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LIPID EMULSION THERAPY: TIPS AND TRICKS

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21/04/2018 Antalya

OBJECTİVES

- Historical perspective
- Mechanisms for lipid emulsion therapy •
- Xenobiotics for which it has been reported •
- Risk-benefit ratio in acute care toxicology.

HAVE YOU HEARD OF “LIPIDS”?

HISTORY

- 1970-80: lipid emulsion bind xenobiotics intravascularly?
- 1997: Unusual toxicity from bupivacaine in patient with abnormal Free Fatty Acid metabolism
- 1998: rats; lipid emulsion shift toxic dose upwards

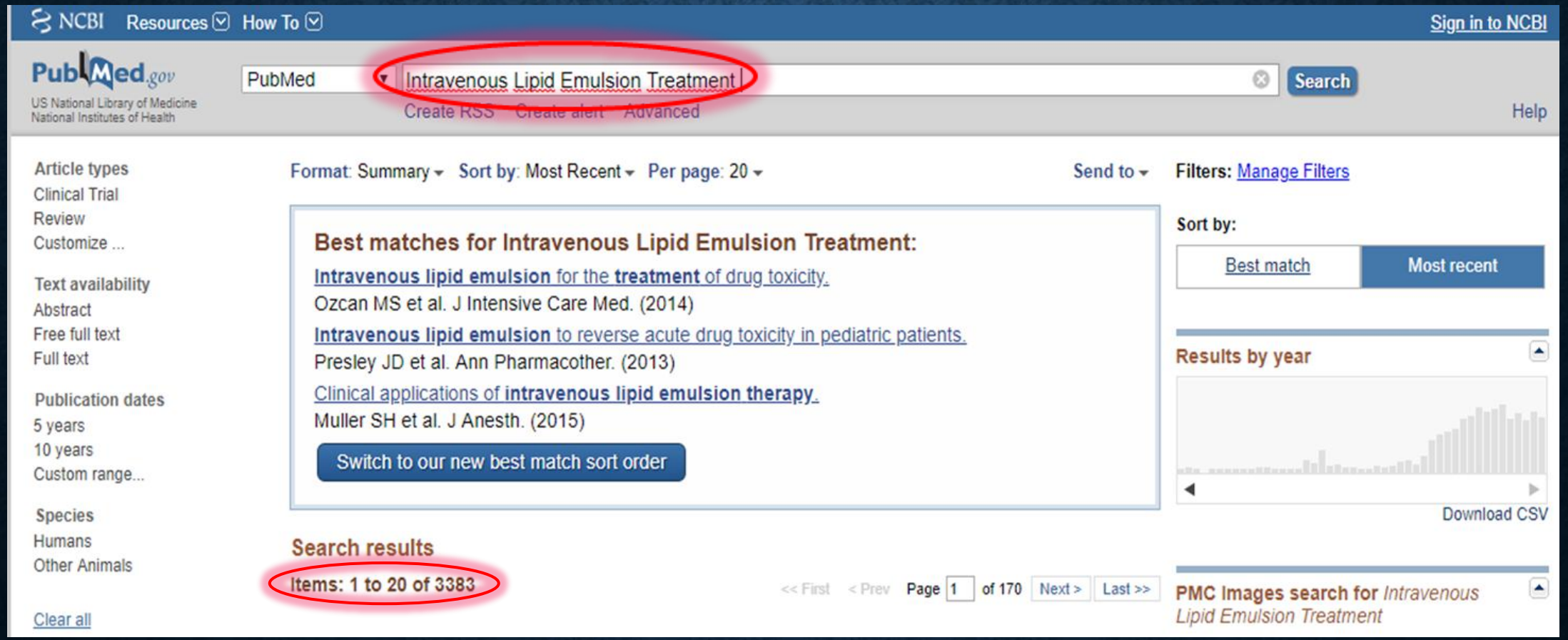
Weinberg et al. Anesthesiology 1998

HOW DOES IT WORK?

- Hypotheses:
- 1.Sequesters lipophilic xenobiotics inside their structures “lipid sink” or “lipid sponge” (in vitro /animal studies) xenobiotics taken away from site causing toxicity
- 2.Substrate for the heart in shock (in vitro / animal studies)
- 3.Alters favorably membranes potentials (2 in vitro studies)
- 4.???????

