Kanıta Dayalı İntravenöz Lipit Tedavisi

Doç. Dr. Hüseyin NARCI

Mersin Tıp Fakültesi

Acil Tıp AD

Sunum Planı

- Giriş
- Tarihçe
- İntravenöz lipid emülsiyonu
  - Etki mekanizması
  - Kontrendikasyonları
  - Komplikasyonları
  - Doz ve uygulama
- Kanıta dayalı kullanımı

Giriş

- İntravenöz lipit emülsiyonu (ILE) geçmişte kalori takviyesi ve esansiyel yağ asidi eksikliğinin tedavisi için kullanılmıştır.
- Günümüzde, zehirlenmelerin tedavisinde anestezi, yoğun bakım, acil tıp uzmanları ve tıbbi toksikologlar için mevcut tedavi seçeneklerinin bir parçası haline gelmiştir.

Giriş

- ILE yağ ve su mikro emülsiyonudur.
  - Soya yağı
  - Yumurta fosfolipidleri
  - Gliserin
- pH= 8.0

Tarihçe

J Clin Anesth. 1997 Dec;9(8):668-70.

Malignant ventricular dysrhythmias in a patient with isovaleric acidemia receiving general and local anesthesia for suction lipectomy.

Weinberg GL[1], Laurito CE, Geldner P, Pygon BH, Burton BK.

⊕ **Author information**

Abstract

We report the occurrence of severe ventricular arrhythmias in a patient with isovaleric acidemia during general anesthesia for suction lipectomy. The timing of events and character of the ECG changes are most consistent with bupivacaine toxicity after subcutaneous injection of tumescence solution containing this local anesthetic. The patient had previously documented carnitine deficiency, a condition which, we speculate, may lower the threshold for bupivacaine induced cardiotoxicity. We review clinical considerations in isovaleric acidemia and conclude that the use of bupivacaine in these patients probably should be avoided.

- Weinberg ve arkadaşları 1997 yılında Bupivakain uyguladıkları bir hastada ventriküler aritmi gelişmesi üzerine bu konuda çalışmaya başlamışlar.
- Hastada ciddi karnitin defekti ve izovalerik asidemi saptamaları üzerine bu hasta grubunda lokal anesteziğe karşı duyarlılık olabileceğini düşündüler.

Tarihçe

ANESTHESIOLOGY
Trusted Evidence: Discovery to Practice

Pretreatment or Resuscitation with a Lipid Infusion Shifts the Dose-Response to Bupivacaine-induced Asystole in Rats

Guy L. Weinberg, MD; Timothy VadeBoncouer, MD; Gopal A. Ramaraju, MD; Marcelo F. Garcia-Amaro, MD; Michael J. Cwik, PhD

We report that lipid infusion reduces bupivacaine-associated cardiotoxicity. Partition experiments suggest that the primary benefit of lipid infusion results from a lipid sink effect. Other mechanisms may be active, however. These preliminary observations suggest a potential means for improved therapy of a serious anesthetic complication.

1998 yılında Weinberg ve ark.nın ratlarda bupivakainin letal dozunu elimine etmesiyle lipid emülsiyonlarının popülaritesi gündeme gelmiştir.

Tarihçe

ANESTHESIOLOGY
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Case Reports | July 2006

Successful Use of a 20% Lipid Emulsion to Resuscitate a Patient after a Presumed Bupivacaine-related Cardiac Arrest

Meg A. Rosenblatt, M.D.; Mark Abel, M.D.; Gregory W. Fischer, M.D.; Chad J. Itzkovich, M.D.; James B. Eisenkraft, M.D.

+ Author Affiliations & Notes

Anesthesiology 7 2006, Vol.105, 217-218. doi:

Size

Bupivakaine bağlı arrest gelişen bir hasta intravenöz lipid emülsiyon tedavisi ile başarılı bir şekilde kurtarıldı.

Tarihçe

Annals of Emergency Medicine
Volume 51, Issue 4, April 2008, Pages 412-415.e1

Toxicology/case report

Use of Lipid Emulsion in the Resuscitation of a Patient With Prolonged Cardiovascular Collapse After Overdose of Bupropion and Lamotrigine

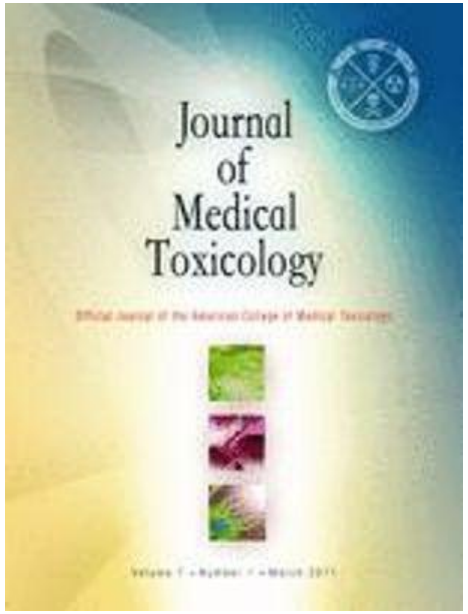
Archie J. Sirianni MD [a], Kevin C. Osterhoudt MD [c, d], Diane P. Calello MD [c, d], Allison A. Muller PharmD [c, d], Marie R. Waterhouse MD [c], Michael B. Goodkin MD [b], Guy L. Weinberg MD [e], Fred M. Henretig MD [c, d]

Animal studies show efficacy of intravenous lipid emulsion in the treatment of severe cardiotoxicity associated with local anesthetics, clomipramine, and verapamil, possibly by trapping such lipophilic drugs in an expanded plasma lipid compartment ("lipid sink"). Recent case reports describe lipid infusion for the successful treatment of refractory cardiac arrest caused by parenteral administration of local anesthetics, but clinical evidence has been lacking for lipid's antidotal efficacy on toxicity caused by ingested medications. A 17-year-old girl developed seizure activity and cardiovascular collapse after intentional ingestion of up to 7.95 g of bupropion and 4 g of lamotrigine. Standard cardiopulmonary resuscitation for 70 minutes was unsuccessful in restoring sustained circulation. A 100-mL intravenous bolus of 20% lipid emulsion was then administered, and after 1 minute an effective sustained pulse was observed. The patient subsequently manifested significant acute lung injury but had rapid improvement in cardiovascular status and recovered, with near-normal neurologic function. Serum bupropion levels before and after lipid infusion paralleled triglyceride levels. This patient developed cardiovascular collapse because of intentional, oral overdose of bupropion and lamotrigine that was initially refractory to standard resuscitation measures. An infusion of lipid emulsion was followed rapidly by restoration of effective circulation. Toxicologic studies are consistent with the lipid sink theory of antidotal efficacy. [Ann Emerg Med. 2008;51:412-415.]

