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1. Klinik Toksikoloji Sempozyumu
28 Eylül 2005

Zehirlenmelerde Kanıta Dayalı Tıbbi Bakım

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Zehirlenmelerde Kanıta Dayalı Tıbbi Bakım

- 'Kanıta dayalı' kavramı
- Toksikolojide kanıta dayalı uygulamalar
- Zehirlenmelerde yaygın olarak uygulanan fakat henüz kanıta dayalı olmayan yaklaşımlar

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Kanıta Dayalı Tıp... yeni değil

- Galileo Galilei (1564-1642)

Bilimde, bir kişinin temel düşünmesi bin kişinin otoritesinden daha değerlidir.

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Otoriteye dayalı - Kanıtta dayalı

- Tedaviler:
 - Bireysel klinik deneyimlere bağılı
 - Tamamen patofizyolojiye dayalı
 - 'Herkesin bildiklerine' bağılı
- Mümkünse tedaviler:
 - tarafsız tekrarlanabilir araştırmalara bağılı
 - Patofizyoloji bilgisi gerekli fakat yeterli değil
 - Araştırma projeleri kanıtın sınıflandırılmasına göre yorumlanır

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Tedavi kararları konusunda 'inanıyorum ki' yeterli değil

- 20 yıldır post-menopozal estrogen

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Tedavi kararlar1 konusunda 'inan1yorum ki' yeterli deęil

- 20 yıldır post-menopozal estrogen
- Gözlemsel, hayvan alıřmalar1, temel laboratuvar alıřmalar1 yeterli deęildir
- Bu tip alıřmalar, hipotezleri oluřturmak için faydalıdır.

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Tedavi kararlar1 konusunda 'inan1yorum ki' yeterli deęil

- 20 yıldır post-menopauzal estrogen
- İzlemsel, hayvan alıřmalar1, temel laboratuvar alıřmalar1 yeterli deęildir
- Rasgele kontrollü alıřmalar !

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'Kanıtta dayalı' kavramı

Kategori	Kanıt tipi	Açıklama
• A	1A	homojen RKÇ'ların derleme
	1B	dar güvenilirlik aralığı olan RKÇ'lar
	1C	önce-sonra : tümü-hiç
• B	2A	homojen kohort çalışmalarından derleme
	2B	bir kohort ya da düşük kalitesi olan RKÇ
	2C	'sonlanım' çalışmaları
	3A	olgu-kontrol çalışmalarından derleme
	3B	bir olgu-kontrol çalışması
• C	4	olgu sunumları
• D	5	çalışmaya dayalı olmayan 'eksper' sözleri
• Z	6	abstraktlar

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Zehirlenmelerde kanıt... bol bol C ve D sınıf önerileri

- the text. If the concentration of the product is not known, it should be assumed to be a concentrated (>20%) product (Grade C).
7. A witnessed "taste or lick" only in a child, or an adult who unintentionally drinks and then expectorates all of a concentrated product without swallowing, does not need referral (Grade C).
 8. Referral is not needed if it has been more than 24 hours since a potentially toxic unintentional exposure, the patient has been asymptomatic, and no alcohol was co-ingested (Grade D).
 9. Gastrointestinal decontamination in the out-of-hospital setting with ipecac syrup, gastric lavage, or activated charcoal is not recommended. Transportation to an emergency department should not be delayed for any decontamination procedures (Grade D).
 10. Patients meeting referral criteria should be evaluated at a hospital emergency department rather than a clinic. A facility that can quickly obtain an ethylene glycol serum concentration and has alcohol or fomepizole therapy available is preferred. This referral should be guided by local poison center procedures and community resources (Grade D).

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Zehirlenmelerde arařtırmaların zorlukları

- Bir 'Zehirlenme Skalası' yok
 - Binlerce madde var
 - her madde için ayrı bir skala oluşturmak pratik değil
 - Ne ölçülür:
ölüm? Ventilatöre baęlı günler? Karacięer markerleri? Acil servis veya hastanede kalıř süresi? Kan basıncı?

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Zehirlenmelerde arařtırmaların zorlukları

- Hasta onamı nasıl, ne zaman alınacak?

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Toksikolojide kanıtın önemi

- İlaça bağlı yan etkileri - ölüm
– Vioxx...
- Fabrika etrafında bir hastalık ortaya çıkmış - atıklarına bağlı mı değil mi?
- Çocuğun özürülü olması ilaca bağlı mıydı?

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CDC Home Search Health Topics A-Z

CDC **MMWR**TM

Recommendations and Reports
January 14, 2005 / 54(RR1);1-24

Case Definitions for Chemical Poisoning

Mercury (Organic)
Clinical Description

Mar Although ingestion of organic mercury is the most typical route of organic mercury toxicity, toxicity might also result from inhalation and dermal exposures, particularly with dimethylmercury. Symptoms of toxicity are typically delayed for >1 month after organic mercury exposure and usually involve the central nervous system. These symptoms might include paresthesias, headaches, ataxia, dysarthria, visual field constriction, blindness, and hearing impairment (58,63-66).

Patel, MD

Laboratory Criteria for Diagnosis

Biologic. A case in which whole blood mercury levels (>10 µg/L) (20,58) are detected, as determined by a commercial laboratory. Urine mercury levels are not useful in evaluating organic mercury poisoning.

Or,

Environmental. Detection of mercury in environmental samples, as determined by NIOSH or FDA.

Case Classification

Suspected. A case in which a potentially exposed person is being evaluated by health-care workers or public health officials for poisoning by a particular chemical agent, but no specific credible threat exists.

Probable. A clinically compatible case in which a high index of suspicion (credible threat or patient history regarding location and time) exists for organic mercury exposure, or an epidemiologic link exists between this case and a laboratory-confirmed case.

Confirmed. A clinically compatible case in which laboratory tests have confirmed exposure.

The case can be confirmed if laboratory testing was not performed because either a predominant amount of clinical and nonspecific laboratory evidence of a particular chemical was present or a 100% certainty of the etiology of the agent is known.

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Toksikolojide ‘kanıta dayalı’ uygulama alanları

Thresholds in Toxic Responses to Chemicals and Radiation and Their Use in Risk Assessment and Regulation

Prepared By:

Richard J. Bull, Ph.D.
MoBull Consulting

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Droperidolun piyasadan çekilmesi: kanıta dayalı bir eylem değildi

Droperidol and the Black Box Warning

To the Editor:

We have read with interest the article by Kao et al¹ and the commentary by Meyer² (April 2003; articles #110 and #111) regarding droperidol. As frequent users of droperidol in our emergency department, we also were curious about the data that prompted the issuance of a black box warning on the product by the US Food and Drug Administration (FDA). After independently conducting an institutional review board–exempted review of data obtained from the FDA through 2 requests under the Freedom of Information Act, we reached the same conclusions about the poor

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Toksikolojide kanıtın önemi

- “X maddeye bağlı Y sonuçları oldu”
 - Kaynak
 - Maruz kalma (temas var mıydı? ne kadar?)
 - Kişiyeye geçen doz (maruz kalmadan çok farklı)
 - Bulgu veya hastalık nedir?

