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pp S81-S94

Lipid Rescue From Bench to Bedside

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THE PLAN...

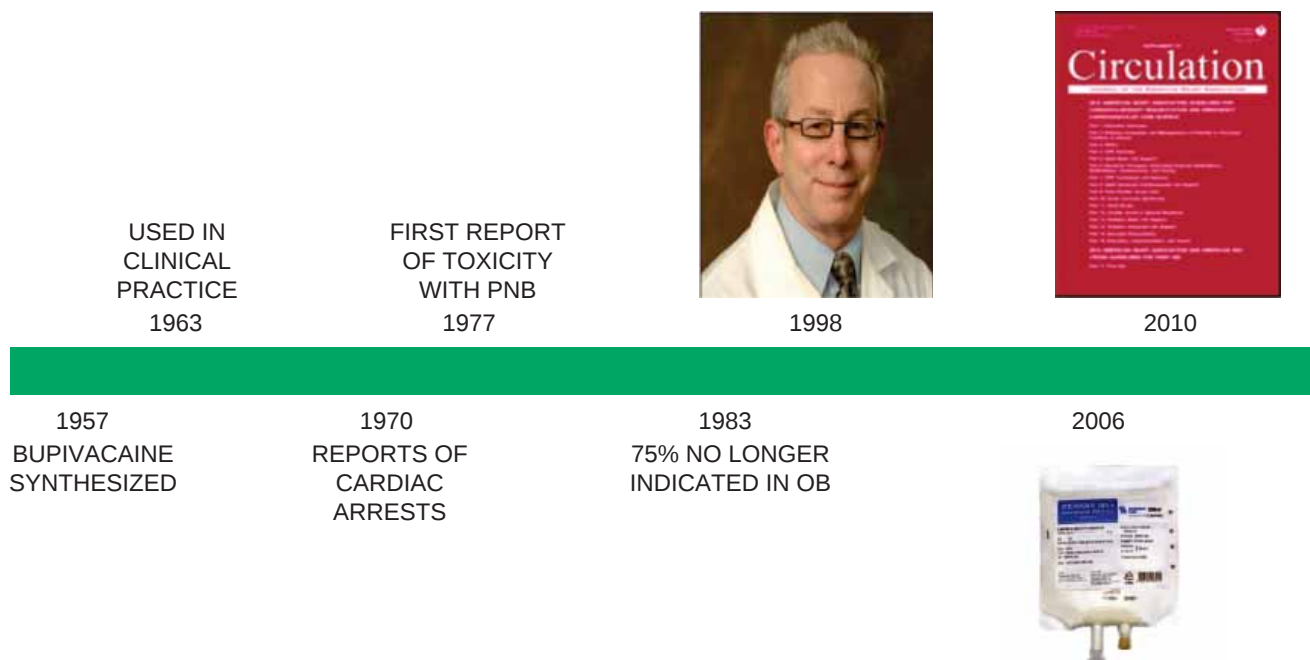
- Science of «lipid rescue»
- Safety of lipid infusions
- Current research
- Diagnosis of LAST
- What's next



www.medigraphic.org.mx

Este artículo puede ser consultado en versión completa en <http://www.medigraphic.com/rma>

TIMELINE OF BUPIVACAINE AND LAST



GUY WEINBERG, M.D.

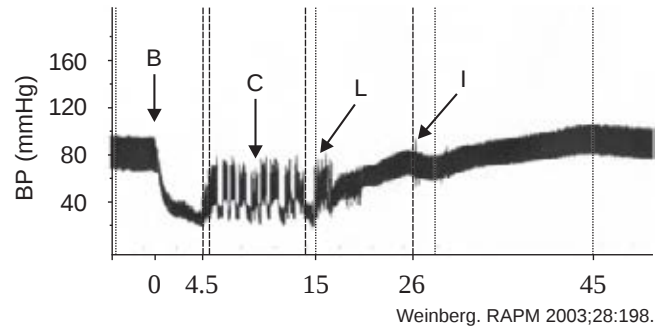
- 16 yr-old female
- Isovaleric acidemia
 - Autosomal recessive dx of leucine catabolism
 - Isovaleryl-CoA dehydrogenase deficiency
 - Carnitine deficiency
 - May sensitize heart to arrhythmias
 - Arrhythmias during axillary liposuction
 - 22 mg (0.4 mg/kg) bupivacaine
- Bupivacaine inhibits carnitine-dependent pathway



