Yeni antidotlar ve İntralipid uygulamalarında güncel durum

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Acil Tıp Kliniği

Sunu Planı

I. Antidot Tanımı
II. Tarihcesi
III. Yeni Antidotlar
IV. İntralipid uygulamalarında güncel durum

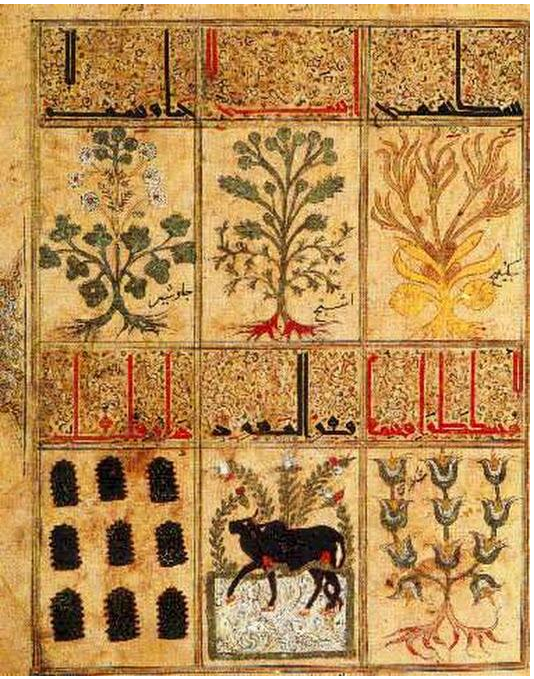
tiryāk "afyon/ ilaç
tiryākī "afyonkeş“

Antidot (Tiryak)

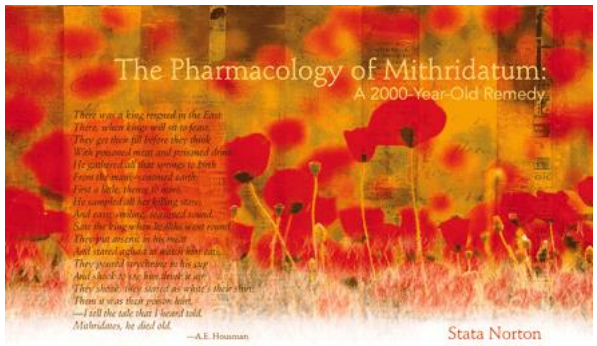
- Panzehir/ Yetim ilaç:

Zehrin etkisini azaltan, etkisini tersine çeviren maddeler 200 MS

Bergamalı Galen



70’den fazla madde içeren Tiryak (antidot)
•Horozlarda çalışma
•Yılan ısırığı sonrası Tiryak verilen horozlar yaşarken verilmeyenler hızla ölmüş



Antidot

Zehiri ;

- etkisizleştiren
- etkisini önleyen
- etkisini azaltan madde

- İdeal antidot
- Hiçbir toksik etkiye sahip olmamalı
- Zehirlenme etkenine özgül olmalı
- Ucuz ve kolay ulaşılabilir olmalı

Zehirlenme Sıklık

- Amerika birleşik devletleri:
- Yılda 3 milyon vaka / : Nüfusun% 1’i-

- ölümcül zehirlenme: 600 / yıl
- 10 000 zehirlenme'de 2 ölüm

Sınıflandırma

4 ana grup

1) kimyasal antagonistler

2) fizyolojik antagonistler

3) farmakolojik antagonistler

4) metabolizma düzeyindeki antagonistler

Kimyasal antagonistler

Zehir	Antidot
Civa, arsenik, bizmut, Kadmiyum	Dimerkaprol
Kurşun	Kalsiyum disodyum EDTA, penisilamin,dimerkaprol
Demir bileşikleri	Desferrioksamin(deferoksamin)
Bakır ve altın bileşikleri	Penisilamin
Heparin	Protamin sülfat
Asetaminofen(parasetamol)	N-asetilsistein
Nitroprusiyat	Hidroksikobalamin

Fizyolojik Antagonistler
(zıt yönde etki)

Konvülsiyon yapıcı maddeler	**diazepam,barbitüratlar**
Vazokonstriktör ilaçlar	nitritler ve diğer vazodilatörler
Amfetaminler	klorpromazin ve türevleri
İzoniazid	pridoksin

Farmakolojik antagonistler

reseptörü bloke ederek antidotal etkinlik

Narkotik analjezikler	**naloksan**
Muskarinik ilaçlar ve antikolinesterazlar	atropin
Atropin	fizostigmin
Histamin	antihistaminikler

Metabolizma düzeyindeki antagonistler

Oral antikoagülanlar	K-vit
Karbonmonoksit	saf oksijen
Methotreksat	folinik asit
Metil alkol ve etilen glikol	etanol
Siyanür	sodyum tiyosülfat
Asetaminofen	N-asetilsistein
Organofosfatlı zehirlenme	pralidoksim, obidoksim
Methemoglobinemi	metilen mavisi

Hastane Antidot stokları

- Kaç tane
- Ne kadar bulundurulmalı
- Dünyadaki durum
- Türkiye deki durum

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Acil hastaları kabul eden tesisler için antidote stokları

Toxicology/concepts

Expert Consensus Guidelines for Stocking of Antidotes in Hospitals That Provide Emergency Care

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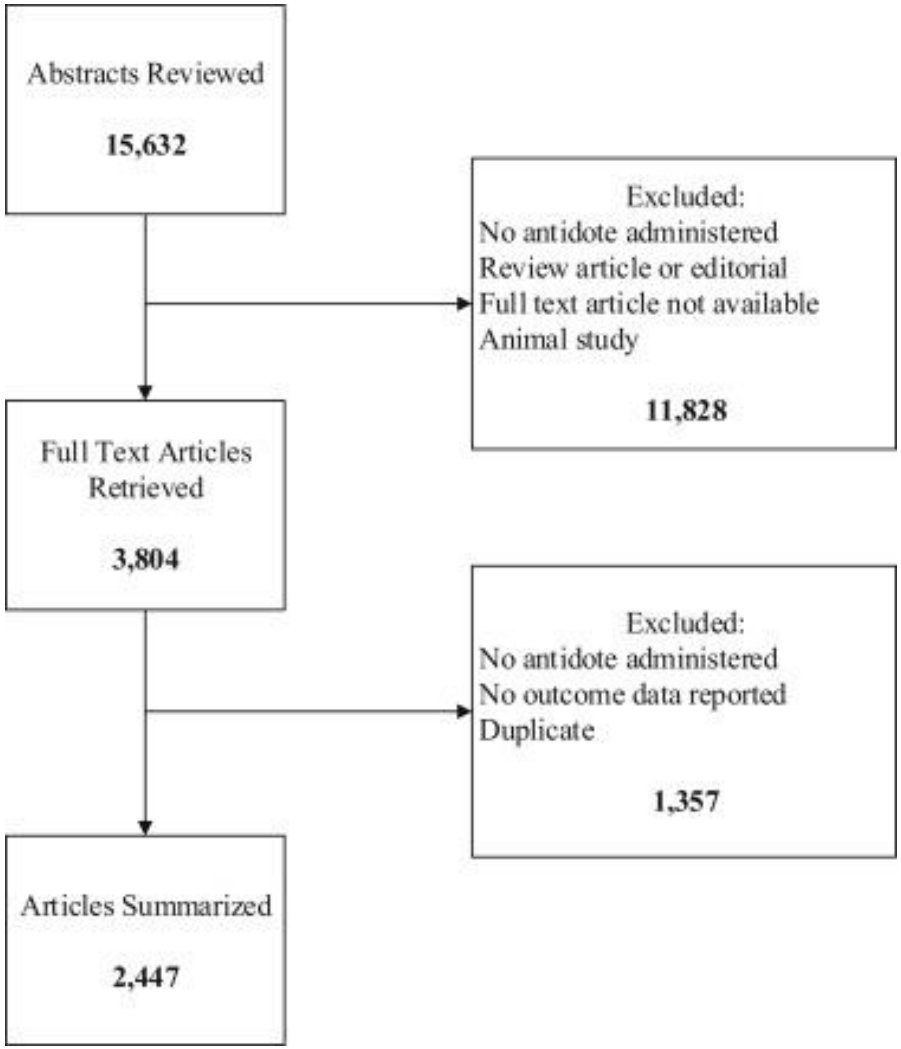
We provide recommendations for stocking of antidotes used in emergency departments (EDs). An expert panel representing diverse perspectives (clinical pharmacology, medical toxicology, critical care medicine, hematology/oncology, hospital pharmacy, emergency medicine, emergency medical services, pediatric emergency medicine, pediatric critical care medicine, poison centers, hospital administration, and public health) was formed to create recommendations for antidote stocking. Using a standardized summary of the medical literature, the primary reviewer for each antidote proposed guidelines for antidote stocking to the full panel. The panel used a formal iterative process to reach their recommendation for both the quantity of antidote that should be stocked and the acceptable timeframe for its delivery. The panel recommended consideration of 45 antidotes; 44 were recommended for