Yüksek doz oral bupropion ve lamotrigin toksisitesi olan hastada, standart resüsitasyon başarısız olduktan sonra İLE tedavisi ile başarı sağlanmış

Tarihçe

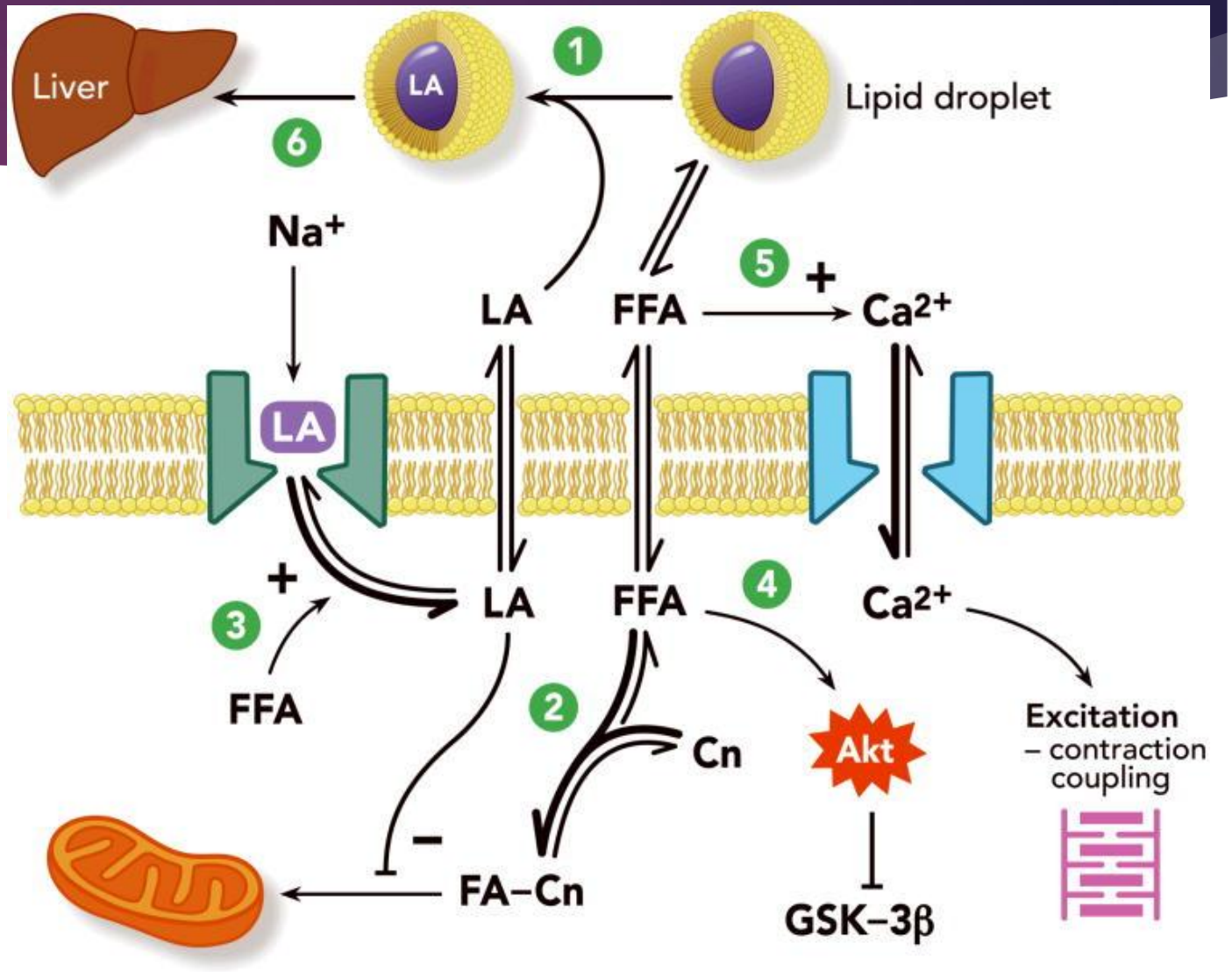
ACMT Position Statement: Interim Guidance for the Use of Lipid Resuscitation Therapy 2011



İntravenöz lipid emülsiyonu
lipit çözünürlüğüne sahip bir ilaca bağlı ciddi toksisite varsa, kardiyak arrest olmasa bile, tedavi için makul bir seçenek olabilir.

Etki mekanizması

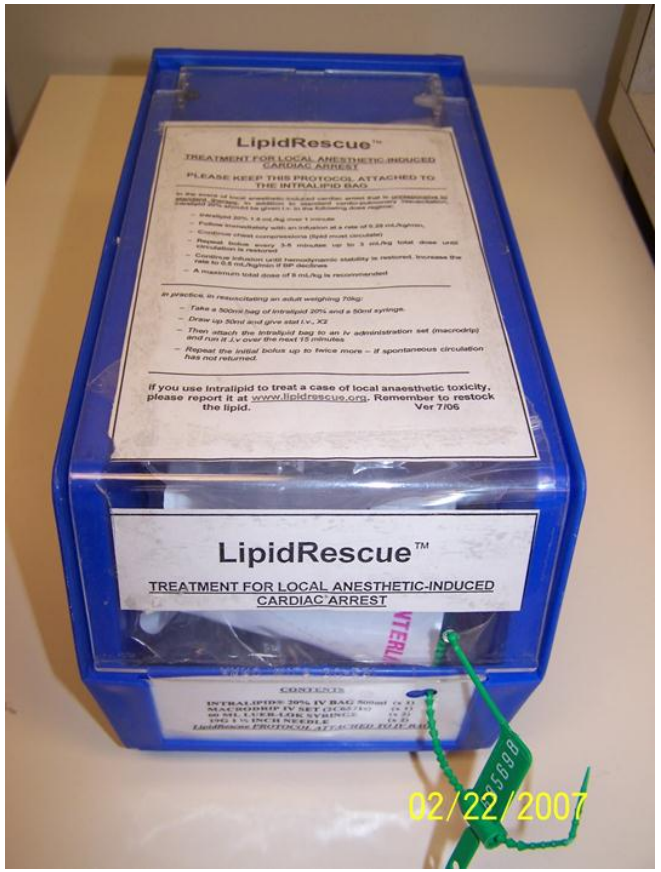
- Lipid Batma (Lipid Sink) Teorisi
- İyonik kanal teorisi
- Biyoenerji teorisi



Butterworth JF 4th. Models and mechanisms of local anesthetic cardiac toxicity: a review. Reg Anesth Pain Med 2010; 35:167–176.