INVESTIGATION

- Measured respiration in cardiac mitochondria oxidizing lipid and non-lipid substrates
 - To see effect of bupivacaine
- Found bupivacaine inhibits key step in mitochondrial transport
- Also...
 - Pretreatment with lipid increases the dose of bupivacaine to induce asystole in rats

- Pretreatment experiment
- 6 rats/treatment group—GA and instrumentation
- Pretreated with 3 mL/kg/min with:
 - Saline
 - Intralipid 10%
 - Intralipid 20%
 - Intralipid 30%
- 0.75% bupivacaine 10mg/kg/min to 10s of asystole
- Concentrations of bupivacaine in plasma to cause arrest:
 - 12.7 mg/kg
 - 17.8 mg/kg
 - 49.8mg/kg
 - 82.0 mg/kg

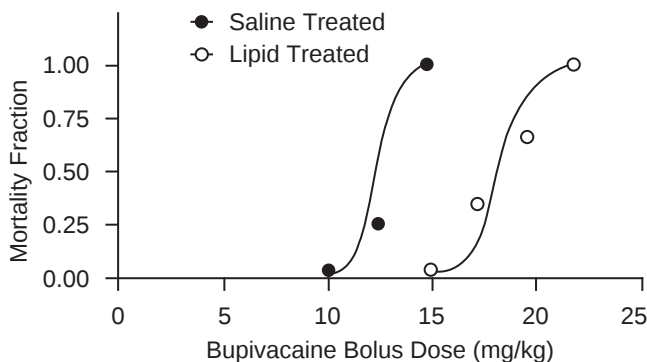


LIPID INFUSIONS ARE:

- Emulsion in water:
 - Soybean oil
 - (predominantly neutral triglycerides)
 - Made isotonic with glycerin
 - Egg lecithin
 - The emulsifying agent
 - NO preservatives
- Particles 0.5 μ m in diameter
- In blood these fat droplets form a lipid compartment
- But not just a lipid sink...

RESUSCITATION

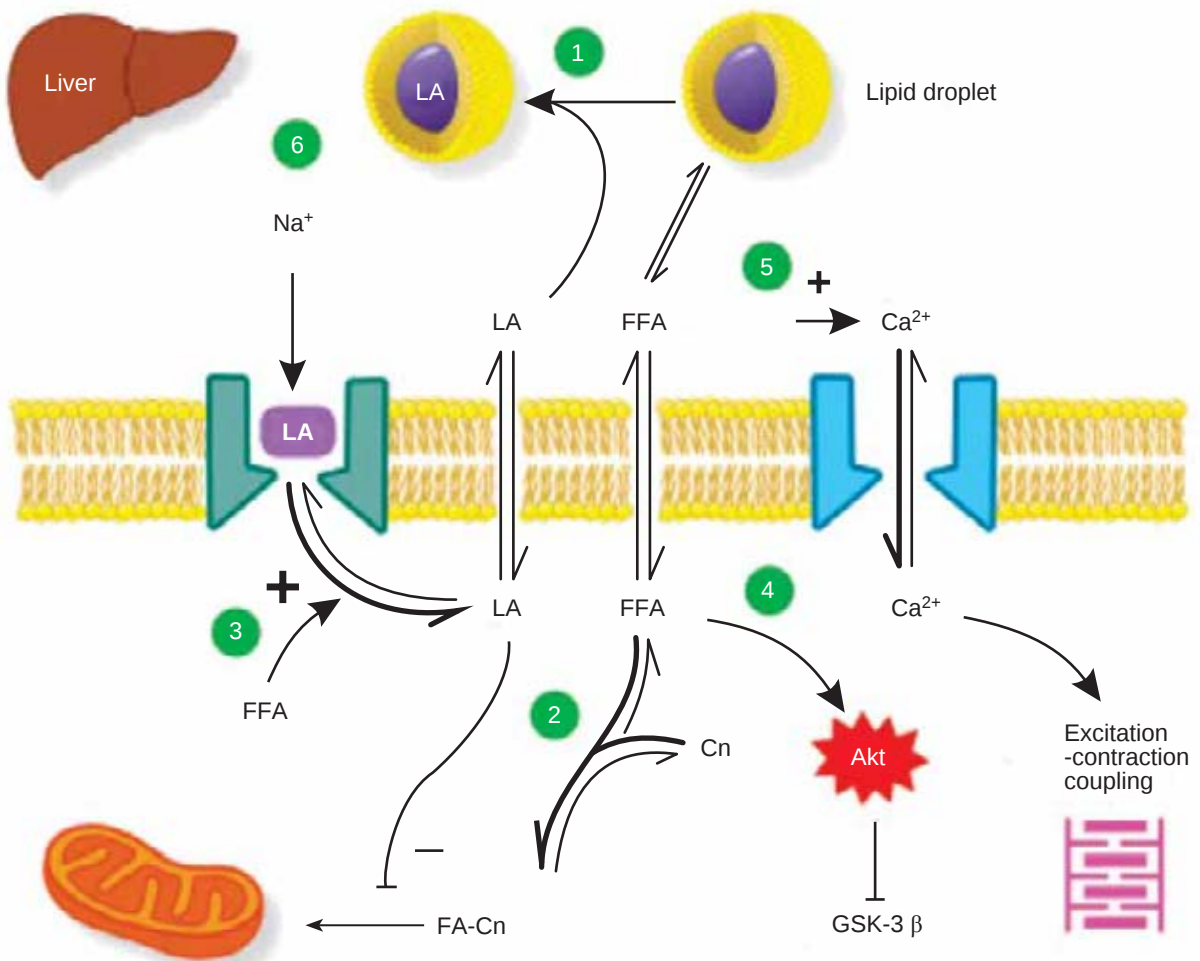
- Anesthetized rats
- Bupivacaine bolus
- Ventilation 100% O₂
- Bolus of:
 - Saline
 - 30% lipid
 - Followed by infusions
- Compressions PRN
- Survival
 - HR > 100 bpm
 - SBP > 60 mmHg
- Lipid shifts dose-response curve to bupivacaine-induced asystole
 - LD50 from 12.5 to 18.5 mg/kg