Abstracts Reviewed
15,632
Excluded:
No antidote administered
Review article or editorial
Full text article not available
Animal study
11,828
Full Text Articles Retrieved
3,804
Excluded:
No antidote administered
No outcome data reported
Duplicate
1,357
Articles Summarized
2,447

- Sınıf I kanıtı genellikle ilacın etkinliğini değerlendirmek için **nadiren** temin edilmiştir.
- Sınıf II kanıt **daha yaygındı**, ama yine de genellikle etkililiğe odaklandı.
- Sınıf III kanıt **bol**, ama son derece değişken. Birkaç makale

44 36 23

Table 2. Antidote stocking recommendations for facilities that accept emergency patients.

Antidote	Poisoning Indication(s)	Strength of Evidence*			Panel Recommendation		
		Is the Drug Effective?	Do Medical Benefits Outweigh Risks?	Is Time an Important Factor?	Should Be Stocked by the Hospital	Should Be Available Within 60 Minutes	Should Be Immediately Available
Acetylcysteine (IV)	Acetaminophen toxicity	I	I	I	Yes	Yes	No
Acetylcysteine (PO)		II	I	I	Yes	Yes	No
Antivenin (*Latrodectus mactans*)	Black widow spider envenomation	II	II	III	Yes	No	No
Antivenin (*Micrurus fulvius*)	Eastern and Texas coral snake envenomation	II	II	III	Yes	Yes	No
Atropine sulfate	Organophosphate pesticide or nerve agent poisoning, carbamate toxicity	II	II	III	Yes	Yes	Yes
Calcium chloride†‡	Fluoride, calcium channel blocking agent	III	III	III	Yes	Yes	Yes
Calcium gluconate†‡	toxicity	III	III	III	Yes	Yes	Yes
Calcium disodium EDTA	Lead poisoning	II	II	III	Yes	No	No
Calcium trisodium pentetate (calcium DTPA)	Internal contamination with plutonium, americium, or curium	III	III	III	Yes	No	No
Centruroides (scorpion) $F(ab')_2$	Scorpion envenomation in pediatrics (A) and adults (B)	I (A) III (B)	I (A) III (B)	II	Yes	Yes	No
Crotalidae polyvalent immune Fab (ovine) (CroFab; FabAV)	North American crotaline snake envenomation	II	I	III	Yes	Yes	No
Cyproheptadine‡	Serotonin toxicity	III	III	III	Yes	No	No
Dantrolene‡	Malignant hyperthermia	II	II	II	Yes	Yes	Yes
Deferoxamine mesylate	Iron poisoning	I	I	III	Yes	Yes	No
Dextrose (D50)	Hypoglycemia	I	II	II	Yes	Yes	Yes
Digoxin immune Fab	Cardiac glycosides toxicity (A) or cardiac steroid toxicity (B)	II (A) I (B)	II (A) I (B)	II	Yes	Yes	Yes
Dimercaprol (BAL)	Heavy metal toxicity (arsenic [A], lead [B], mercury [C])	II (A, B) III (C)	II	II	Yes	Yes	No
DMSA (succimer)	Heavy metal toxicity (arsenic [A], lead [B], mercury [C])	III (A) I (B) II (C)	III (A, C) I (B)	III	Yes	No	No
Ethanol (PO)‡ or	Methanol or ethylene glycol poisoning	II	II	III	Yes	Yes	No
fomepizole§		II	II	III	Yes	Yes	No
Flumazenil	Benzodiazepine toxicity	I	I	II	Yes	Yes	Yes
Glucagon hydrochloride‡	β-Blocker, calcium channel blocker toxicity	III	II	III	Yes	Yes	Yes
Glucarpidase	Methotrexate toxicity	II	II	II	Yes	No	No
Hydroxocobalamin§ or	Cyanide poisoning	II	II	II	Yes	Yes	Yes
sodium nitrite and sodium thiosulfate†		III	III	III	Yes	Yes	Yes
Idarucizumab	Reversal of anticoagulant effects of dabigatran	II	I	II	Yes	Yes	Yes
Leucovorin	Methotrexate or methanol toxicity	II	II	II	Yes	Yes	No
Levocarnitine‡	Valproic acid toxicity	II	II	III	Yes	Yes	No
Lipid emulsion‡	Local anesthetic systemic toxicity	III	III	III	Yes	Yes	Yes
Methylene blue	Methemoglobinemia	II	II	II	Yes	Yes	Yes
Naloxone hydrochloride	Opioid toxicity	I	I	II	Yes	Yes	Yes
Octreotide‡	Sulfonylurea-induced hypoglycemia	I	I	II	Yes	Yes	No
Physostigmine	Anticholinergic syndrome	I	II	III	Yes	Yes	Yes
Phytonadione (vitamin K_1)	Reversal of coumarin-induced coagulopathy	I	I	II	Yes	Yes	Yes
Potassium iodide	Thyroid radioiodine protection	II	II	II	Yes	Yes	No
Pralidoxime chloride	Organophosphorus poisoning	I	I	II	Yes	Yes	No
Protamine sulfate	Reversal of coagulopathy induced by unfractionated (A) or low-molecular-weight (B) heparin	I (A) III (B)	I	II (A) III (B)	Yes	Yes	Yes
3-factor prothrombin complex concentrate‡	Reversal of acquired coagulation factor deficiency induced by vitamin K antagonists	II	II	II	Yes	Yes	Yes
or		I	I	II	Yes	Yes	Yes
4-factor prothrombin complex concentrate§		II	II	II	No	N/A	N/A
Activated prothrombin complex concentrate‡							
Prussian blue	Thallium (A) or radiocesium (B) toxicity	III (A) II (B)	III (A) II (B)	III (A) II (B)	Yes	No	No
Pyridoxine hydrochloride	Isoniazid, hydrazine toxicity	III	III	III	Yes	Yes	Yes
Sodium bicarbonate‡	Tricyclic antidepressant toxicity (A), urine alkalization for salicylate toxicity (B), or cocaine toxicity (C)	III (A, C) II (B)	III (A, C) II (B)	III	Yes	Yes	Yes
Thiamine	Ethylene glycol toxicity (A), thiamine deficiency associated with chronic alcoholism (B)	III (A) I (B)	III (A) II (B)	III (A) III (B)	Yes	Yes	Yes
Uridine triacetate	Fluorouracil or capecitabine overdose regardless of symptoms or early-onset toxicity	III	III	III	Yes	No	No

Table 2. Antidote stocking recommendations for facilities that accept emergency patients.