EVIDENCE TIMELINE

2006	2008	2009	2010	2011	2012
Rosenblatt human bupivacaine presumed cardiac arrest with 20% IVE bolus	Sirianni lamotrigine bupropion Felice JMT 1st review of literature	Cave Systematic Review AEM Meehan Case series abstract	numerous case reports in human and animal poisoning Jamaty ClinTox Systematic Review	Cave EMA Summary of published evidence ObS	Taftachi RCT Levine Case series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5 years
10 years
Custom range...
Species
Humans
Other Animals
Clear all
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Best matches for Intravenous Lipid Emulsion Treatment:
Intravenous lipid emulsion for the treatment of drug toxicity.
Ozcan MS et al. J Intensive Care Med. (2014)
Intravenous lipid emulsion to reverse acute drug toxicity in pediatric patients.
Presley JD et al. Ann Pharmacother. (2013)
Clinical applications of intravenous lipid emulsion therapy.
Muller SH et al. J Anesth. (2015)
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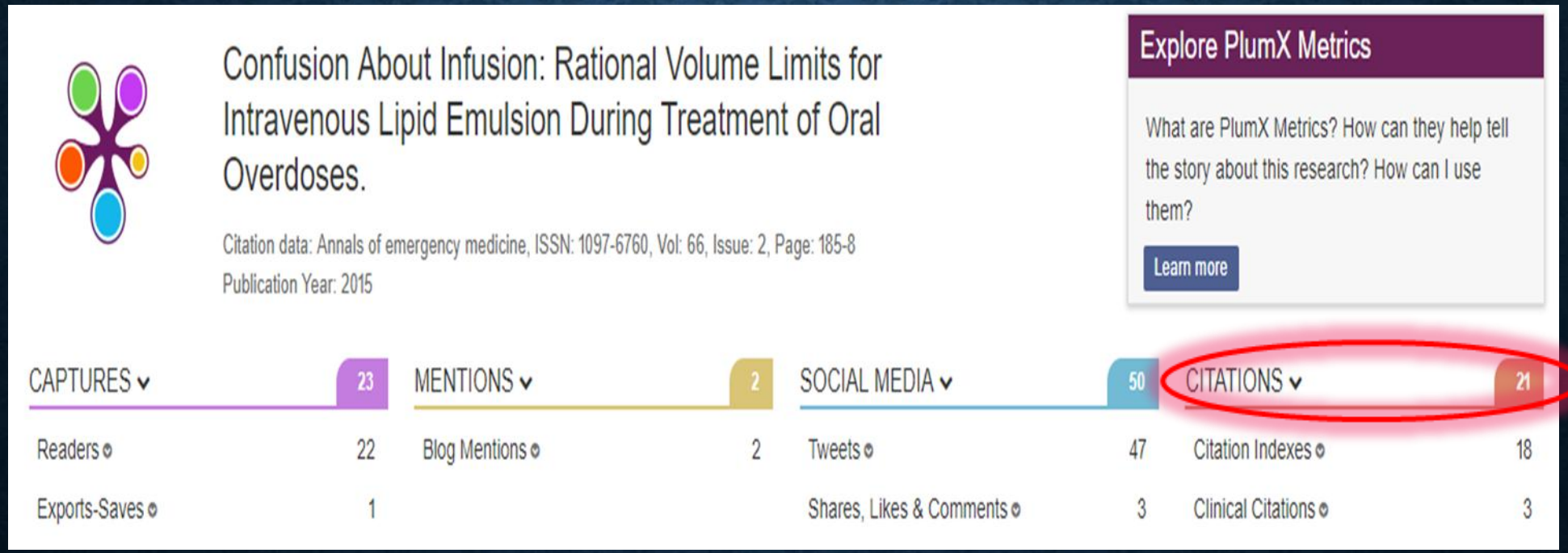
Annals of Emergency Medicine
An International Journal

Confusion About Infusion: Rational Volume Limits for Intravenous Lipid Emulsion During Treatment of Oral Overdoses

Michael R. Fettiplace, MS, Belinda S. Akpa, PhD, Israel Rubinstein, MD, Guy Weinberg, MD

DOI: https://doi.org/10.1016/j.annemergmed.2015.01.020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LIPID DOSE

Confusion About Infusion: Rational Volume Limits for Intravenous Lipid Emulsion During Treatment of Oral Overdoses

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- 1.5 mL / kg bolus followed by 60 minutes of 0.25mL / kg / min infusion.

- Clinicians should be aware that Intralipid can clog renal replacement therapy filters, although renal replacement therapy and intravenous lipid emulsion have been used together without complications.

- Agarwala R, Ahmed SZ, Wiegand TJ. Prolonged use of intravenous lipid emulsion in a severe tricyclic antidepressant overdose. J Med Toxicol. 2014;10:210-214.
- Monteiro N, Silvestre J. Severe diltiazem poisoning treated with hyperinsulinaemia-euglycaemia and lipid emulsion. Case Rep Crit Care. 2013;2013:1-4.
- Assink M, Spronk P, van Kan H, et al. Intravenous lipid emulsion in the treatment of verapamil intoxication. Neth J Crit Care. 2013;17:18-21.