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Toksikolojide KDT'nin sorularında olması gereken bilgiler

- Etkiler
 - Akut? Subkronik? Kronik?
 - Lokal? Sistemik?
 - Reversibl? Irreversibl?
 - Kesin tanı? Yalnız semptom veya bulgu?
- Maruz kalma yolları
 - Hava? Su? Toprak? Gıda? Tek madde? karışım?
 - Süre
 - Süreyen? Arada sırada?
 - Maruz kalma sürekli aynı seviyede?

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Toksikolojide KDT'ın sorularında olması gereken bilgiler

- Doz
 - Akut? Kronik?
 - Dozaj hızı
 - Dozaj süresi
 - Değişen? Aynı?
 - Ölçme: Konulan? Emilen? Hedef organa geçen?
- Diğer
 - İnsan? Hayvan?
 - In vitro? In vivo?
 - Deneysel? Gözlemsel?

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'Literatür'ye destekliyor'

- Özet makalesi: otoriterler diyor
 - Otorite ne kadar konuşmacı olarak gözüküyorsa sözleri o kadar 'ağır'
 - Olumlu araştırma sonuçları
 - Ekspertlerin uzlaşma kararları
- = ekspertlere göre tıbbi bakım

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Fakat 'literatür destekliyor' sistemi yetersiz kaldı

- Sistematik bir şekilde literatürü incelemek
- Sigorta firmaların 'uzlaşma kararlarından' şüphe
- Hekimler, mevcut olan araştırma sonuçlarını uygulamıyordu

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Kanada'daki ilaç firmalarının 'eksper' kitabı

Salty broth for salicylate poisoning? Adequacy of overdose management advice in the 2001 *Compendium of Pharmaceuticals and Specialties*

Jeffrey R. Brubacher, Roy Purssell, Debra A. Kent

Abstract

Background: The *Compendium of Pharmaceuticals and Specialties (CPS)* is a collection of monographs written by pharmaceutical companies and published by the Canadian Pharmacists Association. The *CPS* is widely available and is consulted frequently by Canadian physicians. We examined overdose management advice contained in the *CPS* to see whether it reflects current standards.

Methods: We restricted our review to 10 classes of medication for which an overdose is frequently fatal: acetaminophen, β -blockers, calcium-channel blockers, digoxin, lithium, opioids, salicylates, tricyclic antidepressants, theophylline and

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İlaç firmalarının 'eksper' kitabı

Table 2: Ratings of the monographs in terms of warning against contraindicated interventions for overdose management

Drug (no. of monographs)	Rating:* no. (and %) of monographs			
	Excellent	Good	Fair	Poor
Acetaminophen (22)	0	14	1	7
ASA (12)	0	2	4	6
β-Blockers (19)	0	0	0	19
Calcium-channel blockers (13)	0	7	2	4
Digoxin (1)	0	0	1	0
Lithium (5)	0	0	0	5
Opioids (32)	1	26	0	5
Tricyclic antidepressants (6)	1	0	1	4
Theophylline (aminophylline) (7)	0	0	0	7
Valproic acid (2)	0	2	0	0
Total	2 (2)	51 (43)	9 (8)	57 (48)

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Avukatlara yönelik toksikoloji kılavuzu

Reference Guide on Toxicology

BERNARD D. GOLDSTEIN AND MARY SUE HENIFIN

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CONTENTS

- I. Introduction, 403
 - A. Toxicology and the Law, 404
 - B. Purpose of the Reference Guide on Toxicology, 404

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Uzlaşma

- Uzlaşma, 'bu konu halledilmiştir, tartışmayalım' deyip bir yöntem
- Konsensus ve bilim arasında hiç bir ilişkisi yok.
- Bilimde tekrarlanabilecek sonuçlar önemlidir

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Dioksin diabete neden olur mu?

- İlk rapor: çalışmaların yarısından fazla 'pozitif' veya 'hafif pozitif'

Table 6 Dioxin and diabetes: example of an evidence-based result analysis

Reference	Exposure	Total subjects	Subjects with diabetes	Association shown?	Outcome measure
1	High	55	11	+	GTT
2	High	200		∅	Glucose
3	High	134		±	Glucose
4	High	158	10	-	Diabetes
5	Medium	989	146	+	Diabetes, GTT
6	High	281	26	±	Diabetes, glucose
7	High		132	+	Mortality
8	High		33	±	Mortality
9	High		89	∅	Mortality
10	Low	1197	169	+	Diabetes, GTT
11	Low-mod	69		+	Insulin, GTT

Son rapor: yakından bakıldığında hiç bir 'pozitif' çalışma çok iyi değildi

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İlaçla ilgili araştırma başlanmadan önce yapılması gereken literatür taraması

- Guidelines oluşturulmasında kullanılan kurallar

JHU SOM IRB GUIDELINES FOR DETERMINING AN ADEQUATE AND COMPREHENSIVE LITERATURE SEARCH OF DRUG SAFETY FOR USE BY INVESTIGATOR AND INSTITUTIONAL REVIEW BOARDS

- An adequate and comprehensive literature search for drug safety shall be defined as one that produces sufficient information for the investigator and the Investigational Review Board (IRB) to determine if the drug is sufficiently safe for use in the subjects of the study.
- The adequacy and comprehensiveness of the literature search for drug safety will vary considerably depending on the status of the drug. The adequacy and comprehensiveness spectrum extends from the simplest (for a marketed drug used in a manner approved by the FDA) to the most complex (for a drug that is not approved by the FDA for any condition). The latter situation places the entire responsibility for adequacy and comprehensiveness on the investigator and the IRB.

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Tarama yöntemi net belirlenmeli

LITERATURE SEARCH LOG, SUMMARY, AND BIBLIOGRAPHY

LITERATURE SEARCH LOG

For each source searched include the following information:

Date Search Conducted:

Name of Database:

Host:

Latest update available:

Years Searched:

Please attach a printout of your search strategy (do NOT re-type your search terms on this form – print off the original strategy and attach it to this form).