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Acetylcysteine (IV)	Acetaminophen toxicity	I	I	I	Yes	Yes	No
Acetylcysteine (PO)		II	I	I	Yes	Yes	No
Antivenin (*Latrodectus mactans*)	Black widow spider envenomation	II	II	III	Yes	No	No
Antivenin (*Micrurus fulvius*)	Eastern and Texas coral snake envenomation	II	II	III	Yes	Yes	No
Atropine sulfate	Organophosphate pesticide or nerve agent poisoning, carbamate toxicity	II	II	III	Yes	Yes	Yes
Calcium chloride[†‡]	Fluoride, calcium channel blocking agent toxicity	III	III	III	Yes	Yes	Yes
Calcium gluconate[†‡]		III	III	III	Yes	Yes	Yes
Calcium disodium EDTA	Lead poisoning	II	II	III	Yes	No	No
Calcium trisodium pentetate (calcium DTPA)	Internal contamination with plutonium, americium, or curium	III	III	III	Yes	No	No
Centruroides (scorpion) $F(ab')_2$	Scorpion envenomation in pediatrics (A) and adults (B)	I (A) III (B)	I (A) III (B)	II	Yes	Yes	No
Crotalidae polyvalent immune Fab (ovine) (CroFab; FabAV)	North American crotaline snake envenomation	II	I	III	Yes	Yes	No
Cyproheptadine[‡]	Serotonin toxicity	III	III	III	Yes	No	No
Dantrolene[‡]	Malignant hyperthermia	II	II	II	Yes	Yes	Yes
Deferoxamine mesylate	Iron poisoning	I	I	III	Yes	Yes	No
Dextrose (D50)	Hypoglycemia	I	II	II	Yes	Yes	Yes
Digoxin immune Fab	Cardiac glycosides toxicity (A) or cardiac steroid toxicity (B)	II (A) I (B)	II (A) I (B)	II	Yes	Yes	Yes
Dimercaprol (BAL)	Heavy metal toxicity (arsenic [A], lead [B], mercury [C])	II (A, B) III (C)	II	II	Yes	Yes	No
DMSA (succimer)	Heavy metal toxicity (arsenic [A], lead [B], mercury [C])	III (A) I (B) II (C)	III (A, C) I (B)	III	Yes	No	No
Ethanol (PO)[‡] or	Methanol or ethylene glycol poisoning	II	II	III	Yes	Yes	No
fomepizole[§]		II	II	III	Yes	Yes	No
Flumazenil	Benzodiazepine toxicity	I	I	II	Yes	Yes	Yes
Glucagon hydrochloride[‡]	β-Blocker, calcium channel blocker toxicity	III	II	III	Yes	Yes	Yes
Glucarpidase	Methotrexate toxicity	II	II	II	Yes	No	No
Hydroxocobalamin[§] or	Cyanide poisoning	II	II	II	Yes	Yes	Yes
sodium nitrite and sodium thiosulfate[†]		III	III	III	Yes	Yes	Yes
Idarucizumab	Reversal of anticoagulant effects of dabigatran	II	I	II	Yes	Yes	Yes
Leucovorin	Methotrexate or methanol toxicity	II	II	II	Yes	Yes	No
Levocarnitine[‡]	Valproic acid toxicity	II	II	III	Yes	Yes	No
Lipid emulsion[‡]	Local anesthetic systemic toxicity	III	III	III	Yes	Yes	Yes
Methylene blue	Methemoglobinemia	II	II	II	Yes	Yes	Yes
Naloxone hydrochloride	Opioid toxicity	I	I	II	Yes	Yes	Yes
Octreotide[‡]	Sulfonylurea-induced hypoglycemia	I	I	II	Yes	Yes	No
Physostigmine	Anticholinergic syndrome	I	II	III	Yes	Yes	Yes
Phytonadione (vitamin K_1)	Reversal of coumarin-induced coagulopathy	I	I	II	Yes	Yes	Yes

Potassium iodide	Thyroid radioiodine protection	II	II	II	Yes	Yes	No
Pralidoxime chloride	Organophosphorus poisoning	I	I	II	Yes	Yes	No
Protamine sulfate	Reversal of coagulopathy induced by unfractionated (A) or low-molecular-weight (B) heparin	I (A) III (B)	I	II (A) III (B)	Yes	Yes	Yes
3-factor prothrombin complex concentrate[‡] or	Reversal of acquired coagulation factor deficiency induced by vitamin K antagonists	II	II	II	Yes	Yes	Yes
4-factor prothrombin complex concentrate[§]		I	I	II	Yes	Yes	Yes
Activated prothrombin complex concentrate[‡]		II	II	II	No	N/A	N/A
Prussian blue	Thallium (A) or radiocesium (B) toxicity	III (A) II (B)	III (A) II (B)	III (A) II (B)	Yes	No	No
Pyridoxine hydrochloride	Isoniazid, hydrazine toxicity	III	III	III	Yes	Yes	Yes
Sodium bicarbonate[‡]	Tricyclic antidepressant toxicity (A), urine alkalization for salicylate toxicity (B), or cocaine toxicity (C)	III (A, C) II (B)	III (A, C) II (B)	III	Yes	Yes	Yes
Thiamine	Ethylene glycol toxicity (A), thiamine deficiency associated with chronic alcoholism (B)	III (A) I (B)	III (A) II (B)	III (A) III (B)	Yes	Yes	Yes
Uridine triacetate	Fluorouracil or capecitabine overdose regardless of symptoms or early-onset toxicity	III	III	III	Yes	No	No

Acil hastaları kabul eden tesisler için antidote stokları

- Bu antidotların 44'ünün stokta bulunmalı bunların 23 Hemen ulaşılabilir olmalı

23 Hemen ulaşılabilir olmalı

Atropin	Metilen mavisi
CaClorid-CaGlukonat-	Naloksan
Dantrolen	Fizostigmin
%50 Dex	K vit
DigiFab	Protamin sulfat
Fulumazenil	Protein komplex konsantreleri
Gulucagon	Piridoxin
Hidroxikobalamin-sodyum nitrat/tiyosülfat	Na bikarbonat
İdaricizumab	Tiamin
Lipid Emülsiyon	

100 kg ağırlığındaki bir hastayı tedavi etmek için gerekli olan antidot miktarı

Table 3. Amount of antidote needed to treat one patient weighing 100 kg.

Antidote	Stocking Recommendation, Hours		Notes
	8	24	
Acetylcysteine (IV), g	22	30	Administer intravenously for hepatic failure.
Acetylcysteine (PO), g	28	56	
Antivenin (*L mactans*), vial	1	1	Product has been discontinued by manufacturer; some supplies remain.
Antivenin (*M fulvius*), vial	5	10	Product has been discontinued by manufacturer; some supplies remain.
Atropine sulfate, mg	45	165	
Calcium chloride, g	10	10	Do not administer calcium chloride subcutaneously; should be administered by central venous route, if possible. Calcium gluconate may be given by IV, subcutaneous routes.
Calcium gluconate, g	30	30	
Calcium disodium EDTA, g	0.75	2.25	
Calcium trisodium pentetate (calcium DTPA), g	1	1	
Centruroides (scorpion) $F(ab')_2$, vial	3	3	
FabAV, vial	12	18	
Cyproheptadine, mg	20	36	
Dantrolene, mg	800	2,000	Should be available anywhere general anesthesia is performed.
Deferoxamine mesylate, g	12	36	
Dextrose (D50), g	250	250	D50 as initial treatment may be followed by additional dextrose at lower concentrations.
Digoxin immune Fab, vial	15	15	
Dimercaprol (BAL)	800 mg	2.4 g	
DMSA (succimer), g	1	3	
Ethanol (PO), g	180	360	IV ethanol solution for injection may be administered, if available.
Fomepizole, g	1.5	4.5	
Flumazenil, mg	6	12	
Glucagon hydrochloride, mg	90	250	
Glucarpidase, U	5,000	5,000	Glucarpidase should not be administered until ≥2 h after leucovorin.
Hydroxocobalamin, g	10	10	Can be used safely in patients with smoke inhalation. Red color of drug causes laboratory test interference, technologic dysfunction of dialyzers, and red discoloration of skin and urine.

100 kg ağırlığındaki bir hastayı tedavi etmek için gerekli olan antidot miktarı

urine.

Sodium nitrite, mg, and sodium thiosulfate, g	600 25	600 25	Nitrites cause methemoglobinemia and can impair oxygen delivery; should not be used in smoke inhalation patients with carbon monoxide poisoning.
Idarucizumab, g	5	5	
Leucovorin	300 mg	1 g	
Levocarnitine, g	9	15	Administer IV for acute toxicity
Lipid emulsion (IV), mL	1,250	1,250	Recommendations based on products containing an emulsion of soybean oil, egg phospholipids, and glycerin.
Methylene blue, mg	400	600	
Naloxone hydrochloride, mg	20	40	
Octreotide, μg	75	225	
Physostigmine, mg	4	4	
Phytonadione (vitamin K_1), mg	50	100	Initial dose should be administered IV (not to exceed 10 mg), with subsequent doses administered PO. Patients presenting with elevated international normalized ratio and bleeding should also be treated with prothrombin complex concentrate.
Potassium iodide, mg	130	130	
Pralidoxime chloride, g	7	18	
Protamine sulfate	400 mg	1.2 g	
3-factor prothrombin complex concentrate, IU	5,000	5,000	Vitamin K_1 10 mg IV should be administered concurrently to maintain clotting factor levels after prothrombin complex concentrate levels have diminished.
4-factor prothrombin complex concentrate, IU	5,000	5,000	
Activated prothrombin complex concentrate	N/A	N/A	
Prussian blue, g	12.5	25	
Pyridoxine hydrochloride, g	8	24	
Sodium bicarbonate, g	63	84	
Thiamine	500 mg	1.5 g	
Uridine triacetate, g	20	40	

Antidot ----ilgili alan

Table 4. Considerations for hazard vulnerability assessment.