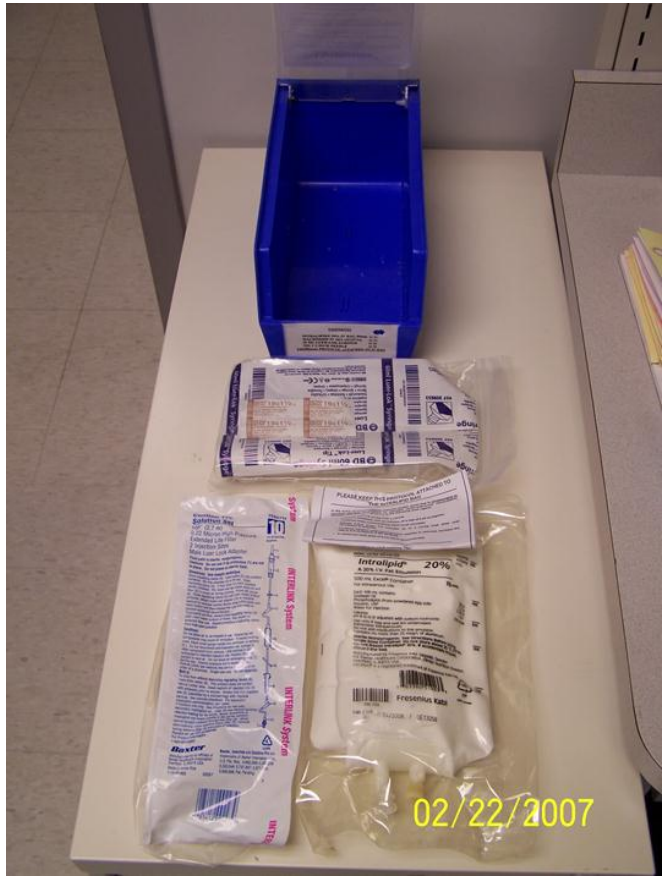
Kontrendikasyonlar

- Lipid metabolizması bozuklukları
- Yumurta alerjisi
- DİKKAT!!!
  - Anemi
  - Şiddetli karaciğer hastalığı
  - Koagülopati
  - Akciğer hastalığı



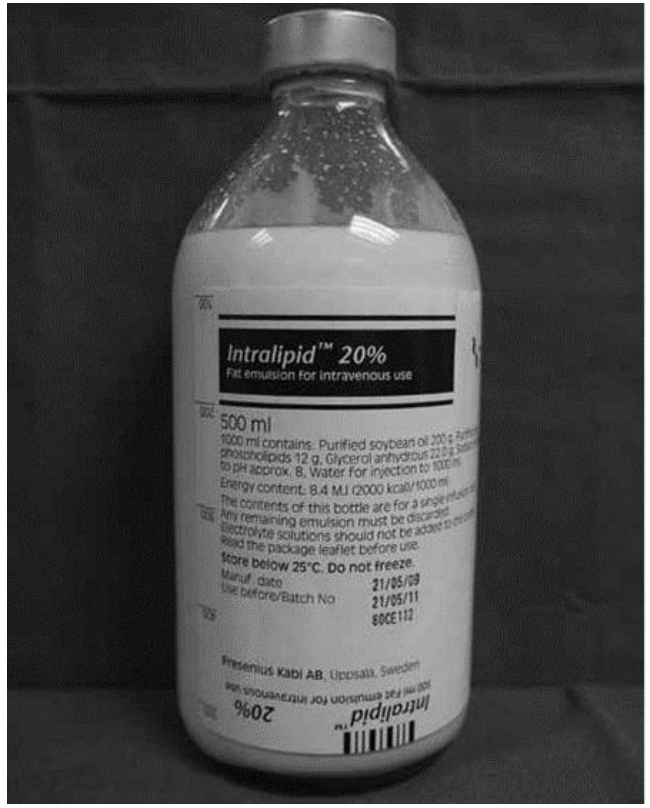
Komplikasyonlar

- Alerjik reaksiyon
- Aşırı sıvı yüklenmesi
- Bozulmuş karaciğer fonksiyonu
- Hiperkoagülabilite
- Pankreatit
- ARDS
- DVT



Doz ve uygulama

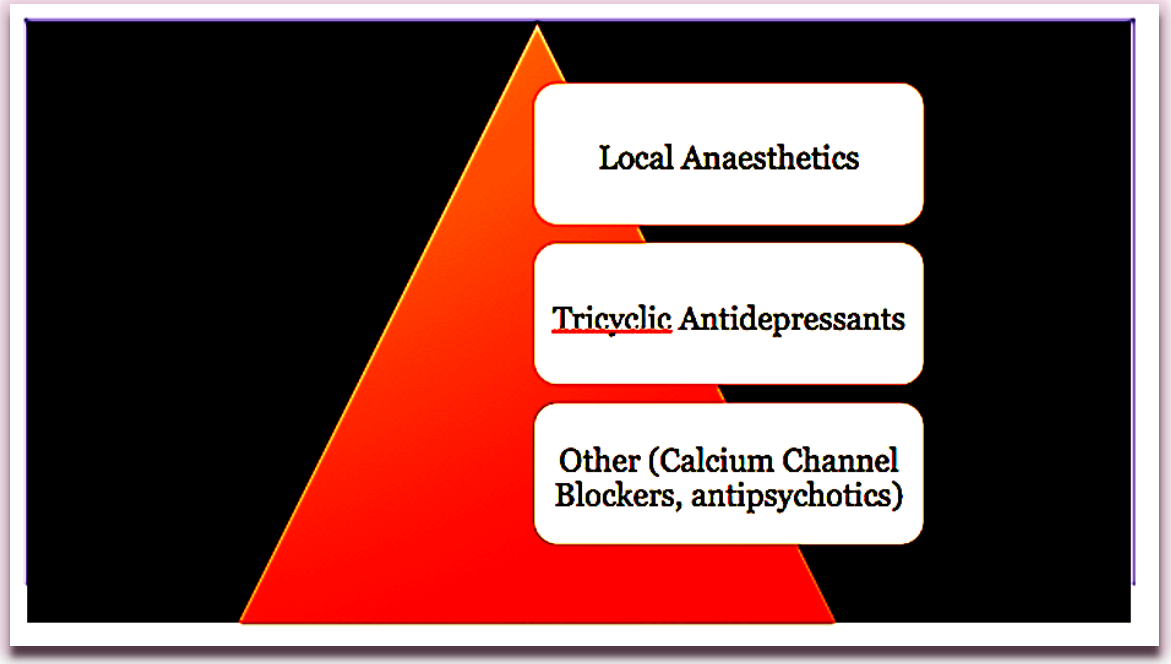
- 1,5 mL/kg IV bolus (1dk'da)
- Sonrasında 0,25 mL/kg/dakika 30-60 dakika infüzyon
- Maksimum doz 10-12 mL/kg.
- Tedavide kullanılan %20 lipid solüsyonudur.