- 12 hounds (22-26 kg) under GA
- Bupivacaine 10 mg/kg injected
- 10 minutes internal cardiac massage
- 20% lipid -or- saline
- 4mL/kg bolus then 0.5 mL/kg/min infusion
- 100 versus 0% survival

POTENTIAL MECHANISMS OF ACTION

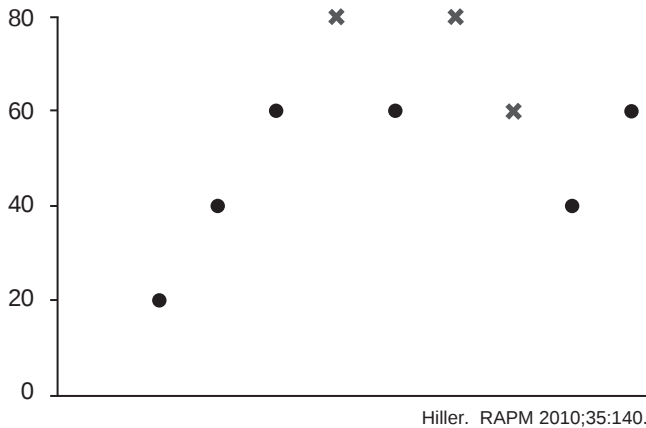
- «Lipid sink»
 - Sequestration of toxins of high lipophilicity
 - Bupiv lipid: aqueous partition coefficient = 11.9:1
- Cytoprotection
 - Akt (protein kinase B) activation
- Competition
 - Inhibition of ion channel binding
- Pharmacokinetics
 - Shunting to sequestering organs
- Inotropic/ionotropic
 - Activation of calcium currents
- Metabolic
 - Reverses the inhibitory effect of bupivacaine on lipid-based mitochondrial respiration



Weinberg. *Anesthesiology* 2012;117:180.

SAFETY OF LIPID INFUSIONS - LD 50 IN RATS

- 20% lipid (20, 40, 60 or 80 mL/kg) or saline
- Over 30 minutes
- Dixon «up-and-down» method
- Recovered and observed for 48 hours
- Euthanized and organs harvested
- Three additional rats given 60 mL/kg
 - Euthanized at 1, 4, 24 hours
 - To identify progression of organ damage



LD₅₀ = 67.72 ± 10.69 ML/KG

- Three animals died
 - 2 at 80 mL/kg, 1 at 60 mL/kg
 - No specific etiology
- No CNS excitation/focal defects/motor abnormalities
 - Lethargy after receiving 80 mL/kg
- No CV changes
- Triglycerides markedly ↑ after all infusions
 - All returned to baseline by 48 hours
- Microabnormalities in lung and liver at 60/80 mL/kg
 - Histopathology worse at 1 hour than 4 and 24 hours
- Supports safety of lipid infusion at current doses

Hiller. RAPM 2010;35:140.

