edilmediğinde ise hayatı tehdit edici olabilir.

Acil servislerde varfarin doz aşımına bağlı INR yüksekliği olan hastalarla sıkça karşılaşılmaktadır. Acil hekimi varfarin kullanan hastada mevcut INR seviyesini ihtiyaç duyulan seviyeye hangi tedavi yöntemleri ile indirebileceğini ve kanaması olan kritik hasta yönetimini bilmelidir. Bu olguyu sunmaktaki amacımız varfarin doz aşımına bağlı kanaması olan bir hastanın yönetiminden edindiğimiz tecrübeyi paylaşarak varfarin intoksikasyonlarıyla ilgili güncel literatür eşliğinde farkındalık oluşturmaktır.

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Olgu Sunumu

81 yaşında kadın hasta halsizlik, iştahsızlık, siyah renkte dışkılama şikâyeti ile acil servise başvurdu. Anamnezinde şikayetlerinin 3 gündür devam ettiği, uygunsuz antibiyotik ve ağrı kesici kullandığı, protez kalp kapağı nedeniylede 5 yıldır varfarin kullandığı öğrenildi. Vital bulgularında tansiyon arteriyel:60/40mmHg, nabız:102 atım/dk idi. Fizik muayenede cilt soluktu, akciğerlerde dinlemekle ronküsler mevcuttu, rektal tuşesinde melena tespit edilen hastanın genel durumu ortaydı. Hastanın kan tetkiklerinde Hgb: 5.14g/dl, Hct: %17.4, platelet: 551000µL, Ptz: 123.8sn, Aptt: 100.4sn, INR: 12.08 tespit edildi. Varfarin alımı durdurulan hastaya tedavi olarak K vitamini 1 mg iv infüzyon, plazma kompleks konsantresi (PCC) 40mg iv infüzyon ve proton pompa inhibitörü (PPI) 80mg iv puşe uygulandı. Bir saat sonra kontrol amaçlı alınan kan tetkiklerinde Ptz: 21.5sn, Aptt: 36.5sn, INR: 1.89 ölçüldü. İleri tetkik ve tedavi amacıyla yoğun bakıma alınan hastaya 3 ünite eritrosit infüzyonu ile birlikte 10mg/saat PPI infüzyonu başlandı. Ertesi günkü kan tetkiklerinde Hgb: 8.84g/dl, INR: 3,83 tespit edildi. Gastroskopi uygulanan hastada aktif kanama odağı tespit edilmedi, takibinde Hgb: 9.5g/dl Hct: %31.2 olan hastanın hemoglobin değerlerinde düşüş olmadı. Düşük molekül ağırlıklı heparin tedavisine başlanan hasta hastaneye yatışının 2. gününde şifa ile taburcu edildi.

Tartışma

Varfarin; atrial fibrilasyon, mekanik kalp kapağı kullanımı, protein C-S eksikliği ve antifosfolipid antibody hastalığı gibi durumlarda halen kullanımına ihtiyaç duyulan bir ilaçtır. Endike olduğu durumların ortak patolojisi trombüs oluşumuna ve embolilere aşırı yatkınlıktır.

Acil servislerde varfarin doz aşımına bağlı kanaması olan hastalara müdahale ederken hastaya ve ihtiyaçlarına göre karar vermek gerekir. (Tablo 1) Bir taraftan hastanın hemodinamisini sağlamak için kanamayı durdurmak diğer taraftan da varfarin kullanımına neden olan altta yatan nedene bağlı tromboemboli riskini göz ardı etmemek gerekir. Bu nedenle mevcut INR seviyesini hedeflenen INR seviyesine mümkün olan en hızlı ve en güvenli şekilde indirmek gerekmektedir.