American College of Medical Toxicology. ACMT Position Statement: Interim Guidance for the Use of Lipid Resuscitation Therapy. *J Med Toxicol* 2011; 7: 81-82.

İLE yayınlar-kanıtlar

- Vaka raporları
- Hayvan çalışmaları
- Sistemik derlemeler
- Vaka serileri



ELSEVIER

The Journal of Emergency Medicine
Volume 48, Issue 3, March 2015, Pages 387-397

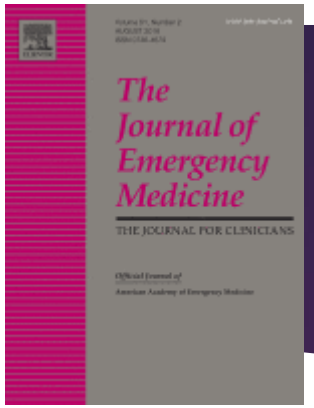
Clinical Review

Intravenous Lipid Emulsion in the Emergency Department: A Systematic Review of Recent Literature

Dazhe Cao MD *† , Kennon Heard MD, PhD †, Mark Foran MD, MPH ‡, Alex Koyfman MD §

94 makale ve 40 konferans özeti % 85 olumlu sonuç tespit edildi.
ILE için en yaygın endikasyon
- lokal anestezik sistemik toksisitesi
- trisiklik antidepresanlar
- verapamil.

Lipitte çözünebilen ilaçlara bağlı ciddi hemodinamik toksisitede, acil doktorları tarafından resüsitasyon için ILE düşünülebilir



USE OF INTRAVENOUS FAT EMULSION IN THE EMERGENCY DEPARTMENT FOR THE CRITICALLY ILL POISONED PATIENT

Samuel H. F. Lam, MD,* Nima Majlesi, DO,† and Gary M. Vilke, MD*

*Department of Emergency Medicine, University of California at San Diego Medical Center, San Diego, California and †Department of Emergency Medicine, Staten Island University Hospital, New York, New York

☐ **Abstract—Background: Multiple case reports of using intravenous fat emulsion (IFE) as an antidote for human poisoning from various xenobiotics have been published over the last decade. Given the rapidly evolving field, emergency physicians may be uncertain about the indications, timing, and dose for IFE treatment. Methods: A PubMed literature search was conducted from January 1996 to November 2015 and limited to human studies written in English and articles with relevant keywords. Guideline statements and nonsystematic reviews were excluded. Studies identified then underwent a structured review of their results. Results: There were 986 papers fulfilling the search criteria screened, and 85 appropriate articles were rigorously reviewed in detail. Recommendations were given on indications, timing, and dose of IFE. Most of these were based on case reports and anecdotal experience. Discussion: In critically ill patients with refractory shock or cardiac arrest after a suspected overdose of local anesthetics or selected xenobiotics, IFE may be considered as a potentially beneficial adjunctive treatment. Despite an abundance of reports on the use of IFE on xenobiotics poisoning, the quality of evidence is suboptimal and fraught with reporting bias. Conclusions: IFE may be an effective antidote in poisonings from various xenobiotics. However, further research is needed to determine its optimal circumstances, timing, and dose of use.** **© 2016 Elsevier Inc. All rights reserved.**

Toplam 986 makaleden uygun olan 85 makale incelendi

ILE, çeşitli ilaçlardan kaynaklanan zehirlenmelerde etkili bir antidot olabilir.
Endikasyonları, zamanlaması ve kullanım dozunu belirlemek için daha fazla araştırmaya ihtiyaç vardır

CLINICAL TOXICOLOGY, 2017
VOL. 55, NO. 7, 617–623
http://dx.doi.org/10.1080/15563650.2017.1288911