REACTIONS

- Contamination
- Direct reactions
 - Pyogenic
 - 10-20 min post-infusion
 - Nausea, vomiting, chills fever, headache chest pain, dyspnea, cyanosis (< 1%)
 - Thrombophlebitis
- Allergy
 - Soybean oil

OTHER CONCERNS

- | | |
|--|---|
| <ul style="list-style-type: none"> • Pulmonary comps— <ul style="list-style-type: none"> — Pts w/nl lung or pulm compromise without ARDS do not demonstrate ↓ oxygenation or pulmonary vascular changes • Pulmonary changes with ARDS 2° to: <ul style="list-style-type: none"> — Enhanced inflammation — Transient | <ul style="list-style-type: none"> • Pancreatitis— <ul style="list-style-type: none"> — All reported cases in patients with concomitant diseases <ul style="list-style-type: none"> - Crohn's - EtOH - HIV |
|--|---|

Large lipid doses will interfere with laboratory studies and have caused chemical hyperamylasemia without symptoms of pancreatitis

Are all formulations of lipid equal?

- Long chain triglyceride (LCT) emulsions more efficient than LCT/medium chain triglyceride (MCT) formulations to bind long-acting LAs
 - Study *in vitro*

Mazoit. Anesthesiology 2009;110:380

- Model of anesthetized and ventilated piglets
- LCT and LCT/MCT both reversed effects
 - QRS duration
 - Atrial-His
 - PQ intervals

Candela. A&A 2010;110:1473

- Caution with extrapolations to humans

BACK TO THE STORY...

A 58 year-old male presents for shoulder surgery

- H/o coronary artery bypass
- Has angina
- ECG
 - Right bundle branch block
 - Left anterior hemiblock
 - Old anterior wall MI
- Meds
 - NTG PRN
 - Lisinopril
 - Atenolol
 - Clopidogrel
 - Aspirin
- Refused further cardiac work-up

THE BLOCK

- ASA monitors, O₂ via nc
 - Midazolam 2 mg
 - Fentanyl 50 µg
- ISB→ stimulation at .34 mA
 - Negative aspiration
- Agents
 - Mepivacaine 300 mg
 - Bupivacaine 100 mg
 - In 5 cm³ aliquots with aspiration between

AND THEN...

- 30 seconds after injection
 - Tonic-clonic seizure
 - O₂ via self-inflating resuscitation bag
 - Propofol 50 mg
- 90 seconds later
 - Seizure restarts
 - Propofol 100 mg
 - V tach → V fib → Asystole
- Endotracheal intubation and CPR

RESUSCITATION

- Full ACLS
 - (At least 6 attendings and 1 resident)
- Central line/arterial line attempts
- Plans for cardiopulmonary bypass

OUR INTERVENTION

- 100 cm³ of 20% lipid infusion IV
- Continued CPR
- Single sinus beat
 - Epinephrine
 - Atropine
- Return to sinus rhythm
- No neurologic sequelae
- (ISB block)



TOO SOON TO CELEBRATE?

QUESTIONS

- Adequacy of cardiac work-up
- Use of propofol to manage seizures
- Appropriate use of defibrillation
- Timeliness of initiation of mechanical ventilation
- Possibility of spontaneous recovery
- Choice of local anesthetic
 - «Retrobupivacaine»

Anaesthesia, 2008, 81, pages 800-801

doi:10.1111/j.1365-2044.2006.04740.x

CASE REPORT

Successful resuscitation of a patient with ropivacaine-induced asystole after axillary plexus block using lipid infusion*

R. J. Litz, M. Popp, S. N. Stehr and T. Koch

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anaesthesia, 2007, 82, pages 516-518

doi:10.1111/j.1365-2044.2007.01805.x

CASE REPORT

Levobupivacaine-induced seizures and cardiovascular collapse treated with Intralipid®

i. Foxall,¹ R. McCahon,² J. Lamb,³ J. G. Hardman⁴ and N. M. Bedford³

Fellow in Regional Anaesthesia, 2 Specialist Registrar, 3 Consultant Anaesthetist, Department of Anaesthesia, Associate Professor and Reader in Anaesthesia, University Department of Anaesthesia, Queen's Medical Centre, Nottingham NG7 2UH, UK

ANESTHESIA
& ANALGESIA

Case Report

Simulation Education in Anesthesia Training: A Case Report of Successful Resuscitation of Bupivacaine-Induced Cardiac Arrest Linked to Recent Simulation Training