Varfarin doz aşımına bağlı INR yüksekliğinin tedavisinde dikkat edilmesi gereken bir durum da rebound INR yükselmesidir. Kan dolaşımındaki varfarinin yarılanma ömrü 44 saate kadar uzayabilmektedir, K vitamininin yarılanma ömrü ise varfarinin yarılanma ömründen kısadır[2]. Özellikle INR değeri 7'nin üzerinde olan asemptomatik veya orta dereceli kanaması olan hastalarda 18- 24 saat sonra K vitaminin tekrar dozları gerekebilir[4]. Bizim sunduğumuz vakada K vitamininin ek dozlarının yapılmasının rebound INR yükselmesini önleyebileceğini düşünmekteyiz.

K vitamini, taze donmuş plazma (TDP), PCC ve rekombinant faktör VIIa koagülopatiyi düzeltmek için kullanılabilecek tedavi seçeneklerindendir. Travma ve ilaca bağlı koagülopatili hastaların müdahalelerinde ise koagülopatiyi düzeltmek için zamanında ve protokollü yaklaşım hastaların prognozlarını iyileştirebilir[1]. Biz de PCC'nin aktif kanaması olmayan fakat varfarin kullanımına bağlı INR yüksekliği olan ve acil cerrahi veya girişimsel işlem gereken hastalarda zaman kazandırabileceğini düşünmekteyiz.

Varfarin kullanan hastalarda kanama riski, INR değerinin yüksekliği ile birlikte artmaktadır. Çeşitli ilaçlar, vitaminler, gıdalar ve bitkisel ürünler varfarin ile etkileşime girerek ilaç dozuna etki edebilir veya kanama riskini artırabilir. Bu nedenle varfarin kullanan hastalar iyi bilgilendirilmeli gerekirse sıkı INR kontrolüne tabi tutulmalıdır. Acil servislerde de varfarin etkisini uzatan ilaç kullanımına sekonder INR yüksekliği ve kanamaya sıkça rastlanmaktadır. Acil servis hekimlerinin varfarin kullanan hastalarda ilaç seçimine dikkat etmesi gerekli hallerde olası kanama riski ve varfarin doz ayarı için hastayı bilgilendirmesi gerekmektedir. Bizim

Tablo 1: Varfarin toksisitesine bağlı acil tedavi yaklaşımı

INR	Kanama durumu	Varfarin kullanım önerisi	Ek tedavi önerisi
<5	yok	Sıradaki 1 dozu atla	yok
5-9	yok	Sıradaki 1-2 dozu atla	K vitamini 1-2.5 mg p.o
9<	yok	İlacı kes	K vitamini 1-2.5 mg p.o
Seviye belirtilmeksizin	var	İlacı kes	K vitamini 10 mg iv yavaş infüzyon + TDP 10-15 mg/kg ya da PCC

TDP: Taze donmuş plazma
PCC: Plazma kompleks konsantresi

sunduğumuz vakada da hastanın düzensiz sıklıkta non-steroid antiinflamatuar (NSAI) ilaç kullanım öyküsü mevcuttu. NSAI'ler gastrointestinal sistem kanamasını bu sistem içerisinde oluşturduğu ülsere lezyondan yapabileceği gibi INR seviyesini artırarak da kanamaya neden olabilir.

Sonuç

Sonuç olarak acil serviste varfarin kullanımına bağlı INR yüksekliğinin tromboembolik hadiselerin de riski göz önüne alınarak tedavisi gerekmektedir. Bu tedavi sırasında rebound INR yüksekliğinin unutulmaması gerekmektedir. Varfarin kullanan hastalarda ilaç önerirken doz etkileşimleri hatırlanmalı ve hastaya mutlaka güncel protokoller ile yaklaşımda bulunulmalıdır.

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Case Report
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Intravenous Lipid Emulsion Treatment in The Verapamil Intoxication

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Abstract

The use of intravenous lipid emulsion therapy (ILE) as an antidote in toxicology has become an increasingly popular in recent years. In pediatric age group, the reported number of cases treated with ILE is very low. Successful results have been reported with ILE therapy in tricyclic antidepressant, verapamil, and beta blocker poisonings in cases that are not responsive to the standard treatment methods. In this article, we present a clinical and laboratory finding of a case that did not respond to standard treatment and was successfully treated with ILE therapy.