Confusion About Infusion: Rational Volume Limits for Intravenous Lipid Emulsion During Treatment of Oral Overdoses

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- Basic science studies demonstrate that lipid concentrations as low as 0.25% can produce **positive inotropic effects**, and clinical cases report that infusions as low as 0.008 mL/kg/min are associated with **profound effects on physiologic parameters.**

and

- 0.25 ml/kg/min higher infusion rates may be avoided by **combining intravenous lipid emulsion with alternative methods** (ie, high-dose insulin, methylene blue).

American Journal of Emergency Medicine 33 (2015) 1111.e1–1111.e4

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journal homepage: www.elsevier.com/locate/ajem

Case Reports

Successful Treatment of Metoprolol-Induced Cardiac Arrest With High-Dose Insulin, Lipid Emulsion, and ECMO☆,☆☆,★,★★,☆☆☆

Cardiovasc Toxicol (2017) 17:223–225
DOI 10.1007/s12012-016-9362-2

Survival After Cardiac Arrest: ECMO Rescue Therapy After Amlodipine and Metoprolol Overdose

Kevin F. Maskell[1] · Nikki Miller Ferguson[2] · Jesse Bain[2] · Brandon K. Wills[1]

Indian J Crit Care Med. 2018 Feb;22(2):111-115. doi: 10.4103/ijccm.IJCCM_417_17.

Extracorporeal Membrane Oxygenation in Drug Overdose: A Clinical Case Series.

Vignesh C[1], Kumar M[2], Venkataraman R[1], Rajagopal S[1], Ramakrishnan N[1], Abraham BK[1].

Author information

	PATIENT 1	PATIENT 2	PATIENT 3
Age	29	19	17
Sex	Female	Male	Female
Drugs Involved In Overdose	Amlodipine 400 mg	Amlodipine 150 mg, Atenolol 750 mg	Propranolol 400mg, Amytriptiline 40 mg, Fluphenazine 100 mg, Gabapentin 600 mg
Apache II	19	31	23
Ingestion to Arrival Time (Hours)	8	20	36
Post Cardiac Arrest Status	-	-	+
Parameters before initiation of ECMO			
MAP (mmHg)	55	75	56
pH/Base Deficit	7.34/-12.4	7.22/-14.2	7.07/-13.8
Lactate	8.42	5.48	25.15
Urine Output	250 ml/h	100 ml/h	70 ml/h
Vasopressor requirement before initiation of ECMO			
Noradrenaline	0.9 mcg/kg/min	1.1 mcg/kg/min	0.66 mcg/kg/min
Adrenaline	1 mcg/kg/min	1.4 mcg/kg/min	1.2 mcg/kg/min
Dopamine	-	32 mcg/kg/min	-
Vasopressin	2.4 units/h	1.8 units/h	2.4units/h
Drug therapies before initiation of ECMO			
Fluids Received	5941 ml	6430 ml	3530ml
Insulin	60 units IV bolus followed by 60 U/h IV infusion	40 units IV bolus followed 40 units/h IV infusion	40 units IV bolus followed 40 units/h IV infusion
Calcium Gluconate	30 ml IV bolus followed by 30 ml/h infusion	30 ml IV bolus followed by 30 ml/h infusion	-
Glucagon	5 mg IV bolus followed by 5 mg/h infusion	5 mg IV bolus followed by 5 mg/h infusion	5mg IV bolus followed by 5mg/h infusion
Lipid Emulsion	90 ml IV bolus followed 900 ml IV over 2 h	100 ml IV bolus followed by 500ml over 2 h	90ml IV bolus followed by 900ml IV over 2 hours
Sodium Bicarbonate	-	-	15mEq/hour
Outcome			
Arrival to ECMO Initiation (Hours)	13	16	17
Duration of ECMO (Hours)	96	72	54
Mechanical Ventilation Days	10	6	10
ICU Length of Stay (Days)	11	8	20
Hospital Length of Stay (Days)	13	13	29

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- Atenolol is Hydrophilic and Log P =0.16
- Amlodipine is Moderate and LogP =2.22

Hansch, C., Leo, A., D. Hoekman. Exploring QSAR - Hydrophobic, Electronic, and Steric Constants. Washington, DC: American Chemical Society., 1995., p. 127

- LogP=lipid-water partition coefficient
- Atenolol Log P =0.16
- LogP<1.72 → hydrophilic