Antidote	Consideration
Acetylcysteine (IV)	Antidote for widely available therapeutic agents
Acetylcysteine (PO)	
Antivenin (*L mactans*)	Geographic/endemic areas
Antivenin (*M fulvius*)	Geographic/endemic areas
Atropine sulfate	Industry, referral patterns from agricultural areas
Calcium chloride	Industry, antidote for widely available therapeutic agents
Calcium gluconate	
Calcium disodium EDTA	Prevalence of lead risk factors such as old housing, industry using lead products
Calcium trisodium pentetate (calcium DTPA)	Receiving hospital for research laboratory
Centruroides (scorpion) $F(ab')_2$	Geographic/endemic areas
FabAV	Geographic/endemic areas, history/experience with exotic bites, consider simultaneous bite victims
Cyproheptadine	All hospitals: serotonin toxicity occurs throughout the United States
Dantrolene	All hospitals: malignant hyperthermia occurs throughout the United States
Deferoxamine mesylate	All hospitals: acute iron ingestion occurs throughout the United States
Dextrose (D50)	All hospitals: acute hypoglycemia occurs commonly throughout the United States
Digoxin immune Fab	Antidote for widely available therapeutic agents
Dimercaprol (BAL)	Industry, prevalence of heavy metal risk factors
DMSA (succimer)	Historical rate of pediatric lead poisoning in hospital service area
Ethanol (PO)	All hospitals: ethylene glycol and methanol are common throughout the United States
Fomepizole	All hospitals: ethylene glycol and methanol are common throughout the United States
Flumazenil	Antidote for widely available therapeutic agents
Glucagon hydrochloride	Antidote for widely available therapeutic agents
Glucarpidase	Hospital catchment area
Hydroxocobalamin	Industry, history, local conditions, community planning, facility service area
Sodium nitrite and sodium thiosulfate	Industry, history, local conditions, community planning, facility service area
Idarucizumab	Only approved antidote for reversal of anticoagulant effects of dabigatran
Leucovorin	Antidote for widely available therapeutic agent
Levocarnitine	Antidote for widely available therapeutic agents
Lipid emulsion (IV)	All hospitals: local anesthetic systemic toxicity occurs throughout the United States
Methylene blue	All hospitals: methemoglobinemia occurs throughout the United States; high number of causative agents
Naloxone hydrochloride	Antidote for widely available and commonly abused agents
Octreotide	Antidote for widely available therapeutic agent
Physostigmine	Antidote for widely available therapeutic agent
Phytonadione (vitamin K_1)	Antidote for widely available therapeutic agents
Potassium iodide	Industry, local conditions
Pralidoxime chloride	Industry, referral patterns from agricultural areas
Protamine sulfate	Antidote for widely available therapeutic agent
3-factor prothrombin complex concentrate	Antidote for widely available therapeutic agents
4-factor prothrombin complex concentrate	
Prussian blue	Industry
Pyridoxine hydrochloride	Industry, history, endemic conditions, community planning, facility service area
Sodium bicarbonate	Antidote for widely available therapeutic agents
Thiamine	All hospitals: ethylene glycol toxicity and thiamine deficiency associated with chronic alcoholism occur throughout the United States
Uridine triacetate	Prevalence of fluoropyrimidine toxicity risk factors

Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi Antidot Merkezi

20 antidot

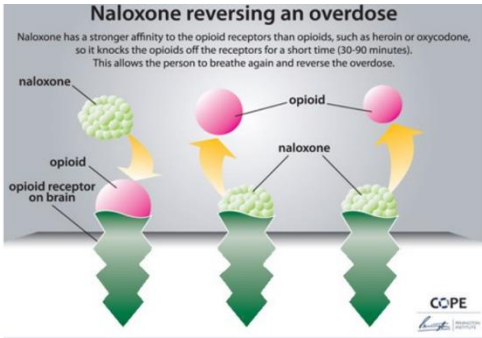
ILAC_ADI	ETKEN_MADDE	TOPLAM_STOK
OTOMATİK ATROPİN ENJEKTÖRÜ (ORDU İLAÇ)	Antidot Atropin sülfat 2 mg ve obidoksim 220 mg içeren 2 ml Enjektör	50
OTOMATİK ATROPİN ENJEKTÖRÜ (ORDU İLAÇ)	Antidot Atropin sülfat 2 mg ve obidoksim 220 mg içeren 2 ml Enjektör	50
BOTULİSM ANTİTOKSİN (BOTULİSMUS ANTİ SERUMU) 250 ML ŞİŞE	Antidot Botilinum ABE Antitoksin 250 ml Şişe	0
BOTULİSMUS POLİVALAN ANTİSERUM (A-B-C-D-E-F-G) 50 ML	Antidot Botilinum ABE Antitoksin 50 ml Şişe	4
DANTROLEN 20 MG 12 FLK	Antidot Dantrolen sodyum 20 mg Ampul	2
DESFERAL 500 MG 10 FLAKON	Antidot Deferoksamin 500 mg Flakon	204
DİGİFAB (DİGOXİN İMMÜN FAB) 40 MG 1 FLAKON (ANTİDOT)	Antidot Digoksin İmmune Fab 40 mg Flakon	42
KELOCYANOR (DİCOBALT EDTA)% 1,5 300 MG/20 ML 6 AMPUL	Antidot Dikobalt edetat 300 mg/20 ml Ampul	6
DİMERCAPROL (BAL) (BRİTİSH ANTİ-LEWİSİTE) 200 MG/2 ML 12	Antidot Dimerkaprol 200 mg/2 ml Ampul	0
METALCAPTASE (D-PENİSİLAMİN) 150 MG /100 KAPSÜL	Antidot D-Penisilamin 150 mg Tablet	0
METALCAPTASE (D-PENİSİLAMİN) 300 MG /100 KAPSÜL	Antidot D-Penisilamin 300 mg Tablet	0
ETİL ALKOL (% 10) 500 CC ŞİŞE	Antidot Etil Alkol 10 % Şişe	175
ANTİCHOLİUM (PHYSOSTİGMİN) 5 AMPUL	Antidot Fizostigmin Salisilat 2 mg Ampul	28
FOMEPİZOLE 1,5 G /1,5 ML (1G /1 ML) ANTİDOT	Antidot Fomepizol Sülfat (4-Metil pirazol) 1 gr/1 ml Ampul	4
FOMEPİZOL (4 METİL PİRAZOL) 100 MG/20 ML 5 AMPUL	Antidot Fomepizol Sülfat (4-Metil pirazol) 100 mg/20 ml Ampul	0
CYANOKİT (HYDROXYCOBALAMİN) FLAKON	Antidot Hidroksokobalamin 5 gr Ampul	1
CALCİUM SODİUM EDTATE 10 AMPUL	Antidot Kalsiyum disodyum EDTA 500 mg/10 ml Ampul	0
METİLEN MAVİSİ 10 ML	Antidot Metilen mavisi 1 % Şişe	40
NALOXON HCI 0,4 MG 1 ML 10 AMPUL	Antidot Nalokson HCl 0.4 mg/ml 1 ml Ampul	64
NALOKSON 04 MG AMPUL	Antidot Nalokson HCl 0.4 mg/ml 1 ml Ampul	0
CONTRATHİON %2 10 FLAKON	Antidot Pralidoksim 20 mg/ml 10 ml Flakon	213
LEGALON-SİL (SİLİBİNİN) 4 FLAKON	Antidot Silibinin 350 mg Flakon	92
DMSA (DİMERCAPTOSUCCİNİC ASİD) SUCCIMER 200 MG KAPSÜL	Antidot Suksimer 200 mg Kapsül	210
DİMAVAL (DMPS SODYUM) 100 MG 20 KAPSÜL	Antidot Unitiyol (DMPS) 100 mg Kapsül	0
DİMAVAL (DMPS SODYUM) 100 MG 9 KAPSÜL	Antidot Unitiyol (DMPS) 100 mg Kapsül	0
DİMAVAL (DMPS SODYUM) 250 MG/ 5 ML 5 AMPUL	Antidot Unitiyol (DMPS) 250 mg/5 ml Ampul	0