Key words: child, verapamil, intoxication, intravenous lipid emulsion

Özet

Toksikolojide bir panzehir olarak intravenöz lipid emülsiyon terapisinin (ILE) kullanımı son yıllarda giderek daha popüler hale gelmiştir. Pediatrik yaş grubunda, ILE ile tedavi edilen bildirilen vaka sayısı çok düşüktür. Standart tedavi yöntemlerine yanıt vermeyen trisiklik antidepresan, verapamil ve beta bloker zehirlenmelerinde ILE tedavisi ile başarılı sonuçlar bildirilmiştir. Bu yazıda, standart tedaviye yanıt vermeyen ve ILE tedavisi ile başarılı bir şekilde tedavi edilen bir olgunun klinik ve laboratuvar bulgusunu sunuyoruz.

Anahtar kelimeler: pediatri, verapamil, zehirlenme, intravenöz lipid emülsiyon

Introduction

Verapamil is a potent calcium channel blocker (CCB) used in the treatment of various cardiovascular diseases such as hypertension, cardiac arrhythmias and angina[1]. Its effect is demonstrated by inhibiting L-type calcium channels in the heart and vascular smooth muscle. In verapamil intoxication, clinical conditions such as bradycardia, metabolic acidosis, hypotension, conduction defects and shock may occur. Treatment is based on the reduction of drug absorption, supportive care and stabilization of cardiac functions[2]. There have been many studies showing the efficacy of lipid emulsion therapy in the overdose of verapamil[3,4].

The use of intravenous lipid emulsion therapy (ILE) as an antidote in toxicology has been an increasingly popular issue in recent years. It has been reported in animal trials and case reports that ILE is a successful antidote for cardiac side effects of drugs such as verapamil, beta blocker, and tricyclic antidepressant[5-7]. In this case report, we aimed to share a case of verapamil intoxication with resistant bradycardia and hypotension within the scope of relevant literature

Case Report

A 16-year-old woman ,weighing 64 kg, ingested 2880 mg of sustained release verapamil-active drug in a suicide attempt. The patient was taken to the nearest health center with complaints of nausea, vomiting and malaise in 30 minutes after taking the drug.

In the health center, a nasogastric tube was inserted and gastric lavage and active charcoal were performed. After developing bradycardia and hypotension, the patient was transferred to our intensive care unit for follow-up and treatment. In the initial evaluation of the case, the patient's fever was 37° C, blood pressure (BP) was 90/60 mm Hg, heart rate (HR) was 60 / min, and peripheral oxygen saturation (SpO2) was 96%. During the physical examination (PE), it was seen that the patient's general condition was moderate, she was conscious, heart sounds were rhythmic, lung sounds were normal, had no organomegaly, and Glasgow Coma Score (GCS) was 14. Hemogram and biochemical tests did not show any features. Electrocardiography (ECG) showed sinus bradycardia (Fig. 1). The blood gas was evaluated as normal. The patient received 0.5 g / kg of activated