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Tıbbi literatürü taramak

Table 1: POCT for Drugs and Ethanol Literature Search – November 15 2003 ¶

Databases Searched: ¶

Medline 1966 – November 2003 ¶

Embase ¶

Cochrane Database ¶

¶

Search Criteria ¶

(Point of Care Testing OR Near Patient Testing OR) ¶

AND (Drugs OR Opiate* OR Cocaine OR Cannabis OR Ethanol OR Alcohol OR

Benzodiazepine* OR Amphetamine* OR MDA OR MDMA OR Ecstasy OR Drugs of Abuse OR Substance Abuse) ¶

Abstracts → = 151 papers ¶

Systematic Review → = 100 papers ¶

Citations in final recommendation → = 81 papers ¶

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Konferanslarda sunulan raporların birçoğu yayınlanmıyor

¶ There is considerable evidence to suggest that a significant proportion of reports of trials published in conference abstracts do not reach full publication (see Scherer RW, Langenberg P. Full publication of results initially presented in abstracts [Cochrane Methodology Review]. In: The Cochrane Library, Issue 3, 2001. Oxford: Update Software. ¶

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Tanı - Tedavi Kılavuzları “Clinical Guidelines”... kanıta dayalı sonuçlarla yapılır

- Soruyu belirlemek
- Soru ile ilgili makalelerin toplanması
 - Tarama tam yapılmalı
 - Hakemli dergilerden
- Değerlendirilip kaliteye göre sıralanması
-

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Kanıta dayalı...

Evidence Based Point of Care Testing for Drugs and Ethanol

¶

¶

Submitted on behalf of the committee by

Dr Ian D. Watson

Members:

Dr Ian D Watson, PhD, FRCPath. University Hospital Aintree, Liverpool, UK

Dr Bertholf, PhD, DABCC, FACB, University of Florida, Jacksonville, FL, USA

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Etilen glikol alımı... ve öneriler

Poison Center	Recommend ipecac?	Recommend gastric lavage?	Recommend charcoal?	Observe at home dose	Referral (toxic) dose	Toxic serum ethylene glycol (mg/dL)
1	No	If <1 hr after ingestion	No	Accidental taste or <mouthful	2 cc/kg or >mouthful	25
2				If estimated serum level <20 mg/dL	Estimated serum level >20 mg/dL	20
3	Yes, if <20 minutes from ingestion	If <1 hr				20
4						20
5		If <1 hr		Adult ≤mouthful of "50% diluted" product	Adult: >mouthful of >50% solution. -All children	20
6		If <2 hr	No		Treat ≥0.2 cc/kg 100%	20
7	For large ingestion if ED >30 minutes away.			"iron-clad lick or taste," <0.5 mL total	-Adult: 15 cc of 100% solution or one mouthful -Child: 3-5 cc or >"taste"	
8		Nasogastric	"Consider"	Estimated peak	Estimated peak	25

Zehrin emilmesini azaltmak

- Mide lavajı
 - 38 F orogastrik boru
 - Trendelenburg
 - 1-2 litre s₁v₁

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Zehrin emilmesini azaltmak

- Mide lavajı
 - 38 F orogastrik boru
 - Trendelenburg
 - 1-2 litre s1v1

Continuing Controversy on Gut Decontamination

One of the most hotly debated problems in emergency medicine is whether, when, and how to remove or neutralize ingested poisons. Many physicians are bemused by the commonly contradictory recommendations that they receive from poisons

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Zehrin emilmesini azaltmak

- Mide lavajı
 - 38 F orogastrik boru
 - Trendelenburg
 - 1-2 litre s1v1
- Merigian et al...

Prospective Evaluation of Gastric Emptying in the Self-Poisoned Patient

KEVIN S. MERIGIAN, MD,* MARTIN WOODARD, MD,†
JERRIS R. HEDGES, MD,‡ JAMES R. ROBERTS, MD,§
ROGER STUEBING,¶ MITCHELL C. RASHKIN, MD¶

of gastric emptying (GE) and me in acutely self-poisoned (BOP) were treated using an on cognitive function exami- Asymptomatic patients (n = 10) and asymptomatic patients (n = 357) ing days, alert patients had nts received gastric lavage. nemptying days, symptom- nical deterioration occurred if GE. AC use did not alter

complication rate.⁹ These studies support reexamination of the use of GE during care of the acutely self-poisoned patient, whether the patient presents without symptoms or with significant cognitive or vital sign abnormalities.

To study the efficacy of GE and AC in acutely overdosed patients, we performed an 18-month controlled prospective alternate-day treatment study. We sought to determine (A) if asymptomatic acutely self-poisoned patients would clinically deteriorate if managed without a GE procedure, (B) if oral AC altered the clinical outcome of asymptomatic poisonings, and (C) if the use of GE procedures significantly altered the

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Prospective Evaluation of Gastric Emptying in the Self-Poisoned Patient

Merigian et al.

- A.K. ile absorbe ediliyorsa...
 - A.K. ve destekleyici bakım
- A.K. ile absorbe edilmiyorsa
 - Alımdan sonra 60 dk içinde gelmişse lavaj ve destekleyici bakım
- [tüm barsak lavajı]

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Zehirlenmiş hasta, şunlar hariç:

Parasetamol
Mantar
Ağır metaller
Demir
MAO inhibit.
Metanol
Etilen glikol



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Prospective Evaluation of Gastric Emptying in the Self-Poisoned Patient Merigian et al.

BLE 6. Most Common Complications in Admitted Symptomatic Patients (Prevalence for Admitted Cases)

	Aspiration Pneumonia	Hypotension	Dysrhythmias	Pulmonary Edema	Seizures
GE + AC (n = 163) (No. adm = 94)	8 (8.5%)*	9 (9.6%)	13 (13.8%)	11 (11.7%)	9 (9.6%)
AC (n = 194) (No. adm = 112)	0 (0.0%)*	5 (4.5%)	12 (10.7%)	9 (8.0%)	4 (3.6%)

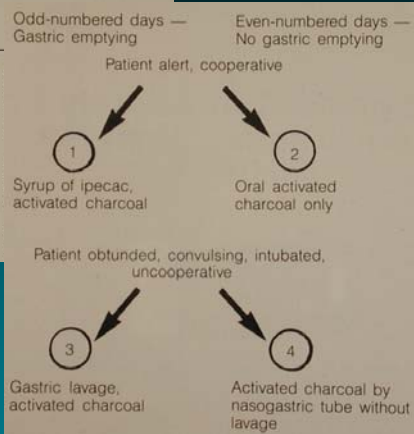
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Management of Acutely Poisoned Patients Without Gastric Emptying

During an 18-month period, 592 acute oral drug overdose patients were studied prospectively in a controlled, randomized fashion to determine the efficacy of gastric emptying procedures in altering clinical outcome. Patients presenting on even-numbered days had no gastric emptying procedures performed, and they were compared to patients presenting on odd-numbered days who received either syrup of ipecac or gastric lavage. Patients were carefully followed for evidence of subsequent clinical improvement or deterioration after initial management. Syrup of ipecac did not significantly alter the clinical outcome of patients who were awake and alert on presentation to the emergency department (ED). Gastric lavage in obtunded patients led to a more satisfactory clinical outcome (P < .05) only if performed within one hour of ingestion. Gastric emptying procedures in the ED for initial treatment of drug overdose are generally not of benefit unless gastric lavage is performed within one hour of ingestion in obtunded patients. [Kulig K,

30-40 F orogastrik tüp (hortum)

1 ve 2, 3 ve 4 no'lu gruplar
arasında fark görülmemiştir.