Hugh M. Smith, MD, PhD

Adam K. Jacob, MD

Luís G. Segura, MD

John A. Dilger, MD

Laurence C. Tischer, MD

Simulation training is rapidly becoming an integral element of the education curriculum of anesthesia residency programs. We report a case of successful resuscitation of bupivacaine-induced cardiac arrest treated with IV lipid emulsion by providers who had recently participated in simulation training involving a scenario nearly identical to this case. Upon debriefing, it was determined that the previous training influenced execution of the following steps: rapid problem recognition, prompt initiation of specific therapy in the setting of supportive advanced cardiac life support measures, and coordinated team efforts. Although the true cause of efficient resuscitation and ultimate recovery cannot be proven, the efficacy of the resuscitation process, including timely administration of lipid emulsion, is evidence that simulation may be useful for training providers to manage such emergencies. (J Intensive Care Med 2008;23:415-416)

Case Report

Anaesthesia, 2008, 81, pages 800-801

doi:10.1111/j.1365-2044.2006.04740.x

CASE REPORT

Successful resuscitation of a patient with ropivacaine-induced asystole after axillary plexus block using lipid infusion*

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Intravenous Lipid Infusion in the Successful Resuscitation of Local Anesthetic-Induced Cardiovascular Collapse After Supraclavicular Brachial Plexus Block

Julie A. Warren, MD

R. Brian Thomas, MD

Alexandru Georgescu, MD

Saurin J. Shah, MD

We describe a case of successful resuscitation with an IV lipid infusion of local anesthetic-induced cardiovascular toxicity after supraclavicular brachial plexus block with mepivacaine and bupivacaine. Lipid therapy was initiated after 10 min of unsuccessful resuscitation and resulted in restoration of cardiovascular activity and hemodynamic stability. This case illustrates the utility of IV lipid therapy in the treatment of local anesthetic toxicity. (J Intensive Care Med 2008;23:415-416)

Case Report

Reversal of Central Nervous System and Cardiac Toxicity After Local Anesthetic Intoxication by Lipid Emulsion Injection

Rainer J. Litz, MD
Thomas Rosenthal, MD
Axel R. Heller, MD
Sebastian N. Stehr, MD

A 71-yr-old man (57 kg, 176 cm, ASA III) received an intrathecal brachial plexus block for surgery of basilar of the cranium. Twenty minutes after intrathecal injection of 40 mL of ropivacaine 1% (Ropivacaine®) and 5 min after supplementation of 10 mL of ropivacaine 1% (Ropivacaine®) using an auxiliary approach, the patient complained of agitation and shivering and became unresponsive to verbal commands. In addition, supraventricular tachycardia with bigeminy occurred. Local anesthetic toxicity was suspected and a dose of 200 mL of a 20% lipid emulsion was infused. Symptoms of central nervous system and cardiac toxicity disappeared within 5 and 75 min after the first lipid injection, respectively. Plasma concentrations of local anesthetics were determined before, 20, and 40 min after lipid infusion and were 4.08, 2.30, and 1.77 µg/mL for ropivacaine and 0.02, 0.35, and 0.24 µg/mL for propofol. These concentrations are below previously reported thresholds of toxicity above 5 µg/mL for both local anesthetics. Signs of toxicity resolved and the patient underwent the scheduled surgical procedure uneventfully under brachial plexus blockade. (Smith Aug 2008;106:1175-7)

Case Report

Successful Resuscitation After Ropivacaine and Lidocaine-Induced Ventricular Arrhythmia Following Posterior Lumbar Plexus Block in a Child

Hugues Lucot, MD
Jean-Yves Thacit, MD
Mohamed Bakouddah, MD
Jean-Xavier Mazoit, MD, PhD
Jean-Marc Malinovsky, MD, PhD

We report the case of a 13-yr-old girl scheduled for liver surgery under general anesthesia and posterior lumbar plexus block. A ventricular arrhythmia developed 15 min after local anesthetic injection. A 20% lipid emulsion was successful in converting the ventricular arrhythmia to a sinus rhythm. This is consistent with previous reports suggesting that lipid emulsion is an effective emergency treatment of local anesthetic toxicity. We recommend the immediate availability of lipid emulsion along with other emergency therapeutics in operating rooms where local anesthesia is used. (Smith Aug 2008;106:1175-7)