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REVIEW

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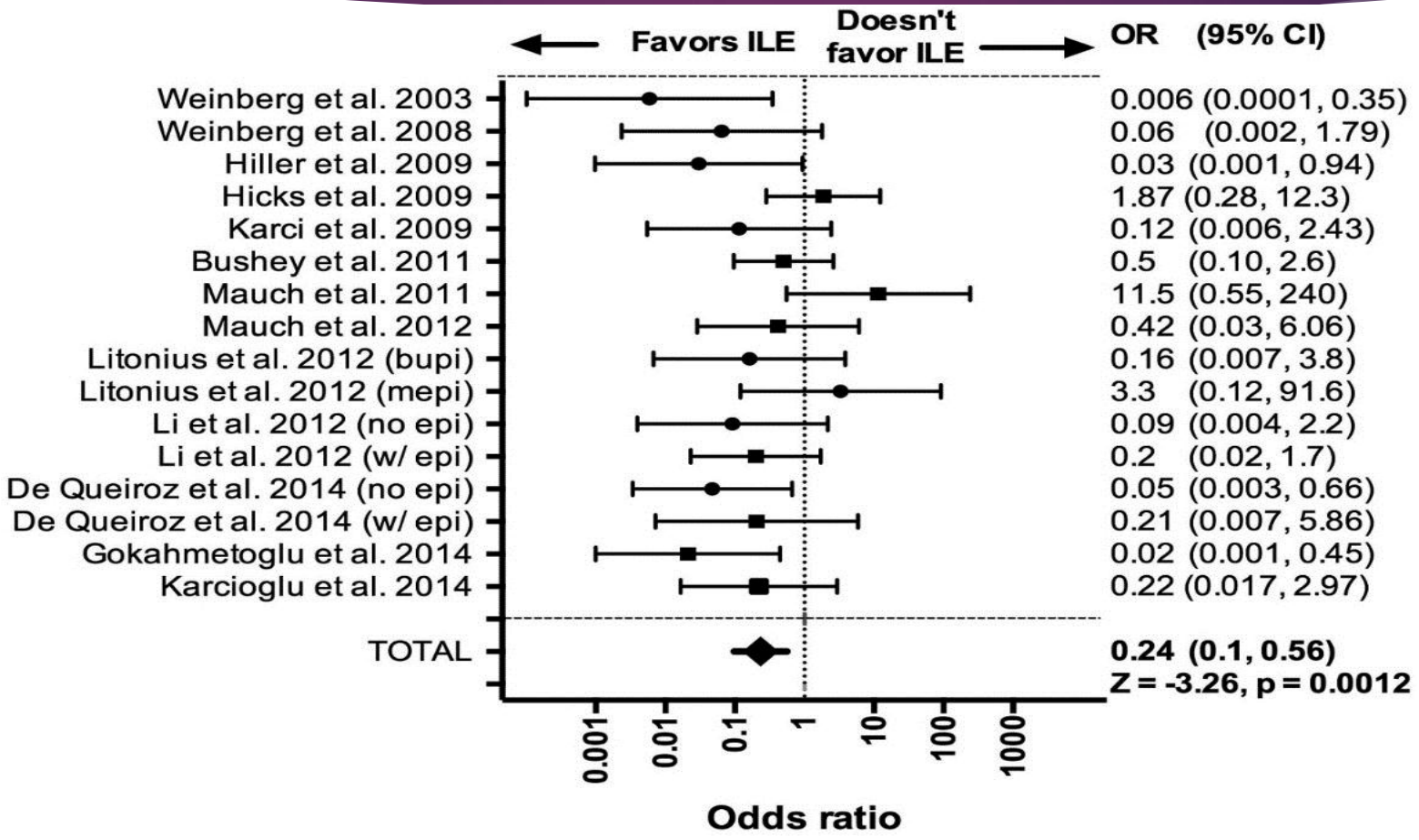
Lipid emulsion improves survival in animal models of local anesthetic toxicity: a meta-analysis

Michael R. Fettiplace[a] and Daniel J. McCabe[b]

[a]Medical Scientist Training Program, University of Illinois College of Medicine, Chicago, IL, USA; [b]Department of Emergency Medicine, John H. Stroger Cook County Hospital, Chicago, IL, USA



Eur Rev Med Pharmacol Sci. 2012 Mar;16 Suppl 1:38-42.

Lipid emulsion improves Glasgow coma scale and decreases blood glucose level in the setting of acute non-local anesthetic drug poisoning--a randomized controlled trial.

Taftachi F[1], Sanaei-Zadeh H, Sepehrian B, Zamani N.

Abstract

BACKGROUND: To date, no study has been performed to evaluate the antidotal effect of intravenous lipid emulsion on the poisoned patients' level of consciousness and routine metabolic profile tests in non-local anesthetic drug overdose.

OBJECTIVES: Our aim was to evaluate the effect of intravenous intralipid administration as an antidote on the poisoned patients' Glasgow Coma Scale (GCS), hemodynamic parameters, arterial blood gas analysis, and routine metabolic profile tests (i.e., urea, glucose, sodium, and potassium) in the setting of non-local anesthetic drug overdose.

MATERIAL AND METHODS: In this randomized controlled trial, a total of 30 patients with non-local anesthetic drug intoxication were enrolled and randomly assigned into case (n=15) and control (n=15) groups. In the case group, all patients received 10 cc/kg intralipid 10% infusion. The patients in the control group just received the supportive care. Patients' demographic and clinical characteristics and results of their laboratory tests were evaluated at presentation and 6 hours after that.

RESULTS: Mean age was 23 +/- 5 and 28 +/- 11 years in cases and controls, respectively. There were no significant statistical differences between these two groups regarding age, gender, elapsed time between intubation and extubation, and need for intubation and/or mechanical ventilation (p = 0.70 and p = 1.00, respectively). Also, systolic blood pressure, pulse rate, mean rate pressure product, respiratory rate, results of arterial blood gas analyses, serum sodium, potassium, urea, and creatinine on presentation and six hours later were not statistically significantly different between the two study groups. However, a significant difference was found between the two groups in terms of GCS difference (p = 0.048) and blood glucose six hours after presentation (p = 0.04).

CONCLUSIONS: In the setting of non-local anesthetic drug overdose, intravenous intralipid infusion can increase GCS and interestingly, decrease the blood glucose.

Lokal olmayan anestezik ilaç doz aşımlarında,İLE infüzyonu GKS'yi artırabilir ve kan glukozunu azaltabilir.

Canadian Journal of Emergency Medicine CAEP

A cohort study of unstable overdose patients treated with intravenous lipid emulsion therapy

Shazma Mithani [a1] [a2], Kathryn Dong [a1] [a2], Ashlea Wilmott [a3], Heather Podmoroff [a4] ...

https://doi.org/10.1017/cem.2016.396 Published online: 23 November 2016

Abstract

OBJECTIVES: Intravenous lipid emulsion (ILE) has been used increasingly over the last decade for a range of drug overdoses. Although the use of ILE in local anesthetic toxicity (LAST) is well established, the hemodynamic effectiveness of ILE in non-LAST poisonings is still unclear. Thus, the primary objective of this study was to examine a cohort of poisoned patients in whom ILE was administered.

METHODS: Consecutive patients were identified by calls to a regional poison center from May 1, 2012 to May 30, 2014. Patients were enrolled if they ingested a drug, developed hemodynamic instability, failed conventional treatment, and received ILE therapy. Data were collected by medical record review. The primary outcome was the change in mean arterial pressure (MAP) in the first hour after ILE administration. Secondary outcomes included survival, length of stay, and the effect of drug class on patient outcome.

RESULTS: Thirty-six patients were enrolled. Agents ingested included calcium channel blockers and beta blockers (10/36, 27.8%), tricyclic antidepressants (5/36, 13.9%), bupropion (3/36, 8.3%), and antiepileptic agents (1/36, 2.8%). Seventeen patients (47.2%) ingested multiple agents. Twenty-five patients survived (69.0%). Overall, MAP increased by 13.79 mm Hg (95% CI 1.43-26.15); this did not meet our a priori definition of clinical significance.