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Effect of Physostigmine and Gastric Lavage in a Datura Stramonium-Induced Anticholinergic Poisoning Epidemic

PHILIP SALEN, MD, RICHARD SHIH, MD, PAUL SIERZENSKI, MD

This study examines the impact of the administration of physostigmine and of nasogastric evacuation of Jimsonweed seeds on intensive-care unit (ICU) use and the length of stay in the hospital after Jimsonweed poisoning. Clinical data for this retrospective study were gathered from records of consecutive patients treated for Jimsonweed poisoning from September to November 1997. Descriptive statistics were used to analyze im-

epines for the treatment of delirium.⁴ The objective of this study was to evaluate the effect of physostigmine and benzodiazepines alone on inte-

necessitated admission of 13 patients to the ICU. The administration of physostigmine did not reduce admissions to the ICU ($P = 0.54$) or reduce length of stay in the hospital ($P = 0.45$) compared with the use of benzodiazepines alone. Nasogastric lavage was performed in 14 (82%) and seeds were recovered in 8 (57%) of those lavaged. The successful removal of Jimsonweed seeds did not decrease ICU use rates ($P = 0.68$) or shorten length of stay in the hospital compared with not recovering seeds ($P = 0.85$). The use of physostigmine and the successful nasogastric lavage of Jimsonweed seeds did not result in decreased intensive-care use or shorter length of stay in the hospital for Jimsonweed-induced anticholinergic toxicity. (Am J Emerg Med 2003;21:316-317. © 2003 Elsevier Inc. All rights reserved.)

Gastrik lavajın yeri

- Ölümcül miktar (?)
- Alımdan hemen sonra (?)
- Maddenin %10'u alınırsa (?)

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Gatrik lavaj: 2004

Position Paper: Gastric Lavage[#]

American Academy of Clinical Toxicology*
European Association of Poisons Centres and Clinical Toxicologists**

ABSTRACT

Gastric lavage should not be employed routinely, if ever, in the management of poisoned patients. In experimental studies, the amount of marker removed by gastric lavage was highly variable and diminished with time. The results of clinical outcome studies in overdose patients are weighed heavily on the side of showing a lack of beneficial effect. Serious risks of the procedure include hypoxia, dysrhythmias,

Zehrin atılımını artırmak

- Forse diürez
- Asit / alkali diürez
- Ardarda aktif kömür

Multiple Doses of Activated Charcoal: Time for Reappraisal?

Multiple-dose charcoal therapy has become a popular treatment for many overdoses. It is generally perceived as a simple, inexpensive, effective, and safe procedure that decreases morbidity and mortality by enhancing drug excretion. However, increased drug clearance has been shown definitively for only a few drugs, and improved outcome has not been demonstrated conclusively for any overdose. Recently, there have been several reports of complications due to this intervention. The role of this pharmacologic curiosity in the management of the acutely poisoned patient requires reassessment. Tenenbein M: Multiple doses of activated charcoal: Time for

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Received for publication

MD, DABEM
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Aktif kömür: verilip yutulmamış

Activated charcoal: the untold story

275 hasta, 47 hasta alımından <1 saat;

Richard M. Lynch, Robert Robertson

Bunlardan yalnız 3 hasta tüm AK yutmuş

Introduction. To identify the prevalence and appropriateness of prescribing activated charcoal in the management of acute poisoning and to document patient compliance with treatment. *Methods.* A prospective study was conducted, between October 1998 and September 1999, on patients attending our accident and emergency department, with a history of overdose. Overdoses were classified as potentially toxic or non-toxic according to the history and/or information received from the National Poisons Information Service. *Results.* Two hundred and seventy five patients presented following overdose; 17% within one hour, 102 were prescribed charcoal (37.1%) but of these, 40 (39%) refused it, and of the 62 patients (61%) who accepted charcoal only 15 (24.2%) took all that was prescribed. Patients were 5.4 times more likely to take charcoal if they had taken a potentially toxic overdose. Of those who presented within one hour and were judged to have taken a potentially toxic overdose, only three patients took the full-prescribed amount. *Conclusion.* We report a substantially greater proportion of patients (39%) refusing charcoal than previously reported (9.9%). The widespread availability of TOXBASE should help redress this discrepancy.

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Aktif kömür ile ilgili yalnız iki klinik çalışma var. Çoğu...

- Hayvanlarda... Gönüllü insanlarda...
 - Daha fazla, daha hızlı atılım
 - Ama gerçek hastalarda morbidite – mortalite konusunda bir değişiklik var mı?
- A.K.ün bağlayamadıkları: metaller, lityum, demir, asitler, alkaliler, alkoller

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1. Klinik Toksikoloji Sempozyumu
28 Eylül 2005

Gönüllü, 3 gm parasetamol, 3 saat sonra oral süperaktif kömür

TABLE 1. Acetaminophen (APAP) Level Results (means \pm SD [95% confidence interval])

	No.	APAP Level ($\mu\text{g/mL}$) (A)	Weight-Corrected APAP Level ($\mu\text{g/mL} \times \text{kg}$) (B)	Weight- and Dose-Corrected APAP Level ($\mu\text{g/mL}$ per mg/kg) (C)
Overall 4-hour levels				
SAC	22	10.8 \pm 4.6 (8.9-12.7)	797 \pm 303 (671-924)	0.30 \pm 0.10 (0.25-0.34)
Controls	24	18.5 \pm 8.2 (15.3-21.8)	1096 \pm 447 (917-1275)	0.39 \pm 0.13 (0.34-0.44)
P value		<.001	.012	.01
Overall 7-hour levels				
SAC	22	1.7 \pm 1.8 (1.0-2.5)	130 \pm 125 (78-183)	0.05 \pm 0.04 (0.03-0.07)
Controls	24	6.1 \pm 4.8 (4.2-8.1)	362 \pm 286 (248-477)	0.13 \pm 0.09 (0.09-0.16)
P value		<.001	.001	.001

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Tek doz aktif kömür...