Antidot etken madde	Antidotun adı
4-metil pirazol (fomepizol sülfat)	FOMEPİZOL
Botulismus polivalan antiserum (A-B-E)	BOTULİSMUS ANTİTOKSİN
Calcium ededate sodyum	CALCIUM EDEDAT DE SODIUM %5
Dicobalt EDTA	KELOCYANOR %1.5
Digoksin immün fab	DIGIFAB
Dimercaprol	BAL
DMPS	DIMAVAL
D-penisilamin	METACAPTASE
Etil alkol	ETİL ALKOL %10
Hydroxocobalamin	CYANO KİT 2.5 mg
Metilen mavisi	METİLEN MAVİSİ %1
Physostigmine	ANTICHOLIUM
Pralidoksim	CONTRATHION
Silibinin	LEGALON-SIL
Succimer (DMSA)	SUCCICAPTAL

Ulusal Zehir Danışma Merkezi antidot listesi

114

Opioid Toksisitesinde İntranazal Nalokson



Randomize kontrollü çalışma

- Toplam **100 opioid overdozu olan hasta**
- iki grup : **50 iv, 50 intranazal nalokson grubu (her bir gruba 0.4 mg)**
- Sonuçları değerlendirirken;

–nalokson öncesi ve sonrası bilinç düzeyi (GKS),
–vital bulgular,
–yanıt zamanı,
–oksijen saturasynu,
–hastanede kalış süresi
–ve yan etkiler değerlendirilmiş

TYD

Koma antidot
O2
Glikoz
Naloksan
Tiamin

- **Sonuç: İntranazal naloksan,opioid overdozuna bağlı SSS depresyonu ve solunum depresyonunda kullanıldığında iv naloksan kadar etkili**

- CARNEY, Leiah. Naloxone Therapy in Opioid Overdose Patients: Intranasal or Intravenous?. 2017.

Yüksek konsantrasyonlu intranazal nalokson (2 mg / mL), opioid doz aşımı semptomlarının tersine çevrilmesi için intramüsküler nalokson (2 mg) 'inkine benzer bir etkiye sahip gibi görünmektedir ve istenmeyen olaylarda bir fark yoktur.

Chou, Roger, et al. "Management of suspected opioid overdose with naloxone in out-of-hospital settings: A systematic review." *Annals of internal medicine* 167.12 (2017): 867-875.

AGENT	INDICATION	ADULT DOSE	PEDIATRIC DOSE	ROUTE	COMMENTS
Atropine	Organophosphate toxicity	1–3 mg	0.05 mg/kg	IV, IM	Double dose every 5 minutes until effect
Pralidoxime	Organophosphate toxicity	1–2 g bolus	25–50 mg/kg	IV, IM	Given over 30 minutes Dose can be repeated based on response

Alternative dosing options are: 2 g bolus over 20 minutes followed by an infusion of 500 mg/h for up to 7 days, 1 g/h every 4 hours, or 30 mg/kg followed by infusion of 8 mg/kg per hour

Magnesium sulfate - calcium channel blocking drugs as antidotes for acute organophosphorus insecticide poisoning

	no antidot
Carbamates	Aldicarb, carbaryl
Chlorinated hydrocarbons	Dichlorodiphenyltrichloroethane (DDT), gamma-hexachlorocyclohexane (lindane)
Substituted phenols	2,4-dinitrophenol (DNP)
Chlorophenoxy pesticides	2,4,5-trichlorophenoxyacetic acid (2,4,5-T), 2,4-dichlorophenoxyacetic acid (2,4-D)
Bypyridyl pesticides	N,N'-dimethyl-4,4'-bipyridinum dichloride (paraquat), 1,1'-ethylene-2,2'-bipyridyldiylium dibromide (diquat)
Pyrethrins/pyrethroids	Permethrin
Glyphosate	N-(phosphonomethyl)glycine
Insect repellent	N,N-Diethyl-meta-toluamide (DEET)

- Çok miktarlarda pestisit yutulduğunda, Pralidoxime

OP-toksisite olasılığını artırır

Eddleston, Michael. "Are oximes still indicated for acute organophosphorus insecticide self-poisoning?." (2018): 1-2.

- Clinical Research
- **Salbutamol in acute organophosphorus insecticide poisoning – a pilotdose-response phase II study**
- **Fazle Rabbi Chowdhury**,Md. Mustafezur Rahman,Parash Ullah,Abdul Mumith Ruhan,Md. Shafiqul Bari,M. M. Jahangir Alam, show all
- Pages 820-827 | Received 22 Nov 2017, Accepted 09 Feb 2018, Published online: 20 Feb 2018
- Download citation
- https://doi.org/10.1080/15563650.2018.1440587
-
-
- Dili Seçin▼
- Translator disclaimer
- **Abstract**
- **Background:** Treatment of acute organophosphorus (OP) insecticide poisoning is difficult, with many patients dying despite best care. Pre-clinical studies have shown benefit from salbutamol, possibly due speeding alveolar fluid clearance or reducing bronchoconstriction. In this small pilot dose-response study, we aimed to explore whether addition of nebulized salbutamol to standard care might improve resuscitation.
- **Methods:** We performed a single-blind phase II study comparing the effect of two different doses of nebulized salbutamol versus saline placebo, in addition to standard treatment. Primary outcome was oxygen saturations over the first 60 min of resuscitation; secondary outcomes included heart rate, incidence of dysrhythmias, time to 'atropinization', atropine dose required, and mortality.
- **Result:** Seventy-five patients were randomized to receive 5 mg (Salb5, *n* = 25) or 2.5mg (Salb2.5, *n* = 25) of salbutamol, or saline placebo (NoSalb, *n* = 25), by nebulizer. Oxygen saturations did not differ between groups over the first 60 min of resuscitation (median AUC NoSalb: 1376 [95% CI 1282 to 1470], Salb2.5: 1395 [1305 to 1486], Salb5: 1233 [1100 to 1367]; *p* = .9898). Heart rate was also similar across the three arms. Median time to full atropinization, and atropine dose required, were the same for all three arms (NoSalb 15.0 [10–16] min and 12.6 [8.0–13.4] mg, Salb2.5 15.0 [10–16] min and 12.6 [9.3–16.8] mg, and Salb5 15.0 [10–20] min and 12.6 [10.7–20.6] mg; *p* = .4805 and *p* = .1871, respectively). Three (12%) patients died in the Salb2.5 and Salb5 groups and two (8%) in the NoSalb group.
- **Conclusion:** This pilot study, within the limitations of its small size and variation between patients, found no apparent evidence that administration of nebulized salbutamol improved resuscitation of patients with acute OP insecticide self-poisoning. The data obtained provides a basis to design further studies to ultimately test the role of salbutamol in OP insecticide poisoning.
- Keywords: Salbutamol, nebulization, organophosphorus, insecticide, poisoning

Organofosfor / biyopolimerlerle

- Moleküler modellemenin yeni yöntemleri,
- ilaç tasarımında acil sorunların çözülmesine, biyokatalizörlerin ve biyosensörlerin yönlendirilmiş evrimine ve diğer birçok araştırma alanlarına yardımcı olmaktadır.

- biyopolimerlerle
- (poliglutamik ve poliaspartik asitin çeşitli modifikasyonlarının yanı sıra hidroksietil nişasta ve süksinillenmiş jelatin ile)

- hekzahistidin ile etiketlenmiş organofosfor hidrolaz (His6-OPH) bazlı enzim-polielektrolit komplekslerinin (EPC'ler) yapıları, moleküler yerleştirme kullanılarak farklı pH'larda simülasyonu.
- Lyagin, Ilya V., and Elena N. Efremenko. "Biomolecular engineering of biocatalysts hydrolyzing neurotoxic organophosphates." *Biochimie* 144 (2018): 115-121.