SCIATIC BLOCK

- 83 yr-old 75 kg, TKA with GA plus:
 - Continuous FNB
 - Single-injection sciatic block
- Block with NS technique
- During injection of bupivacaine 130 mg
 - LOC
 - Tonic-clonic seizure
 - Pulselessness

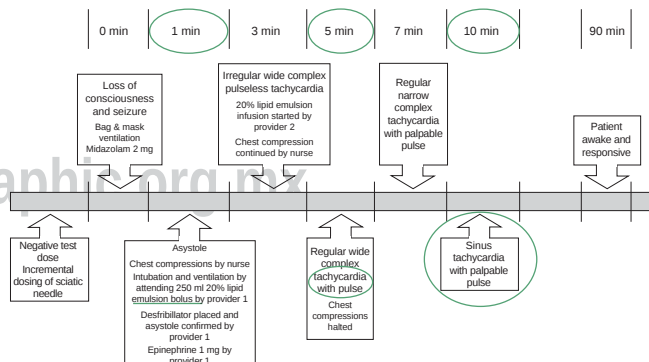
SIMULATION TRAINING



LIPID EMULSION 3 ML/KG



Smith. A&A 2008;106:1581-4.

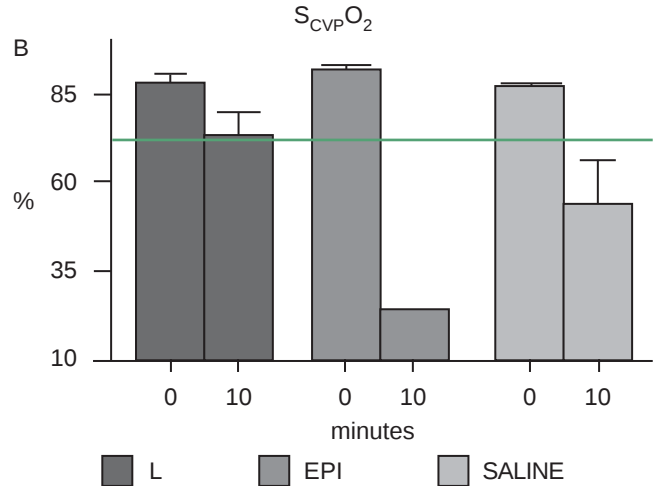


Smith. A&A 2008;106:1581-4.

VERSUS EPI VERSUS SALINE

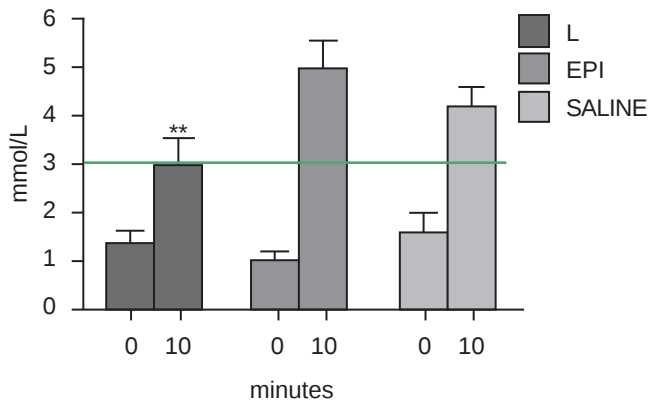
- Rats + isoflurane + bupiv 20 mg/kg
- 100% O₂ + chest compressions
- Boluses of resuscitation drugs at 2.5 and 5 min
 - 30% lipid
 - Saline
 - Epinephrine 30 µg/kg
- Continuous ECG, arterial pressure
- RPP, pH, lactate, S_{CVP}O₂

Weinberg. Anesthesiology 2008;108:907.