Single-Dose Oral Activated Charcoal in the Treatment of the Self-Poisoned Patient: A Prospective, Randomized, Controlled Trial

2002

Kevin S. Merigian [1*](#); Kari E. Blaho [2](#)

Oral activated charcoal (OAC) is a universally accepted treatment of the overdose patient. Although the benefits of OAC have been suggested, there are no conclusive clinical data indicating that OAC affects outcome in overdose patients. This study was a prospective, randomized, controlled trial to determine the effects of OAC treatment in the self-poisoned adult patient. Adult patients presenting to the emergency department (ED) with a history of oral overdose were assigned to treatment with OAC (50 g) or supportive care only on an even-odd day protocol. Patients did not undergo gastric evacuation procedures in the ED. The outcome measures were clinical deterioration, length of stay in the ED or hospital, and complication rate. Over a 24-month period, 1479 patients were entered into the study. There were no significant differences in outcome parameters between the OAC treatment group and controls when comparing the length of intubation time, length of hospital stay, and the complication rates associated with the overdose. There was a higher incidence of vomiting and longer length of ED stay associated with OAC treatment. The results of this study indicated that oral drug overdose patients do not require gastric evacuation or charcoal administration. OAC provided no additional benefit to supportive care alone, was associated with a higher incidence of vomiting and a longer length of ED stay, and did not improve clinical outcome.

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28 Eylül 2005

A randomized clinical trial of activated charcoal for the routine management of oral drug overdose

G.M. COOPER¹, D.G. LE COUTEUR², D. RICHARDSON³ and N.A. BUCKLEY⁴

From the ¹Pharmacy, University of Canberra, Bruce, ²Centre for Education and Research on Ageing and ANZAC Research Institute, University of Sydney, Concord Repatriation General Hospital, Concord, and Departments of ³Emergency Medicine and ⁴Clinical Pharmacology and Toxicology, Canberra Clinical School, The Canberra Hospital, Canberra, Australia

Received 23 November 2004 and in revised form 23 June 2005

Summary

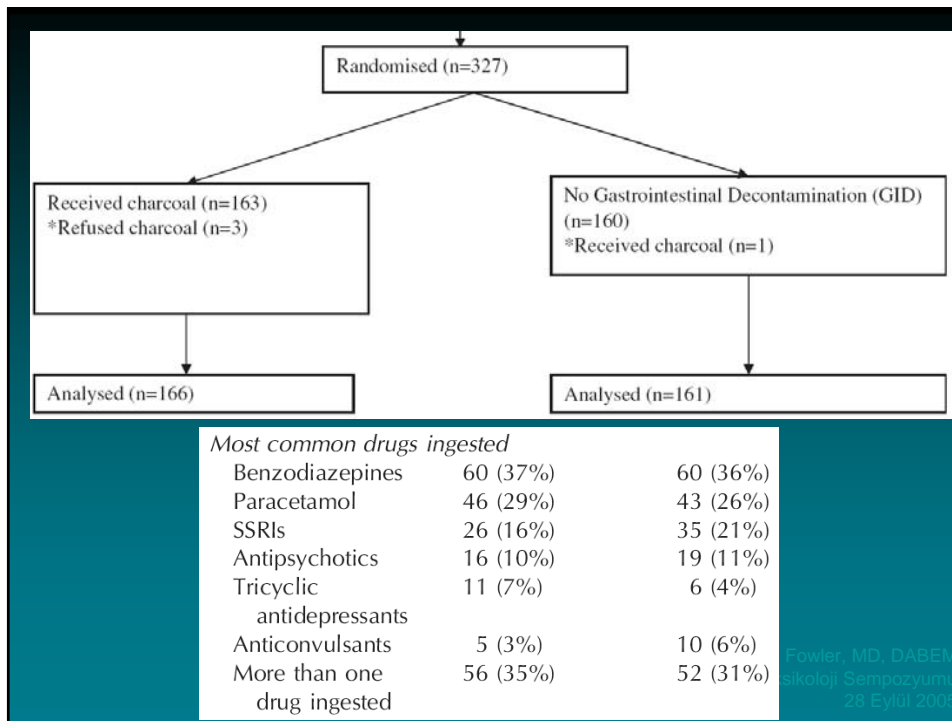
Background: Activated charcoal (AC) is commonly used for the routine management of oral drug overdose.

Aim: To determine whether the routine use of activated charcoal has an effect on patient outcomes.

Design: Randomized controlled unblinded trial.

Methods: We recruited all adult patients presenting with an oral overdose at The Canberra Hospital, excluding only transfers, late presenters, those

excluded from the trial. Only seven were excluded due to the severity of their ingestion. The most common substances ingested were benzodiazepines, paracetamol and selective serotonin reuptake inhibitor antidepressants. More than 80% of patients presented within 4 h following ingestion. There were no differences between AC and no decontamination in terms of length of stay (AC 6.75 h, IQR 4–14 vs. controls 5.5 h, IQR 3–12; $p=0.11$) or secondary outcomes



Primer sonlanımlar: kalış süresi ve GKS

Table 2 Primary outcome of length of stay (LOH, hours): overall and in subgroups according to time to presentation and Glasgow Coma Score (GCS)

Subgroup	No gastrointestinal decontamination	Charcoal	p (Mann Whitney)
Overall	5.5 (3.0–12.0)	6.8 (4.0–14.0)	0.11
Unknown ingestion time (n=29)	5.0 (3.0–9.0)	7.0 (4.0–24.0)	0.24
≤2 h post ingestion (n=189)	5.0 (3.0–9.8)	6.0 (4.0–12.0)	0.33
2–4 h post ingestion (n=57)	8.0 (3.0–16.0)	6.0 (4.0–16.5)	0.50
>4 h post ingestion (n=52)	7.5 (3.3–14.0)	9.5 (4.5–18.5)	0.36
GCS 15 (n=234)	5.0 (3.0–11.5)	5.8 (4.0–12.0)	0.09
GCS <15 (n=93)	9.0 (5.0–28.0)	12.0 (4.5–36.0)	0.52

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Aktif kömür: 2004

Abundant in vitro binding studies, in vivo mortality studies, volunteer studies, and comparison studies of overdose patients have demonstrated the capacity of AC to adsorb numerous toxic compounds and decrease their systemic absorption [2,3,5,6]. However, controlled studies showing clear clinical benefits from the administration of AC to poisoned patients remain sparse [7-9].

weight. Charcoal does not bind to metals (eg, iron and lithium) or to alcohols or caustics/corrosives.