Organofosfor /bispiridinyum

- Organofosfor zehirlenmesine karşı Hücre kültürü ortamı (*in vitro)*

insan a7-nikotinik asetilkolin reseptörlerinin bispiridinyum bileşikleri ile duyarsızlaştırılması

➢ bispiridinyum propan MB327

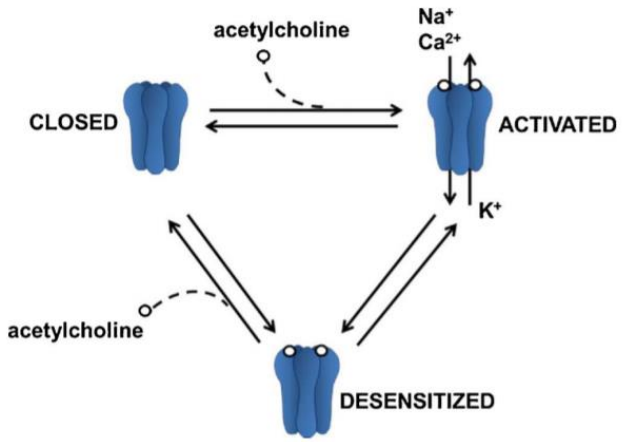


Fig. 1. Simplified schematic model of conformational transitions of nAChRs including closed, open and desensitized states consequent to binding of acetylcholine (Faghih et al., 2008). For further details see text.

➢ yeniden uyarlamış ve ortalama kanal açık süresini uzatmıştır

Scheffel, Corinna, et al. "Counteracting desensitization of human α7-nicotinic acetylcholine receptors with bispyridinium compounds as an approach against organophosphorus poisoning." *Toxicology letters* 293 (2018): 149-156.

- Levocarnitine‡ Valproic acid toxicity
- Valproic acid kullanımına bağlı Hiperamonemiye bağlı ensefalopatide

MUÑIZ, Antonio E. Valproic Acid Overdose Review of a Case With Electrocardiographic Changes. *The Journal of emergency medicine*, 2017, 53.3: 333-338.

- Octreotide‡ Sulfonylurea-induced hypoglycemia

- Prussian blue :

Thallium (A) or radiocesium (B) toxicity

- Sodium bicarbonate‡ Tricyclic antidepressant toxicity (A),
- urine alkalization for salicylate toxicity (B), or
- cocaine toxicity (C)

- Thiamine:100mg
- Ethylene glycol toxicity (A),
- chronic alcoholism

Fomepizol

Metanolün toksik metabolitine dönüşmesini durdurmak için alkol dehidrojenaz inhibitörleri olarak işlev görür.

Fomepizole, 15 mg / kg'lık bir yükleme dozuyla intravenöz olarak verilir ve daha sonra 4 doz için her 12 saatte bir 10 mg / kg veya metanol konsantrasyonu normal bir asit-baz statüsüyle 32 mg / dL'den az oluncaya kadar bakım dozajı verilir.

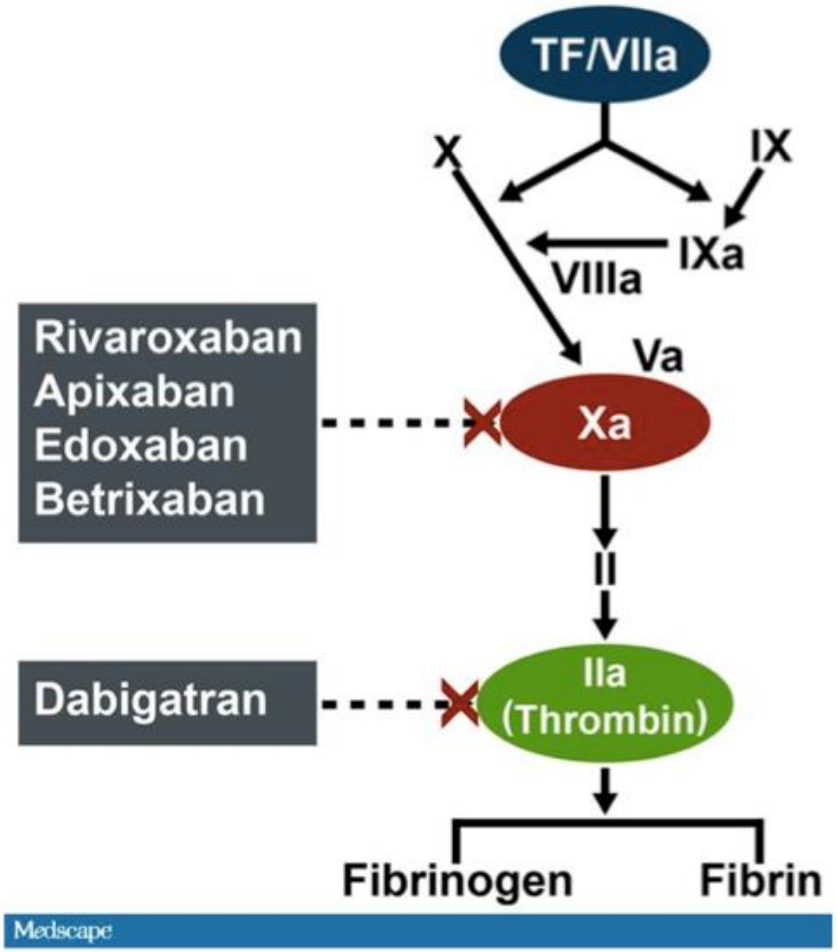
4 dozun ötesinde ek dozlama yapılması gerekiyorsa, artan metabolizmanın otodüksiyonuna bağlı olarak dozlama her 12 saatte bir 15 mg / kg'a yükselir.

Diyaliz sırasında, fomepizol diyaliz edilebilir olduğu gibi her 4 saatte bir dozlanmalıdır.

Ashurst, John V., and Thomas M. Nappe. "Toxicity, Methanol." (2018).

Yeni Kuşak Antikoagülanların Antidotu

- Bu ajanlarla meydana gelen kanamalarda şu an kullanılan tedavi yolu:
- –Destek tedavi (sıvı, eritrosit, kanama kaynağı kontrolü)
- –Antikoagülanların kesilmesi
- –Erken alımlarda aktif kömür
- •Nonspesifik prokoagülanlar (prothrombin Kompleks konsantreleri ve aktive faktör VIIa) ciddi kanamalarda kullanılmış.



Dabigatran	**İdarucizumab** 
Rivaroksaban, apiksaban ve edoksaban	**Andexanet alfa (**Andexxa) FDA **enzimatik olarak inaktive edilmiş faktör Xa'nın kesilmiş formu olup, faktör Xa inhibitörlerine (*rivaroksaban, apiksaban ve edoksaban) bağlanarak etkilerini geri döndürür***
edoksaban	Ciraparantag
Subkutan fondaparinuks ve in vivo LMWH	**Aripazine** **küçük bir sentetik molekül olup (~500 Da) *oral dabigatran, apiksaban, rivaroksaban yanında subkutan fondaparinuks ve in vivo LMWH etkilerini geri döndürür.***

edoksaban

- Ciraparantag
- Çift kör bir Faz II'de, 80 plasebo kontrollü sağlıklı yetişkin erkekler, ciraparantag
- ***Edoksaban etkilerini tersine çevirmiştir***

- BURNETT, Allison; SIEGAL, Deborah; CROWTHER, Mark. Specific antidotes for bleeding associated with direct oral anticoagulants. *BMJ: British Medical Journal (Online)*, 2017, 357.

- **Dabigatran yalnızca %35 proteine bağlanır ve diyalizabıldır.**
- •Rivaroksaban ve apiksaban ise %90 proteine bağlanır ve diyalize edilemez.