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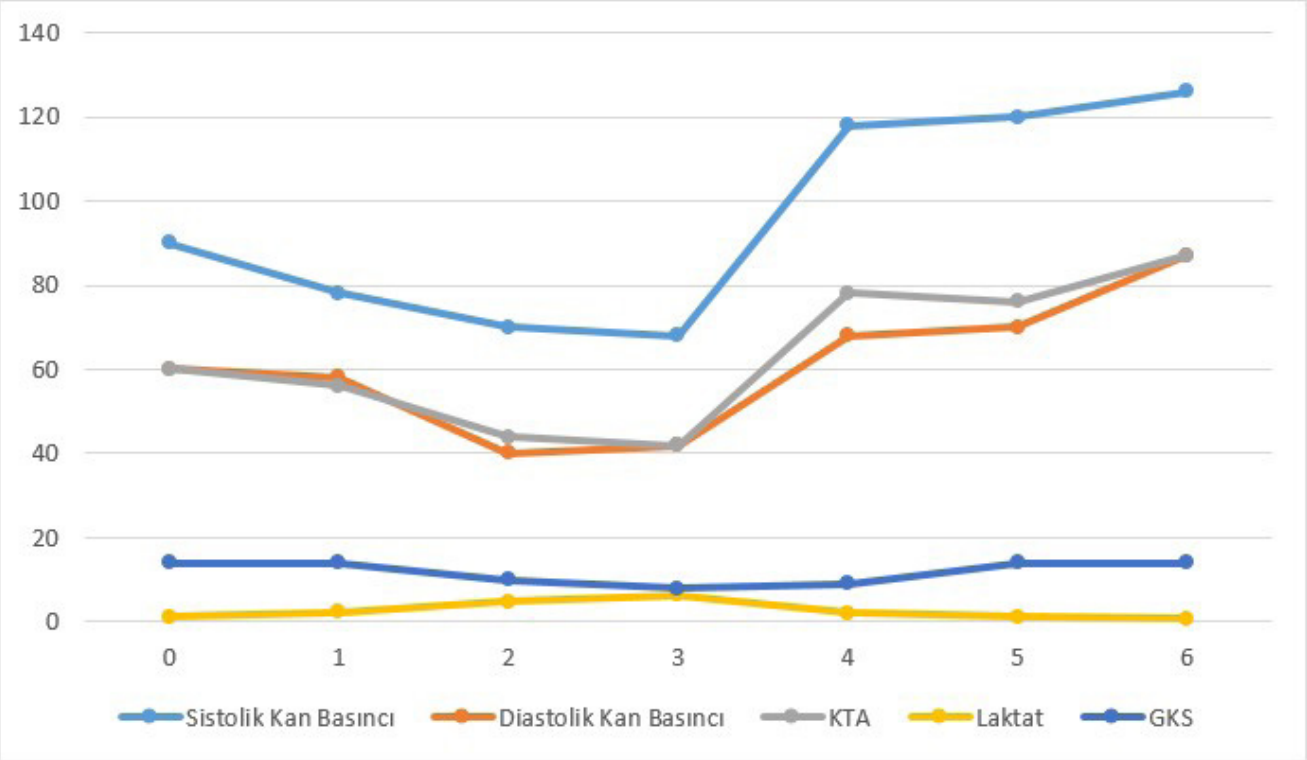
Grafik 1: Hastanın yoğun bakım takipleri



charcoal and fluid support, ECG monitoring and close haemodynamic follow-up were conducted.

During the second hour of follow-up, intravenous calcium, fluid and dopamine treatment were given to the patient with blood pressure (BP): 70/40 mm Hg and HR: 44 / min. Neuroadrenaline and adrenaline therapy were initiated in patient with hypotension and bradycardia. At the third hour of the follow-up, the patient's blood gas pH was 7, 24, PaO2 was 92 mmHg, PaCO2 was 56 mmHg, HCO3 was 14.3 mmol / L, BE was -13.5, and lactate was 6.3 mEq. As confusion occurred and GCS was 8, the patient was intubated (Figure 1).

At the same time, hyperinsulin / euglycemia (HIE), glucagon and ILE therapy were started, respectively. A 1.5 ml / kg 20% lipid emulsion, iv bolus for 1 minute followed by a 0.25 ml / kg / min 30 minute infusion was started to the patient who did not respond to initial treatment. In approximately 10 minutes, the pulse rate and blood pressure values attained normal levels and the ECG returned to normal sinus rhythm. The inotropic support of the patient was reduced and cut at the 24th hour because the patient reached normal blood pressure and pulse rate. The patient was extubated. The patient whose cardiac evaluation was normal without complication on follow-up was discharged on the 4th day.

Discussion

Verapamil, a lipophilic calcium channel blocker, reduces the level of cytosolic calcium by inhibiting voltage-dependent L-type calcium channels found in the smooth muscle of the myocardium and veins and reducing calcium entry into these cells. Verapamil has the most potent negative inotropic effect among CCB. Cardiotoxic effect of verapamil overdose may cause more deaths than all other CCBs. In a study conducted in the United States in 2004, 10513 high-dose calcium channel blocker cases were identified. 5202 of those were high-dose verapamil, and 356 had major toxic effects[8].