Conclusion: Charcoal should not automatically be administered to every patient presenting with an overdose. The benefits (decreased systemic delivery of the drug) must be weighed carefully against the risks (aspiration of vomitus and charcoal).

EM
TM
28 Eylül 2008

Tüm barsak lavajı: 2004

Position Paper: Whole Bowel Irrigation[#]

American Academy of Clinical Toxicology*
European Association of Poison Centres and Clinical Toxicologists**

ABSTRACT

Whole bowel irrigation (WBI) should not be used routinely in the management of the poisoned patient. Although some volunteer studies have shown substantial decreases in the bioavailability of ingested drugs, no controlled clinical trials have been performed and there is no conclusive evidence that WBI improves the outcome of the poisoned patient. Based on volunteer studies, WBI should be considered for potentially toxic ingestions of sustained-release or enteric-coated drugs particularly for those patients presenting greater than two hours after drug ingestion. WBI should be

CO zehirlenmesinden sonra, geç nöropsikiyatrik sorunlar

Study objective: Carbon monoxide (CO) poisoning is a major clinical problem. The risk of morbidity and the most effective treatment have not been clearly established. We measured the incidence of delayed neurologic sequelae in a group of patients acutely poisoned with CO and tested the null hypothesis that the incidence would not be affected by treatment with hyperbaric oxygen (HBO).

Design: We conducted a prospective, randomized study in patients with mild to moderate CO poisoning who presented within 6 hours. Patients had no history of loss of consciousness or cardiac instability.

Interventions: The incidence of DNS was compared between groups treated with ambient pressure 100% oxygen (2.8 ATA for 30 minutes followed by 2.0 ATA oxygen for 90 minutes). DNS were defined as development of new symptoms after oxygen treatment plus deterioration on one or more subtests of a standardized neuropsychological screening battery.

Results: In 7 of 30 patients (23%), DNS developed after treatment with ambient-pressure oxygen, whereas no DNS developed in 30 patients after HBO treatment ($P < .05$). DNS occurred 6 ± 1 (mean \pm SE) days after poisoning and persisted 41 ± 8 days. At follow-up 4 weeks after poisoning, patients who had been treated with ambient pressure oxygen and had not sustained DNS exhibited a worse mean score on one subtest, Trail Making, compared with those treated with HBO and with a control group matched according to age and education level. There were no differences between the control group and the hyperbaric oxygen group.

Conclusion: DNS after CO poisoning cannot be predicted on the basis of a patient's clinical history or CO level. HBO treatment decreased the incidence of DNS after CO poisoning.

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Hiperbarik oksijen ile daha az...

Study objective: Carbon monoxide (CO) poisoning is a major clinical problem. The risk of morbidity and the most effective treatment have not been clearly established. We measured the incidence of delayed neurologic sequelae in a group of patients acutely poisoned with CO and tested the null hypothesis that the incidence would not be affected by treatment with hyperbaric oxygen (HBO).

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CO kan düzeyi ve semptomlar: maruz kalma süresine göre

Relationship between the measure of ambient carbon monoxide (CO) level, symptoms of poisoning and the carboxyhaemoglobin level

F. Van Trimpont

SMUR Mons-Borinage, Emergency Ward, CHU Ambroise Pare, Boulevard Kennedy 2, 7000 Mons, Belgium

On the scene, SMUR team, three ambulances and a fire truck were faced with 21 CO poisoning cases (without a portable expired CO tester to objective exposure). The ambient CO measured by the firemen in the three incriminated rooms in relation with the symptoms was used to allow the triage of the victims in the neighbouring hospitals in order to decide possible transfers to the hyperbaric chamber. **Results:** The patients might be divided in three groups:

	Group 1 (n = 8)	Group 2 (n = 8)	Group 3 (n = 5)
ppm measures	1135	360	440
Length of stay (min)	30 (locker 1)	30 (locker 2)	5 (toilets)
Symptoms	Headache, dizziness, nausea	Dizziness, nausea	None
HbCO (%) levels of different victims	24.9 19.5 22 30.4 21 25 27.5 22	10.6 5.7 9.8 6 4 6 16.7 18.8	1.3 2 3 0.7 3
Average level of HbCO (%)	24	9.7	1.4

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CO ve normobarik oksijen tedavisi

- Geriye dönük, 1 yılda 4 hasta belirlenmiş
- 1 yıl sonra bütün nöropsikiyatrik test sonuçları normal sınırlarda idi.
- HBO'yu kullanmadan normal sonuçlar elde edilebilir

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Etilen glikol alımı (hastane öncesinde)

Is a self-harm, malicious, abuse or misuse intent suspected?	YES → refer to emergency department.
NO ↓	
Is patient symptomatic? (e.g., lethargic, dizzy, vomiting)	YES → refer to emergency department.
NO ↓	
Did patient ingest a potentially toxic dose?	YES → refer to emergency department.
1. For "concentrated" products (>20%):	
• Child (age <6 years): more than a witnessed taste or lick?	
• Adult: one "swallow" (10-30 mL) or more?	
2. For very dilute solutions (<20%):	
• More than calculated mL/kg toxic dose (Formula 2)?	
3. An unknown amount, unknown concentration, or unable to estimate maximum amount ingested?	
NO ↓	
Is a child's home situation of concern (e.g., family/caregiver seems unreliable)?	YES → consider referral to emergency department.
NO ↓	

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Etilen glikol alımı... ve öneriler

Poison Center	Recommend ipecac?	Recommend gastric lavage?	Recommend charcoal?	Observe at home dose	Referral (toxic) dose	Toxic serum ethylene glycol (mg/dL)
1	No	If <1 hr after ingestion	No	Accidental taste or <mouthful	2 cc/kg or >mouthful	25
2				If estimated serum level <20 mg/dL	Estimated serum level >20 mg/dL	20
3	Yes, if <20 minutes from ingestion	If <1 hr				20
4						20
5		If <1 hr		Adult ≤mouthful of "50% diluted" product	Adult: >mouthful of >50% solution. -All children	20
6		If <2 hr	No		Treat ≥0.2 cc/kg 100%	20
7	For large ingestion if ED >30 minutes away.			"iron-clad lick or taste," <0.5 mL total	-Adult: 15 cc of 100% solution or one mouthful -Child: 3-5 cc or >"taste"	
8		Nasogastric	"Consider"	Estimated peak	Estimated peak	25