The lipophilicity	Toxic Agent	LogP
Lipophilic, LogP≥1.72[1,2]		
	Tetrahydrocannabinol	7,22
	Amitriptyline	4,81
	Imipramine	4,80
	Biperiden	4,28
	Fluoxetine	4,05
	Paroxetine	3,70
	Dexibuprofen	3,67
	Opipramol	3,45
	Clozapine	3,23
	Bupropion	3,12
	Essitalopram	3,08
	Phenytoin	2,47
	Olanzapine	3,00
	Valproic Acid	2,75
	Warfarin	2,70
	Mirtazapine	2,70
	Alprazolam	2,65
	Carbamazepine	2,45
	Venlafaxine	2,38
	Malathion	2,36
	Amlodipine	2,22
	Questapine	2,09
	Metoprolol	1,87
	Bisoprolol	1,87
	Amphetamie	1,85
Hydrophilic , LogP<1.72[1,2]		
	Paracetamol	0,46
	Methylphenidate	0,20
	Theophylline	-0,13
	Monocrotophos	-0,40
	Pregabalin	-0,55

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ABSTRACT

Previous case reports have described the administration of lipid emulsion therapy in lipophilic drug intoxication cases. Here, we aimed to share the data and outcomes of patients administered lipid therapy, especially those with a worsened general status despite receiving initial antidotal and extracorporeal therapies. A total of 65 patients who presented to the emergency room and received lipid therapy between January 1, 2014 and January 1, 2017 were included in this study. Each patient was given a 20% ClinOleic (Baxter) infusion of 1.5 mL/kg for 1–3 minutes and then 100 mL/h (0.025 mL/kg/min). The toxic drugs were divided into low or high permeability groups according to their lipid/water partition coefficients (LogP). Of the 65 patients, 55.4% (n=36) were female and 44.6% (n=29) were male. These patients were grouped according to a 1.72 lipid/water cut-off value. The lipid therapy was administered in addition to antidotal therapy in two patients in the hydrophilic group and five patients in the lipophilic group. The only variable that was significantly restored 12 hours after the lipid therapy was the respiratory rate, which was 16.0 (15.5–17.3) breaths/min in the hydrophilic group and 20.0 (18.0–22.0) breaths/min in the lipophilic group (p=0.003). We believe that lipid therapy can be used as a last resort in intoxication cases, especially in patients with decreased Glasgow Coma Scale scores and worsened vital findings despite antidotal and extracorporeal therapies, regardless of whether the causative agent is hydrophilic or lipophilic.

Keywords: lipophilicity, lipid emulsion therapy, toxicity, hydrophilicity, lipid/water partition coefficient, emergency service

	Lipophilic (n=59)	Hydrophilic (n=6)	pValue
Duration of hospitalization			
EmergencyIntensiveCare	2.0(1.0-4.0)	2.5(0.8-6.0)	0.670
Observationunit	1.0(1.0-2.0)	1.5(1.0-2.5)	0.479
Total time (day)	3.0(2.0-5.0)	3.5(2.8-7.0)	0.365
GKS			
Admition	13.0(4.5-15.0)	15.0(8.5-15.0)	0.213
Afterlipid 12th hour	15.0(14.0-15.0)	15.0(11.0-15.0)	0.867
24th hour	15.0(14.0-15.0)	15.0(14.0-15.0)	0.955
MeanArterielPressure			
Admition	88.9±16.3	95.7±18.0	0.388
12th hour	83.3±14.2	83.3±10.8	0.997
24th hour	83.4±15.1	90.7±10.6	0.302
Respiratory rate			
Admition	20.0(18.0-22.0)	16.0(15.5-17.3)	**0.003**
12th hour	18.0(16.0-21.0)	21.0(15.5-25.5)	0.255
24th hour	19.0(15.5-22.0)	18.0(14.0-20.0)	0.417

Journal of Clinical Toxicology

Thomas et al., J Clin Toxicol 2017, 7:6
DOI: 10.4172/2161-0495.1000368

Case Report Open Access

Intravenous Lipid Emulsion Therapy and VA-ECMO rescue therapy for Massive Venlafaxine and Clonazepam Overdose

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[2]*Department of Anesthesiology, Division of Critical Care Medicine, CCM Fellowship Program Director, Vancouver General Hospital, Vancouver, Canada*

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TAKE HOME A MESAGE

- Although it has negative effects in lipid renal replacement therapy theoretically, such problems were rare in practice in studies conducted.

- Lipid will save you time until you reach antidotes, ECMO or other extracarporal therapies.


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