Intoxication usually starts at 1-5 hour after ingestion of the drug, while it might be up to 48-72 hours in slow-release formulations[9]. In verapamil intoxication, cardiovascular, gastrointestinal, central nervous system related and metabolic effects can be seen. Treatment is based on reduction of drug absorption, supportive care and stabilization of cardiac functions[10]. When its effect on the cardiovascular system is examined, bradycardia and hypotension are the most common findings[9]. Findings of central nervous system include vertigo, confusion, hallucinations, epileptic seizures, and coma. In the onset of neurological symptoms, direct toxic effects have also been observed although cerebral hypoperfusion has been mainly considered[10].

Metabolic acidosis and hyperglycemia are the most common metabolic effects. Hypoperfusion occurs elevation of lactate level in resulting metabolic acidosis. In this case, blood gas analysis revealed that metabolic acidosis developed with lactate elevation. No response to advanced cardiac life support theraphy that was received, hypotension

and bradycardia continued, and there was a consciousness change and a decrease in GCS, which was thought to be due to decreased cerebral perfusion.

There are two hypotheses related to the ILE mechanism. In 1998, Weinberg et al. argued that the ILE formed a separate compartment for drugs after being intravenously injected. This mechanism is referred to as the Lipid Sink Theory and is still considered the most valid opinion[5]. Ion Channel Theory is an alternative theory that was put forward in the following years. In these studies, it was claimed that ILE increased myocardial energy substrates and high-energy phosphate content in the heart, or triglyceride levels increased the calcium level through calcium ion channels in cardiomyocytes[11]. Sirianni (2008) was the one clinically using lipid emulsions on a 17-year-old girl in whom cardiac arrest developed after taking bupropion and lamotrigine and no response to advanced cardiac life support therapy was received. She was treated successfully with ILE therapy [7]. Reported ILE treatment in pediatric age group is relatively small. Hendron et al. successfully used the ILE therapy on a 20-month-old girl who took high-dose tricyclic antidepressant, was unresponsive to standard treatment, and had resistant convulsions and ventricular tachycardia. She had no complication and was discharged on the 3rd day without sequelae[12]. Levine et al. applied ILE therapy in addition to standard treatment to a 13-year-old female patient who took high-dose amitriptyline, developed seizure, and then ventricular tachycardia and arrest. She was discharged on the 28th day without sequelae[13]. Our patient who developed severe hypotension and bradycardia after taking high dose verapamil and was non-responsive to standard treatment was successfully treated with ILE therapy, and cardiac functions improved. She was discharged on the 4th day of follow-up without sequelae.

Despite the widespread use of ILE, no standard dose proposal is available. There are different opinions about the subject: some publications suggest infusion after the dose to be given as bolus; while others suggest only low-dose and relatively long-standing infusions[14, 15]. In pediatric age group intoxication, the same indications as the adult and the same treatment doses are recommended as a treatment. In this case, 1.5 mL / kg of 20% lipid emulsion was applied as iv bolus for 1 minute followed by 0.25 mL / kg / min for 30 minutes infusion.

The most important and frequent problem caused by the use of ILE as an antidote is that excessive amounts of triglyceride prevents serum laboratory analysis and causes allergic reaction, acute lung injury, pancreatitis, and venous thromboembolism. Levine et al.[13] reported a case of pancreatitis after ILE. Nonetheless, there was no complication after ILE application in our case.

In conclusion, the use of intravenous lipid emulsion therapy for lipophilic drug intoxication has become an increasingly popular in recent years. In pediatric age group intoxication, the same indications as the adult and the same treatment doses are recommended as a treatment. Clinicians should be aware of these treatment indications, treatment doses, possible complications and side effects, and should consider ILE treatment as an alternative treatment method in cases that do not respond to standard treatments.

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