Ekstrakorporeal Tedaviler

- Hemodiyaliz
- Sürekli düşük seviyeli diyaliz (SLED) ,
- Aralıklı hemofiltrasyon (IHF) ve hemodiafiltrasyon (UHDV)
- Sürekli renal replasman tedavi (CRRT)
- Hemoperfüzyon (HP)
- Terapötik Plazma değişimi (TPE) , exchange transfüzyon
- Periton diyalizi (PD)
- Albümin diyalizi
- Beyin omurilik sıvısı değişimi
- Ekstrakorporeal membran oksijenizasyonu (ECMO)

Table 1 | Number of ECTRs performed in the US, 2010–2014

Poison	Number of ECTRs performed
Ethylene glycol	2072
Lithium	1924
Salicylate	1520
Acetaminophen	959
Ethanol	423
Methanol	345
Metformin	319
Benzodiazepines	308
Cardiac glycosides	260
Calcium channel blockers	205
Valproic acid	183
Beta adrenergic antagonists	134
Atypical antipsychotics	130
Methadone	97
Oxycodone	86
NSAIDs	81
Tricyclic antidepressants	69
Cocaine	68
Heroin	67
Isopropanol	62

ECTR, extracorporeal treatment.

GHANNOUM, Marc, et al. Use of extracorporeal treatments in the management of poisonings. *Kidney international*, 2018.

GHANNOUM, Marc, et al. Use of extracorporeal treatments in the management of poisonings. *Kidney international*, 2018.

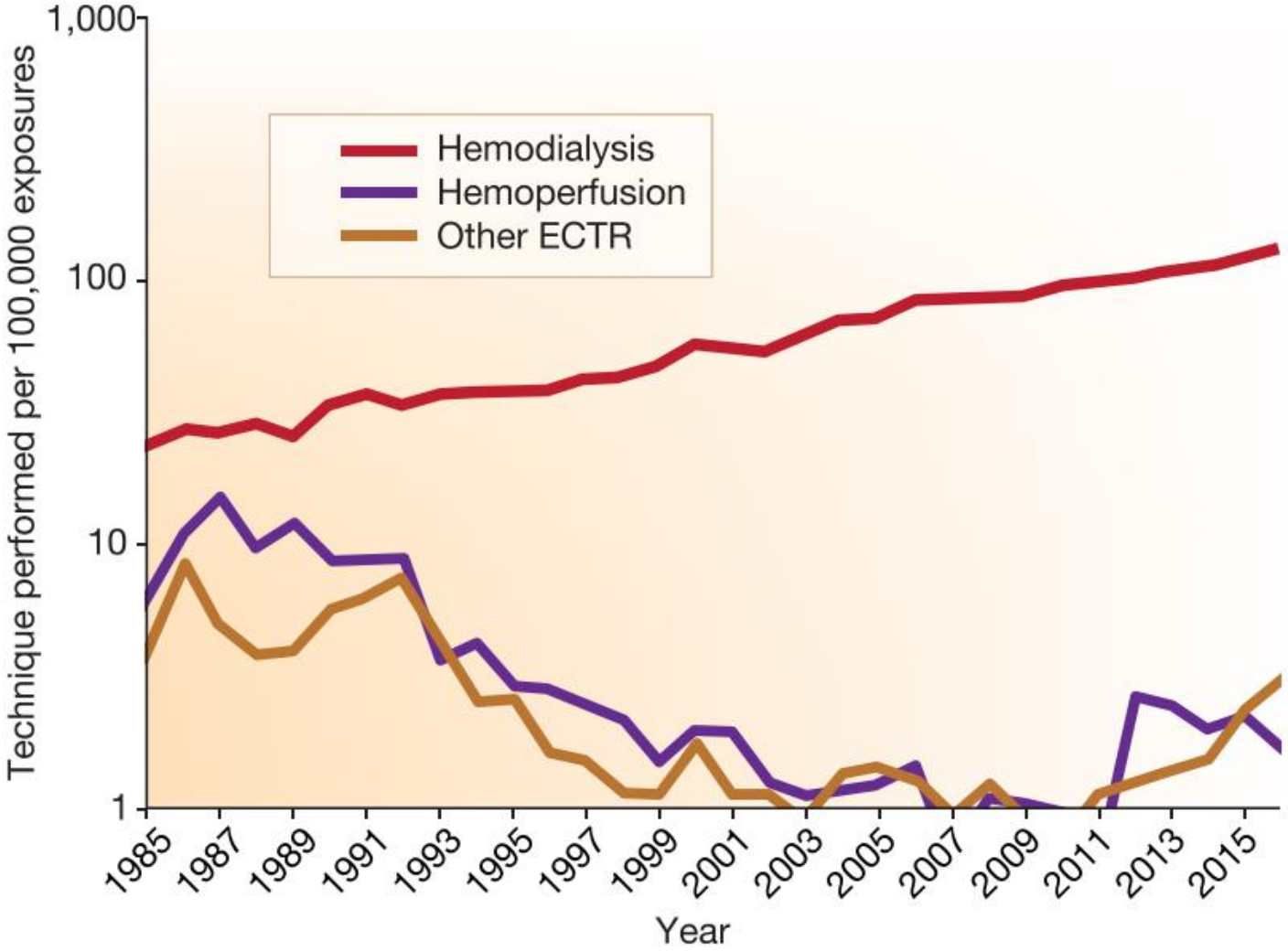


Figure 2 | US poison center trends in the use of hemodialysis, hemoperfusion, and other extracorporeal treatments.

Level of recommendation for ECTR according to the poison, as reviewed by EXTRIP

Recommendation against	Suggestion against	Neutral	Suggestion for	Recommendation for
Tricyclic antidepressants Digoxin		Phenytoin	Acetaminophen Carbamazepine	Barbiturates Lithium Methanol Metformin Salicylates Thallium Theophylline Valproate

ECTR, extracorporeal treatment.
Planned review has not yet been completed for *Amanita*, baclofen, bromates, chloroquine, dabigatran, dapsone, diethylene glycol, ethylene glycol, isoniazid, fluoride, isopropanol, methotrexate, organophosphate, paraquat, and quinine.

GHANNOUM, Marc, et al. Use of extracorporeal treatments in the management of poisonings. *Kidney international*, 2018.

Asetaminofen-Ekstakorporeal Tedavi

- **Karaciğer disfonksiyonu öncesinde yüksek asetaminofen kan düzeyleriyle beraber erken mitokondriyal disfonksiyon belirtileri**
- **(metabolik asidoz, erken koma ve artmış laktat düzeyleri) varsa ekstrakorporeal tedavi (aralıklı hemodiyaliz) önerilir.**

Karbamazepin-Ekstakorporeal Tedavi

- Karbamazepin **orta derecede dializabl**

–Tedaviye refrakter multipl nöbet varlığı,

–Hayatı tehdit eden aritmiler,

–Mekanik ventilasyon gerektiren solunum depresyonu veya uzamış koma,

– Multipl aktif kömür ve destek tedaviye rağmen yüksek karbamazepin düzeyi ile ısrarlı önemli toksisite varlığı.

- **İntermitten hemodiyaliz önerilen yöntem**
- intermitten hemoperfüzyon , sürekli renal replasman alternatif

- **Ghannoum M, Yates C, Galvao TF, Sowinski KM, et al.; EXTRIP workgroup. Extracorporeal treatment for carbamazepine poisoning: systematic review and recommendations from the EXTRIP workgroup. Clin Toxicol (Phila). 2014;52(10):993-1004.**

Dabigatranın Ekstrakorporeal tedavi

- Akut kanama sırasında dabigatranın temizlenmesi için bir strateji olarak önerilmesine rağmen,

dabigatran ile ilişkili, yaşamı tehdit eden diğerdurumlarda Ekstrakorporeal tedavi yararlı olabilir.

International Journal of Hematology
April 2017, Volume 105, Issue 4, pp 532–535 | Cite as

Dabigatran overdose: a case report of acute hepatitis. Extracorporeal treatment

Authors | Authors and affiliations

Mariagrazia Porru, Antonella Mameli, Maria E. Cianchetti, Mario Musu, Paola Schirru, Maria F. Ruberto, Doris Barcellona, Francesco Marongiu

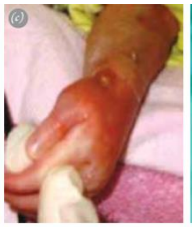
Case Report
First Online: 01 December 2016

Abstract

Dabigatran is an oral, direct thrombin inhibitor approved by international regulatory agencies for stroke prevention in patients with paroxysmal or persistent non-rheumatic atrial fibrillation (AF). The benefits of dabigatran are widely described, but its use in the geriatric population is not without risk. Chronic kidney disease is a common comorbidity with AF, and thus frequent checks of renal function in elderly patients are recommended. We report a case of dabigatran intoxication in an elderly man affected by heart failure and worsening renal function, who developed acute hepatitis and coma, which was successfully treated with continuous veno-venous hemodiafiltration. Although extracorporeal therapy has been suggested as a strategy for clearing dabigatran during acute bleeding, this approach may be useful in other dabigatran-related, life-threatening conditions, such as that described in this report.