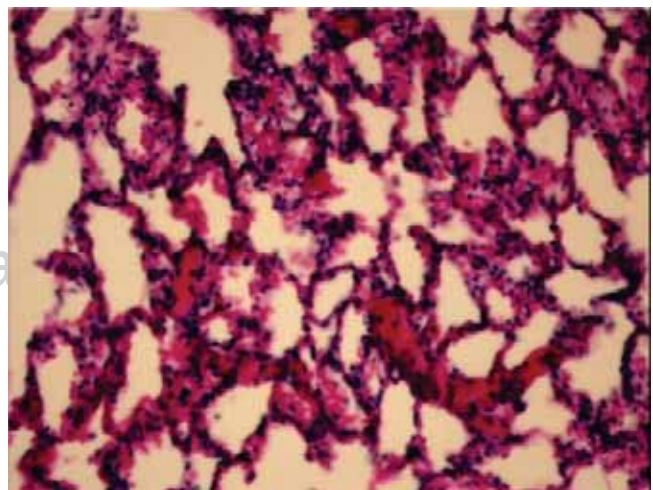
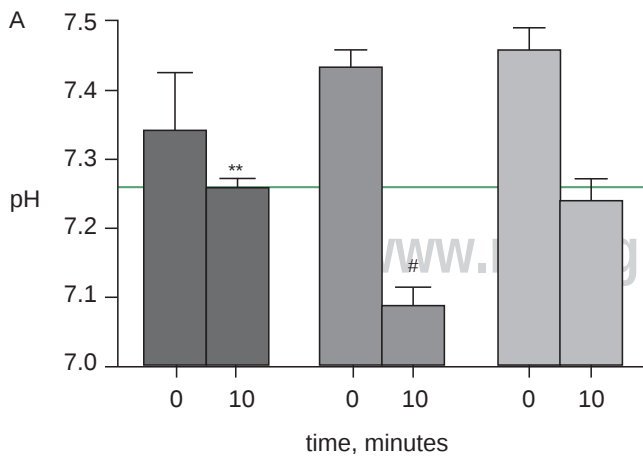
Weinberg. Anesthesiology 2008;108:907.

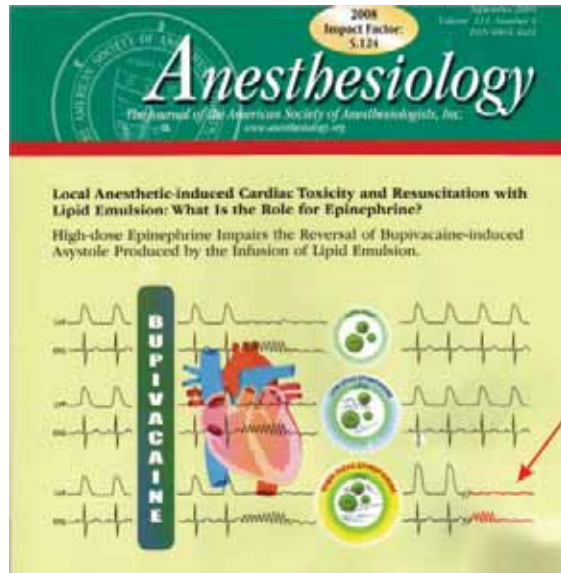
Blood Lactate



- All metrics improved more with lipid
- 80% rats with Epi had pulmonary edema
- 100% w/epi had ectopy
- Epi might worsen:
 - Tissue perfusion
 - Cardiac output
 - O₂ delivery
- Epi exerts direct metabolic effects that ↑ lactate
- Quality of recovery after epi no better than controls
 - May even be worse

pH





IS HYPERADRENERGIC STIMULATION DETRIMENTAL?

- Epinephrine
 - Is arrhythmogenic
 - ↑ myocardial oxygen demand
 - ↓ subendocardial perfusion
 - Causes pulmonary edema
- LA cardiac toxicity ↓ contractility, worsened by acidosis
- Repeat boluses may aggravate toxicity
 - By causing intense vasoconstriction
 - Increasing lactate



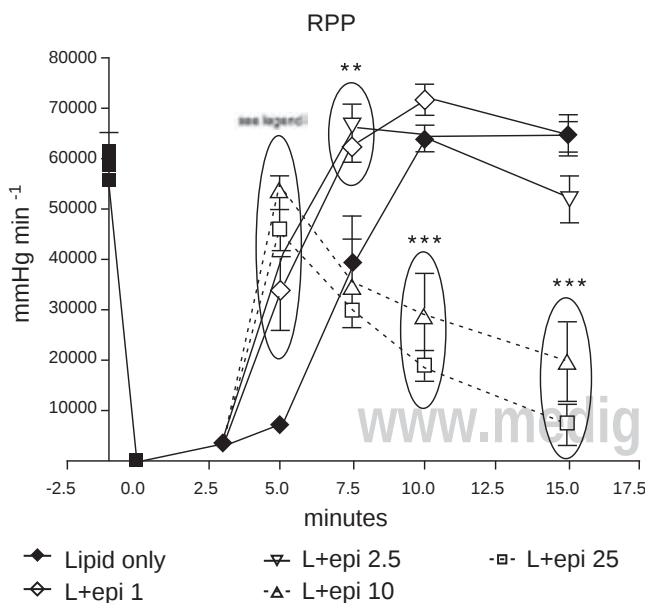
EPINEPHRINE IMPAIRS RESUSCITATION

- 30 rats/6 groups
- Bupivacaine 20 mg/kg
- All tx at 3 minutes
- 30% lipid + epi
- Lipid alone had slower but more sustained recovery
- Epi > 10 µg/kg improved initial return but not sustainable
- Pulmonary edema