Metanol zehirlenmesi

Rethinking the Toxic Methanol Level

M. A. Kostic, M.D.,^{1,*} and R. C. Dart, M.D., Ph.D.^{1,2,*}

¹Rocky Mountain Poison and Drug Center, Denver Health Authority, Denver, Colorado, USA

²University of Colorado Health Sciences Center, Denver, Colorado, USA

ABSTRACT

Introduction: Treatment thresholds for methanol poisoning are based on case reports and published opinion. Most guidelines recommend treatment for a methanol level ≥ 20 mg/dL in a nonacidotic patient. No supportive data have been offered nor has the time of the exposure been addressed. For instance, no distinction has been drawn between a methanol level drawn 1 hr vs. 24 hr from ingestion. We analyzed all published cases of methanol poisoning to determine the applicability of the 20 mg/dL threshold in a nonacidotic patient, specifically those arriving early for care (within 6 hr) with a peak or near-peak blood methanol concentration. *Methods:* Using predefined search criteria, a systematic review of the world

D. DABEM
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EYLÜL 2008

Metanol zehirlenmesi: 6 saat içinde gelen, asidozu olan

Data from 16 patients who presented within 6 hr of ingestion and became acidotic.^a

Blood methanol, mg/dL	Time, hr ^b	Arterial pH	Serum HCO ₃ , mEq/L	Outcome
10	2	7.25	14.5	Full recovery
20	2	7.40	20	Full recovery
23	3.5	7.42	20	Full recovery
31	1	7.37	21	Full recovery
126	2	7.34	17	Full recovery
160	1	7.36	21	Full recovery
230	5	7.36	14	Full recovery
230	5	7.36	13	Full recovery
265	4	7.24	13	Full recovery
345	3	7.26	14	Optic neuropathy
373	2	7.41	10	Full recovery
410	4	6.9	5	Alive
420	4	7.09	14	Full recovery
500	4	7.28	12	Alive, ?VI ^c
560	5	6.99	12.5	Dead
570	4	7.32	21	Alive, VI

BEM
yumu
2008

Metanol zehirlenmesi: 6 saat içinde gelen, asidozu olmayan

Data from 6 patients who presented within 6 hr of ingestion and did not become acidotic.^a

Blood methanol, mg/dL	Time, hr ^b	Arterial pH	Serum HCO ₃ , mEq/L	Outcome
35	1	7.43	23	No effect
37	3.5	7.44	23	No effect
46	2	7.39	22	No effect
110	4.5	7.42	25	No effect
377	4	7.39	22	No effect
410	1.5	7.38 (Pa _{co2} = 38)	ND ^c	Myoglobinuric renal failure, recovered
129	30	ND	28	No effect

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28 Eylül 2008

Metanol zehirlenmesi

- Erken başvuran hastalar için kd tedavi yok
- Kimi bireyler 2-5 saat sonra hasta olur
- Şu anda birçok kişi gereksiz tedavi görüyor (standart s₁n₁r >20-25 mg/dL kabul edilirse)
- Prospektif çalıřma: semptomsuz, erken başvuran, düşük metanol düzeyi olan

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FOMEPIZOLE FOR THE TREATMENT OF METHANOL POISONING

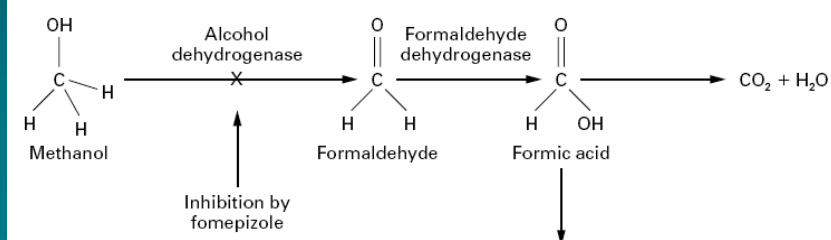
JEFFREY BRENT, M.D., PH.D., KENNETH McMARTIN, PH.D., SCOTT PHILLIPS, M.D., CYNTHIA AARON, M.D., AND KEN KULIG, M.D., FOR THE METHYLPYRAZOLE FOR TOXIC ALCOHOLS STUDY GROUP*

ABSTRACT

Background Methanol poisoning may result in metabolic acidosis, blindness, and death. The inhibition of alcohol dehydrogenase is fundamental to the treatment of methanol poisoning. We performed a multicenter study to evaluate fomepizole, an inhibitor of alcohol dehydrogenase, in the treatment of patients with methanol poisoning.

Methods We administered intravenous fomepizole to 11 consecutive patients who presented with methanol poisoning at a participating center. Serial clinical and laboratory studies, including measurements of plasma formic acid and fomepizole, were performed. The outcomes measured were the preservation of visual acuity, the resolution of metabolic aci-

an attempt to inhibit methanol metabolism.^{2,5,6} There are problems with the therapeutic use of ethanol. Intravenous preparations are often not available, and the pharmacokinetic characteristics of ethanol are erratic, making it difficult to maintain adequate plasma concentrations.^{7,8} Thus, plasma ethanol must be measured often and appropriate dose adjustments made. Furthermore, patients treated with ethanol need to be closely monitored because they are intoxicated and at risk for liver injury and hypoglycemia. In fact, there has never been a prospective study of the efficacy of ethanol in the treatment of methanol poisoning; all the clinical data are from case reports and retrospective case series.



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1 2008

Metanol zehirlenmesinde fomepizol

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF 11 PATIENTS WITH METHANOL POISONING.*

MENTAL STATUS AT PRESENTATION	TIME TO TREATMENT	ARTERIAL pH	PLASMA METHANOL	PLASMA FORMIC ACID	PLASMA ETHANOL	INITIAL VISUAL ACUITY†	HEMO-DIALYSIS	OUTCOME
	hr		mg/dl	mmol/liter	mg/dl			
Awake	12.7	7.46	75.3	ND	151.2	20/100	Yes	Recovered
Comatose	Unknown	7.21	66.9	20.6	104.3	FC‡	Yes	Recovered
Somnolent	6.3	7.38	38.8	ND	10.7	U	No	Recovered
Comatose	>24.0	6.90	129.0	21.0	198.9	U	Yes	Recovered
Awake	23.5	7.34	37.4	5.33	67.8	20/20	No	Recovered
Lethargic	26.4	7.38	612.1	9.89	89.1	FC§	Yes	Recovered
Awake	3.3	7.44	36.7	0.48	ND	20/20	No	Recovered
Awake	3.5	7.42	23.0	0.64	ND	20/20	No	Recovered
Awake	23.5	7.42	300.0	ND	10.9	20/20, 20/25	Yes	Recovered
Comatose	Unknown	7.01	71.3	27.7	ND	U	Yes	Died
Comatose	Unknown	6.90	484.0	43.1	ND	U	Yes	Died

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Metanol zehirlenmesi

- Birçok klinik protokolde kalsiyum folinat (Leucovorin) yer alıyor

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Metanol zehirlenmesi

- Kalsiyum folinat (Leucovorin) önerisinin 'kanıtı':
- 1980 yılında, maymun çalışması
- Sodyum folat ile...