CONCLUSIONS: Our study did not find a clinically important improvement in MAP after ILE administration. Until future research is done to more definitively study its efficacy, ILE should remain a potential treatment option for hemodynamically unstable overdose patients only after conventional therapy has failed.

ILE uygulamasından sonra OAB'ta klinik olarak önemli bir iyileşme bulunamadı. ILE hemodinamik olarak anstabil hastalarda geleneksel tedavi başarısız olduktan sonra potansiyel bir tedavi seçeneği olarak kalmalıdır

TOXICOLOGY/ORIGINAL RESEARCH

Intravenous Lipid Emulsion Therapy for Severe Diphenhydramine Toxicity: A Randomized, Controlled Pilot Study in a Swine Model

Shawn M. Varney, MD*; Vikhyat S. Bebarta MD; Susan M. Boudreau, RN, BSN; Toni E. Vargas, PA-C; Maria Castaneda, MS; Lee A. Zarzabal, MS

*Corresponding Author. E-mail: smvarney@gmail.com.

Conclusion: In our study of diphenhydramine-induced hypotensive swine, we found no difference in hypotension, QRS widening, or diphenhydramine levels in aqueous layers between intravenous lipid emulsion and sodium bicarbonate.
[Ann Emerg Med. 2016;67:196-205.]

Sodyum bikarbonat ile intravenöz lipit emülsiyonu arasında hipotansiyon veya sağkalımı iyileştirmede bir fark tespit edilmemiştir. QRS genişlemesi ve ilaç konsantrasyonları düzelmemiştir.

Journal of the Formosan Medical Association

Volume 115, Issue 11

FULL TEXT ARTICLE

Intravenous lipid-emulsion therapy in a patient with cardiac arrest after overdose of diphenhydramine

Jiun-Hao Yu, Dong-Yi Chen, Hsien-Yi Chen and Kuo-Hua Lee

Journal of the Formosan Medical Association, 2016-11-01, Volume 115, Issue 11, Pages 1017-1018, Copyright © 2016

ILE uygulaması, hipotansiyon ve QRS genişliğinde belirgin iyileşme ile sonuçlandı

What are the adverse effects associated with the combined use of intravenous lipid emulsion and extracorporeal membrane oxygenation in the poisoned patient

Hwee Min D. et al.Volume 53, 2015 - Issue 3

ILE ve ekstrakorporeal membran oksijenasyonunun kombine kullanımının, VA-ECMO devrelerinde yağ birikimi ve kanın pıhtı oluşumunun artmasıyla ilişkili olabileceğine dair in vitro ve klinik kanıtlar vardır

J. Med. Toxicol. (2014) 10:307–310
DOI 10.1007/s13181-014-0382-7

OBSERVATION (CASE REPORTS)

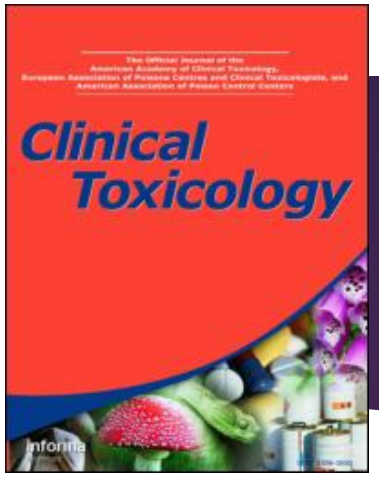
Asystole Immediately Following Intravenous Fat Emulsion for Overdose

Jon B. Cole · Samuel J. Stellpflug · Kristin M. Engebretsen

We report two cardiac arrests that occurred immediately after IFE administration. An association with IFE or interaction with other resuscitation medications should be contemplated. IFE should be considered with caution when used in pre-arrest circumstances.

2015 AHA İleri Yaşam Desteği

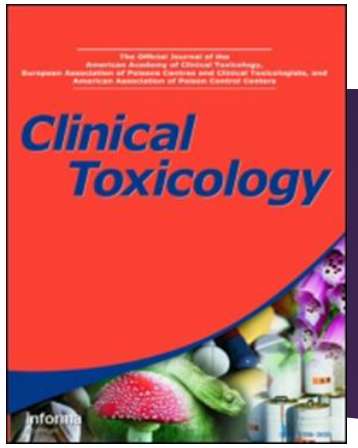
- Özellikle bupivakain toksisitesinden dolayı nörotoksisite/ kardiyak arrest hastalarında standart resüsitasyon tedavisi ile birlikte ILE uygulamak mantıklı olabilir (Class IIb, LOE C-EO).
- Diğer ilaç zehirlenmelerinde standart resüsitatif önlemlere yanıtsız hastalarda İLE uygulamak mantıklı olabilir (Class IIb, LOE C-EO).



Zehirlenmelerde intravenöz lipid emülsiyon tedavisi kanıta dayalı öneriler

- American Academy of Clinical Toxicology,
- European Association of Poison Centres and Clinical Toxicologists
- American College of Medical Toxicology
- Asia Pacific Association of Medical Toxicology
- American Association of Poison Control Centers
- Canadian Association of Poison Control Centers

Sophie Gosselin et al. (2016) Evidence-based recommendations on the use of intravenous lipid emulsion therapy in poisoning, Clinical Toxicology, 54:10, 899-923,



Zehirlenmelerde intravenöz lipid emülsiyon tedavisi kanıta dayalı öneriler

Tavsiye gücü
Level 1: Güçlü tavsiye
Level 2: Zayıf / şartlı öneri
Neutral : Olumlu yada olumsuz görüş birliği yok
No recommendation: Öneri yok
Kanıt düzeyi
Grade A: Yüksek düzeyde kanıt
Grade B: Orta düzeyde kanıt
Grade C: Düşük kanıt düzeyi
Grade D: Çok düşük kanıt düzeyi

Table 1. Intravenous lipid emulsion (ILE) in poisoning: clinical situations.