Kalsiyum glukonat ekstravazasyonu

- Kalsiyum glukonat ekstravazasyonu, yumuşak dokuların nekrozu ve kalsifikasyonu gibi ciddi lezyonlara neden olabilen bir süreçtir.



- **Sodyum tiyosülfat ve hiyalüronidaz**, kalsiyum glukonat ekstravazasyonundan sonra kalsiyum birikimlerinin gelişmesini önler.

- COMPAÑA, Francisco Javier Pacheco, et al. The Use of Antidotes for Calcium Gluconate Extravasation: An Experimental Study in Mice. *Plastic and reconstructive surgery*, 2018, 142.3: 699-707.

Antidotların **Intraosseous** uygulanması

- digoxin immune FAB,
- sodium bicarbonate,
- calcium chloride,
- lipid emulsion,
- insulin,
- fomepizole
- hydroxocoablamin
- IM : atropine , pralidoxime

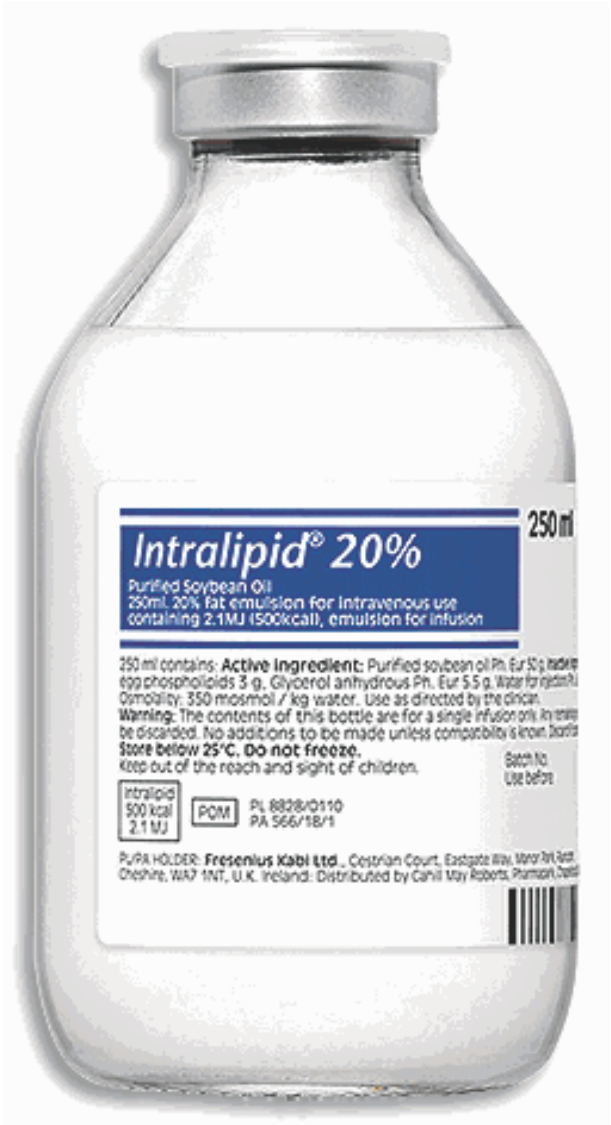
ELLIOTT, Audrée, et al. Intraosseous administration of antidotes–a systematic review. *Clinical Toxicology*, 2017, 55.10: 1025-1054.

Lipid emulsion

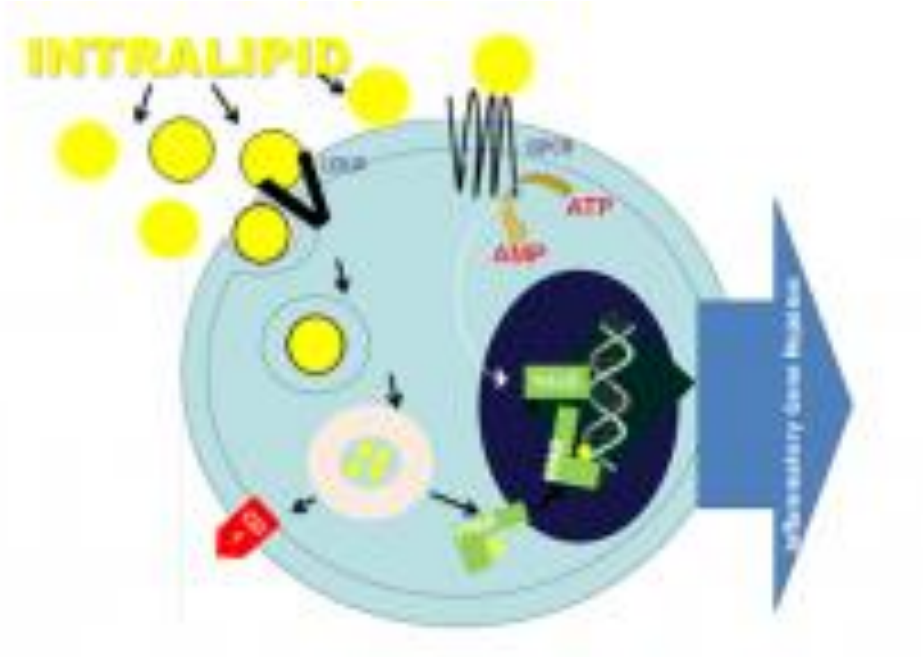
- Endikasyon:
- Lokal anestezik sistemik toksisitesi

(intravasküler uygulama/ Yüksek dozlarda kullanımı toksisitenin en sık nedenleridir)

İntravenöz Lipid Emülsiyonu



- Total parenteral beslenme amaçlı
- Lipofilik olan ilaç zehirlenmelerinde hemodinamik anstabil hastaların resüsitasyonunda etkin bir antidot



- Rotschild L, et al. Lipid emulsion in clinical toxicology. Scand J Trauma Resusc Emerg Med 2010;18:51.

Lipofilik İlaçlar

- Amlodipine • Verapamil • Metoprolol • Bupivacaine • Diphenhidramine • Propranolol • Tricyclic antidepressants • Organophosphates • Bupropion • Carvedilol • Quetiapine • Flecainide

Lipid infüzyonu;

- Lipid sink (lipid çamuru)
- Kalp kası için enerji Substratı
- İyon kanalları üzerine etkileri
- Myokard sodyum kanallarını blokajının kaldırılması
- Voltaja bağımlı çalışan kalsiyum kanallarından kalsiyumun içeri girişini artırır

Tedavi Protokolü

- İlk bolus dozu 1.5 ml/kg
- **Arrest söz konusu ise 3 doz tekrar edilebilir**
- **Her 5 dakikada/total 3 doz**
- 10- 12.5 (FDA) ml/kg üzerine çıkılmamalı
- Bolus süresi 15-30 dk.
- Ardından 0.25 ml/kg/saat infüzyon

(3 dakika için)

- **Sonra 0.025 mL/kg/dakika 6.5 saate kadar**

(trigliserid düzeyleri takip edilmeli 1000mg/dL altında olmalı)

Fettiplace MR, Akpa BS, Rubinstein I, Weinberg. Confusion About Infusion: Rational Volume Limits for Intravenous Lipid Emulsion During Treatment of Oral Overdoses. Ann Emerg Med 28 Feb 2015 [Epub ahead of print]

LE tedavisinden sonra

- Kreatinin
- Lipaz
- ALT
- CK
- bilirübin seviyeleri ölçülemezken
- kolorimetrik testlerle ölçülen serum glukoz seviyesi ve serum magnezyum ve albumin değerleri yanlış çıkar

- Grunbaum AM, et al. Clin Toxicol (Phila) 2012;50:812-7

Lipid emulsion

- Lokal anestezik sistemik toksisitesi
- İlaç etkili mi? III
- Tıbbi faydalar risklerden ağır basıyor mu? III
- Zaman bir Önemli Faktör? Evet
- Hastane stoklarında olmalı Evet
- Mevcutta hemen bulunmalı

Teşekkürler