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28 Eylül 2005

Organophosphorous Poisoning : an Evidence Based Approach

Dr Surjit Singh

MJAFI 2004; 60 : 2-4

Key Words : Organophosphorous poisoning; Randomized controlled trial

Acute organophosphorous poisoning (OPP) occurs following dermal, respiratory or oral exposure [1]. Organophosphorous compounds (OPCs) can be classified into low volatile compounds eg. chlopyriphos, dimethoate, dichlorvos, methyl parathion etc. used for

of these patients involves washing of skin and of vomiting or gastric lavage to remove OPC and stomach, administration of activate atropine, glycopyrrolate, oximes and s compounds in addition to ventilatory support

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Organofosfat...

- Araştırma çok, rasgele kontrollü çalışma yok

Sodium bicarbonate : Animal studies suggest that increasing pH with sodium bicarbonate may reduce mortality rate and this effect is independent of acidosis [25,26]. At present, a few uncontrolled studies are available [5] to show its benefit but no RCTs are available.

failure [22]. Two RCTs are available from Vellore (India) [17-19], suggesting that oximes do not benefit and with 12 gm over 3 days increase the risk of death, intermediate syndrome and requirement of ventilation. However, the studies have been criticized for randomization bias and inadequate dose. It is suggested that 2-PAM infusion should be given till patient recovers

[11]. In India, as suicide is still an offence and gastric lavage is being done routinely, for medico-legal reasons to collect gastric sample and for therapeutic reasons, it will be better to carry out RCTs to see whether it benefits the patients.

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Organofosfatlar ve pralidoksim (Cochrane review 2005)

- 2 RKÇ, toplam 182 hasta
- Metodoloji zayıf
 - Baseline nitelikleri aynı değildi
 - Kullanılan doz az
 - Maruz kalma - tedavi başlama süresi uzun
 - Farklı organofosfat maddeler
- Plasebo ile pralidoksim arasında fark yok

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Flumazenil: tedavi mi? zehir mi?

Flumazenil—Treatment or Toxin

Donna L. Seger, M.D.*

Vanderbilt University Medical Center, Nashville, Tennessee, USA

ABSTRACT

Flumazenil is frequently administered to the poisoned patient. Seizures may be precipitated and re sedation may occur in patients who awakened following flumazenil administration. Seizures may increase morbidity and mortality of the overdose. Benefit: Risk ratio of administering flumazenil should be determined in each overdose patient. Indications for flumazenil are limited.

Yeni tedaviler...

Aminophylline Reversal of Antihypertensive Agent Toxicity

Donald J Roberge MD, MPH, FAAEM, ACMT, M Laurie Rossetti DO, and James M Rosetti
Department of Emergency Medicine and the Internal Medicine Residency Program,
St Francis Medical Center, 400 45th Street, Pittsburgh, PA 15202

Hypotension occurred following a combined beta blocker (atenolol), angiotensin converting enzyme inhibitor (quinapril), and tricyclic antidepressant (fluvoxamine) overdose. In another instance heart block and hypotension was noted in association with a beta blocker (atenolol) overdose. Crystalloid infusion was ineffective in both cases, but toxicity was rapidly reversed with aminophylline administration. The recognized inotropic and chronotropic properties make it a potentially valuable therapeutic agent in the treatment of antihypertensive agent toxicity.

On following overdose of multiple antihypertensive agents, the risk of severe hypotension due to adverse drug interaction related to concomitant use of more than one antihypertensive medication, may be difficult to treat. Therapeutic interventions vary, depending on the agent(s) ingested, but include crystalloid infusion, atropine, chronotropes and inotropes (eg atropine, calcium channel blockers, diuretics, vasopressors (eg catecholamines), pacemakers, and aortic balloon counterpulsation devices

Presenting ED vital signs were heart rate 64, blood pressure 80/50, temperature 36.8 C (oral), respiratory rate 12, oxygen saturation 96% (ambient oxygen). The patient was conversant, though mildly somnolent, and the physical examination was remarkable only for morbid obesity (BMI 45.5 mm), sluggishly-reactive pupils. Hemogram, panel of chemistries and chest radiography were normal. ECG demonstrated a normal sinus rhythm with normal cardiac intervals. A urine toxicology screen

DOI: DABEM
1. Klinik Toksikoloji Sempozyumu
28 Eylül 2008

Yeni tedaviler...

Insulin-Glucose as Adjunctive Therapy for Severe Calcium Channel Antagonist Poisoning

Tony H. Yuan; William P. Kerns II; Christian A. Tomaszewski; Marsha D. Ford; Jeffrey A. Kline

Carolinas Medical Center, Charlotte, North Carolina

ABSTRACT

Case Report: This case series documents the clinical courses of 4 patients after verapamil overdose and 1 patient after amlodipine-atenolol overdose. All subjects had hypodynamic circulatory shock (hypotension, bradycardia, and acidosis) that was not adequately responsive to conventional treatment. After initiation of insulin-dextrose infusion, the hemodynamic status of all 5 patients stabilized and all patients survived. Plasma drug concentrations are reported for all cases and verapamil levels were extremely high in 2 patients (371

D. DABEM
Sempozyumu
EYLÜL 2005

Zehirlenmelerde kanıtta dayalı tıbbi bakım

- Birçok konuda yeterince 'kanıt' yok
 - Türkiye'de gastrik lavaj
 - Aktif kömür
 - Flumazenil
 - Pralidoksim
 - fomepizol
 - Yeni tedaviler
 - Antihipertansif ajan zehirlenmesi

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1. Klinik Toksikoloji Sempozyumu
28 Eylül 2005

Zehirlenmelerde kanıtta dayalı tıbbi bakım

- Birçok konuda yeterince 'kanıt' yok
- Kanıtı bulmak için sistematik literatür taraması
- Araştırılması gereken konu çok

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**Kanıtta dayalı tedavileri
uygulamak istiyorsak,
ilk önce bizim kanıtta dayalı
araştırma projeleri
yapmamız gerekli.**

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Kurşun zehirlenmesi!



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**Kurşun
zehirlenmesi...**

**250 adet mermi
yutmuş!**



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nu
28 Eylül 2005