Statements	Clinical situations
ILE is indicated in cardiac arrest, after standard ACLS is started	
ILE is indicated in life-threatening toxicity	As first-line therapy As part of treatment modalities If other therapies fail (in last resort)
ILE is indicated in non-life-threatening toxicity	As first-line therapy As part of treatment modalities If other therapies fail (in last resort)

Lokal anestezikler: Bupivakain

- Kardiyak arrest: kullanımı öneriliyor (1D)
- Yaşamı tehdit eden toksisite: tedavi yöntemlerinin bir parçası olarak (2D) ve diğer tedaviler başarısız olursa son çare olarak (1D) öneriliyor.
- Yaşamı tehdit etmeyen toksisitede: nötral öneri

Diğer tüm lokal anestezikler

- Kardiyak arrest: nötral öneri
- Yaşamı tehdit edici toksisite: diğer tedaviler başarısız olursa / son çare olarak (2D) kullanılması öneriliyor
- Yaşamı tehdit etmeyen olmayan: nötral öneri

Amitriptilin

- Kardiyak arrest: nötral öneri
- Yaşamı tehdit eden toksisite: diğer tedaviler başarısız olursa / son çare (2B) öneriliyor, birinci basamak tedavide tavsiye edilmiyor (2D).
- Yaşamı tehdit etmeyen toksisite: birinci basamak tedavi (1D) olarak kullanılmamalı ve tedavinin bir parçası değil (2D).

Diğer trisiklik antidepresanlar

- Kardiayak arrest: nötral öneri
- Yaşamı tehdit eden toksisite: birinci basamak tedavide tavsiye edilmiyor (2D)
- Yaşamı tehdit etmeyen toksisite: hiçbir durumda ILE kullanılması önerilmez (2D)

Beta reseptörü antagonistleri (Lipid soluble)

- Kardiyak arrest: nötral öneri
- Yaşamı tehdit eden toksisite: nötral öneri
- Yaşamı tehdit etmeyen toksisite: birinci basamak tedavide önerilmiyor (2D)

Beta reseptör antagonistleri (Non-lipid soluble)

- Kardiyak arrest: nötral öneri
- Yaşamı tehdit eden toksisite: birinci basamak tedavide tavsiye edilmiyor (2D)
- Yaşamı tehdit etmeyen toksisite: birinci basamak tedavide (2D) veya tedavi yöntemlerinin (2D) bir parçası olarak kullanılması önerilmiyor.

Kalsiyum kanal blokerleri:diltiazem ve verapamil

- Kardiyak arrest: nötral öneri
- Yaşamı tehdit eden toksisite: birinci basamak tedavide tavsiye edilmiyor (2D)
- Yaşamı tehdit etmeyen toksisite: birinci basamak tedavide önerilmiyor (2D)

Kalsiyum kanal blokerleri: dihidropiridinler

- Kardiyak arrest: nötral öneri
- Yaşamı tehdit eden toksisite: birinci basamak tedavide tavsiye edilmiyor (2D)
- Yaşamı tehdit etmeyen toksisite: hiçbir durumda ILE kullanılması önerilmiyor (2D)

Antidisritmik Class 1

- Kardiyak arrest: nötral öneri
- Yaşamı tehdit eden toksisite: nötral öneri
- Yaşamı tehdit etmeyen toksisite: birinci basamak tedavide önerilmiyor (2D)

Appendix 5. Vote results

Toxins	Cardiac arrest	Life-threatening toxicity			Non-life-threatening toxicity		
		As first line therapy	As part of treatment modalities	If other therapies fail (in last resort)	As first line therapy	As part of treatment modalities	If other therapies fail (in last resort)
Local anesthetics							
Bupivacaine	**Recommended (M:7, LQ:7, DI:0.2)**	Neutral (M:6, DI:0.5)	**Suggested (M:7, LQ:6, DI:0.2)**	**Recommended (M:8, LQ:7, DI:0.2)**	Neutral (M:5, DI:0.5)	Neutral (M:5, DI:0.5)	Neutral (M:6, DI:0.5)
All other local anesthetics	Neutral (M:6, DI:0.3)	Neutral (M:5, DI:0.4)	Neutral (M:6, DI:0.5)	**Suggested (M:7, LQ:6, DI:0.4)**	Neutral (M:5, DI:0.7)	Neutral (M:5, DI:1.0)	Neutral (M:6, DI:0.3)
Non-local anaesthetics							
Antidysrhythmics Class 1	Neutral (M:5, DI:0.3)	Neutral (M:4, DI:0.7)	Neutral (M:5, DI:0)	Neutral (M:6.5, DI:0.5)	***Not suggested* (M:3, UQ:5, DI:0.7)**	Neutral (M:5, DI:0.6)	Neutral (M:5, DI:0.4)
Amitriptyline	Neutral (M:6, DI:0.5)	***Not suggested* (M:2.5, UQ:4.5, DI:0.3)**	Neutral (M:5, DI:0.5)	**Suggested (M:7, UQ;5, DI:0.4)**	***Not recommended* (M:1, UQ:2, DI:0.1)**	***Not suggested* (M:3, UQ:4, DI:0.5)**	Neutral (M:5, DI:0.8)
Other tricyclic antidepressants	Neutral (M:5.5, DI:0.3)	***Not suggested* (M:2, UQ:5, DI:0.8)**	Neutral (M:5, DI:0.9)	Neutral (M:6, DI:0.6)	***Not suggested* (M:1, UQ:4, DI:0.3)**	***Not suggested* (M:2, UQ:5, DI:0.8)**	***Not suggested* (M:3, UQ:5, DI:0.8)**
Baclofen	Neutral (M:5, DI:0.1)	Neutral (M:5, DI:0.7)	Neutral (M:5, DI:0)	Neutral (M:5, DI:0.3)	***Not suggested* (M:2, UQ:5, DI:0.7)**	Neutral (M:4, DI:0.7)	Neutral (M:5, DI:0.7)
Beta receptor antagonists (lipid-soluble)	Neutral (M:6, DI:0.3)	Neutral (M:4, DI:0.4)	Neutral (M:5, DI:0.3)	Neutral (M:6, DI:0.3)	***Not suggested* (M:2, UQ:5, DI:0.8)**	Neutral (M:4, DI:0.7)	Neutral (M:5, DI:0.6)
Beta receptor antagonists (Non lipid-soluble)	Neutral (M:5, DI:0.5)	***Not suggested* (M:2, UQ:4, DI:0.5)**	Neutral (M:4, DI:0.7)	Neutral (M:5, DI:0.3)	***Not suggested* (M:1, UQ:3.5, DI:0.2)**	***Not suggested* (M:1, UQ:5, DI:0.8)**	Neutral (M:5, DI:0.8)
Bupropion	Neutral (M:6, DI:0.5)	***Not suggested* (M:2, UQ:5, DI:0.4)**	Neutral (M:5, DI:0.4)	**Suggested (M:7, LQ:5, DI:0.7)**	***Not suggested* (M:2, UQ:5, DI:0.8)**	Neutral (M:4, DI:0.8)	Neutral (M:5, DI:0.8)
Calcium channel blockers Diltiazem and verapamil	Neutral (M:6, DI:0.5)	***Not suggested* (M:2, UQ:5, DI:0.8)**	Neutral (M:5, DI:0.1)	Neutral (M:6, DI:0.1)	***Not suggested* (M:1, UQ:4, DI:0.5)**	Neutral (M:4, DI:0.7)	Neutral (M:5, DI:0.7)
Calcium channel blockers Dihydropyridines	Neutral (M:5, DI:0.3)	***Not suggested* (M:2, UQ:5, DI:0.5)**	Neutral (M:5, DI:0.2)	Neutral (M:6, DI:0.5)	***Not suggested* (M:1, UQ:4.5, DI:0.3)**	***Not suggested* (M:2, UQ:5, DI:0.8)**	***Not suggested* (M:2, UQ:5, DI:0.8)**
Cocaine	Neutral (M:5, DI:0.3)	***Not suggested* (M:2, UQ:5, DI:0.5)**	Neutral (M:5, DI:0.7)	Neutral (M:6, DI:0.4)	***Not suggested* (M:1, UQ: 3.75, DI:0.3)**	***Not suggested* (M:2, UQ:5, DI:0.8)**	Neutral (M:5, DI:0.8)
Diphenhydramine	Neutral (M:5, DI:0.3)	***Not suggested* (M:1, UQ:4, DI:0.2)**	Neutral (M:5, DI:0.4)	Neutral (M:6, DI:0.6)	***Not recommended* (M:1, UQ:2, DI:0.1)**	***Not suggested* (M:1, UQ:4, DI:0.2)**	***Not suggested* (M:2, UQ:5, DI:0.8)**

Appendix 5. Vote results

Toxins	Cardiac arrest	Life-threatening toxicity			Non-life-threatening toxicity		
		As first line therapy	As part of treatment modalities	If other therapies fail (in last resort)	As first line therapy	As part of treatment modalities	If other therapies fail (in last resort)
Other antihistamines	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Ivermectin	Neutral (M:5, DI:0)	Neutral (M:4.5, DI:0.7)	Neutral (M:5, DI:0)	Neutral (M:5, DI:0.4)	***Not suggested*** **(M:2, UQ:5, DI:0.8)**	Neutral (M:5, DI:0.8)	Neutral (M:5, DI:0.7)
Other insecticides	Neutral (M:5, DI:0)	***Not suggested*** **(M:3, UQ:5, DI:0.8)**	Neutral (M:5, DI:0.3)	Neutral (M:5, DI:0.4)	***Not suggested*** **(M:2, UQ:5, DI:0.8)**	Neutral (M:4, DI:0.7)	Neutral (M:5, DI:0.4)
Lamotrigine	Neutral (M:6, DI:0.4)	***Not suggested*** **(M:3, UQ: 5, DI:0.8)**	Neutral (M:5, DI:0.4)	Neutral (M:6.5, DI:0.4)	***Not suggested*** **(M:1.5, UQ: 5, DI:0.5)**	***Not suggested*** **(M:3, UQ:5, DI:0.8)**	Neutral (M:5, DI:0.8)
Malathion	Neutral (M:5, DI:0)	***Not suggested*** **(M:3, UQ:5, DI:0.7)**	Neutral (M:5, DI:0.1)	Neutral (M:5, DI:0.2)	***Not suggested*** **(M:2, UQ:5, DI:0.8)**	Neutral (M:4, DI:0.6)	Neutral (M:5, DI:0.3)
Other pesticides	Neutral (M:5 DI:0.1)	***Not suggested*** **(M:2, UQ:5, DI:0.8)**	Neutral (M:5, DI:0)	Neutral (M:5, DI:0.3)	***Not suggested*** **(M:2, UQ:5, DI:0.5)**	Neutral (M:5, DI:0.8)	Neutral (M:5, DI:0.5)
Olanzapine	Neutral (M:5, DI:0.3)	Neutral (M:5, DI:0.7)	Neutral (M:5, DI:0.1)	Neutral (M:5, DI:0.4)	***Not suggested*** **(M:2, UQ:5, DI:0.8)**	Neutral (M:5, DI:0.7)	Neutral (M:5, DI:0.7)
Other antipsychotics	Neutral (M:5, DI:0.3)	***Not suggested*** **(M:3, UQ:5, DI:0.7)**	Neutral (M:5, DI:0)	Neutral (M:5, DI:0.4)	***Not suggested*** **(M:2, UQ:5, DI:0.8)**	Neutral (M:5, DI:0.7)	Neutral (M:5, DI:0.6)
Selective Serotonin Reuptake Inhibitors	Neutral (M:5, DI:0.1)	Neutral (M:4, DI:0.8)	Neutral (M:5, DI:0.1)	Neutral (M:5, DI:0.3)	***Not suggested*** **(M:2, UQ:5, DI:0.8)**	Neutral (M:5, DI:0.7)	Neutral (M:5, DI:0.6)

Zehirlenmelerde intravenöz lipid emülsiyon tedavisi kanıta dayalı öneriler

- Çoğu zehirlenmemelerde ILE kullanılmasını önerecek bir kanıt bulunamamıştır.
- ILE tedavisinin birçok spesifik yönü klinik ortamda doğrulanmamıştır.
- Hayvan modellerinden elde edilen sonuçların doğrudan klinik uygulaması zordur.
- ILE etkinliğine ilişkin hayvan çalışmalarının büyük kısmı intravenöz ilaçlar ile yapılırken, ancak klinik zehirlenmelerin çoğu oral maruziyetin sonucudur.

Sonuçlar

- Lokal anestezik toksisitede lipid emülsiyon kullanımı için en iyi kanıt bupivakain toksisitesidir.
- Trisiklik antidepresanlar, beta blokerler ve kalsiyum kanal blokerleri de dahil olmak üzere birçok ilaç toksisitesinde lipit emülsiyon kullanımı için kanıt düzeyi çok düşüktür.
- Randomize kontrollü yüksek kalitede çalışmalara ihtiyaç vardır.

Sonuçlar

- Kaliteli destekleyici bakım uygulanmış
- Başka tedavi seçeneği olmayan
- Hemodinmaik olarak anstabil veya kardiyak arrest olan hastalarda İLE bir tedavi seçeneği olabilir.

TEŞEKKÜRLER