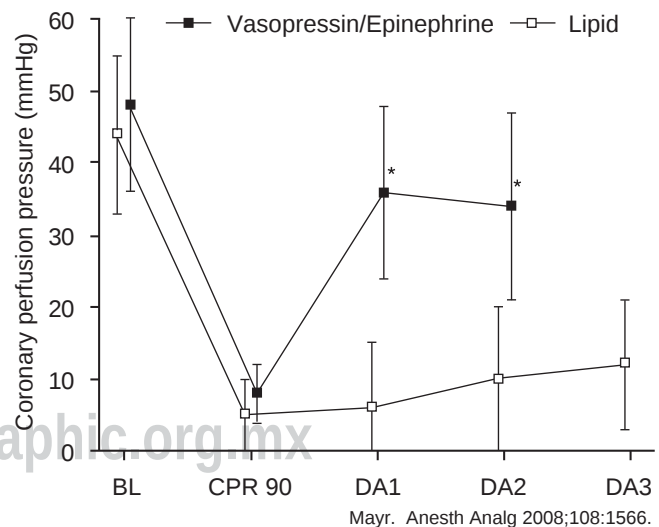
VASOPRESSIN + EPI ↑ CPP MORE THAN LIPID IN A PORCINE MODEL OF BUPI-INDUCED ARREST

- 10 adult pigs with GETA
- 5 mg/kg bupivacaine
- CPR begun 1 minute post-arrest x 2 minutes
- Randomized
 - 4 mL/kg lipid → 0.5 mL/kg/min
 - Vasopressin + epi (0.4/45, 0.4/45, 0.8/200 U/kg and µg/kg) every 5 minutes
- 5 in the vasopressor group survives, 0 in lipid

Mayr. Anesth Analg 2008;108:1566.



Hiller. Anesthesiology 2009;111:498.



Mayr. Anesth Analg 2008;108:1566.

Pig in a Poke: Species Specificity in Modeling Lipid Resuscitation

Guy Weinberg, MD,*† and Israel Rubinstein, MD†§

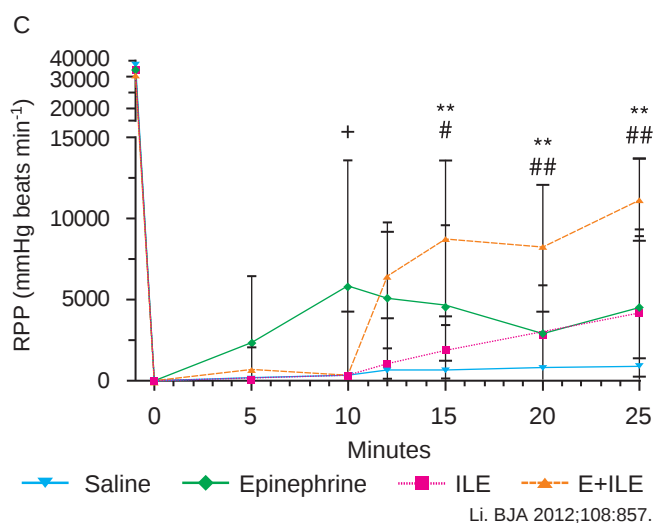
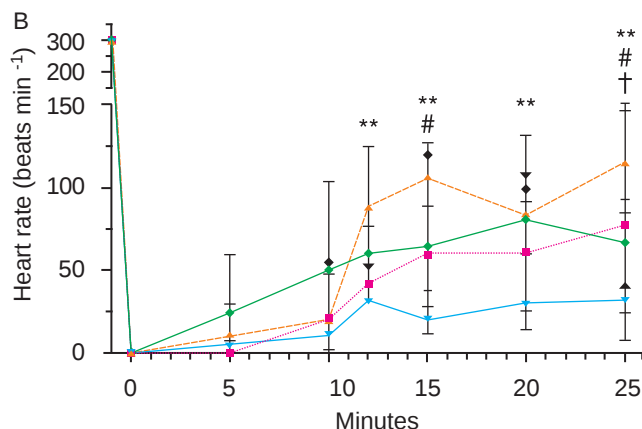
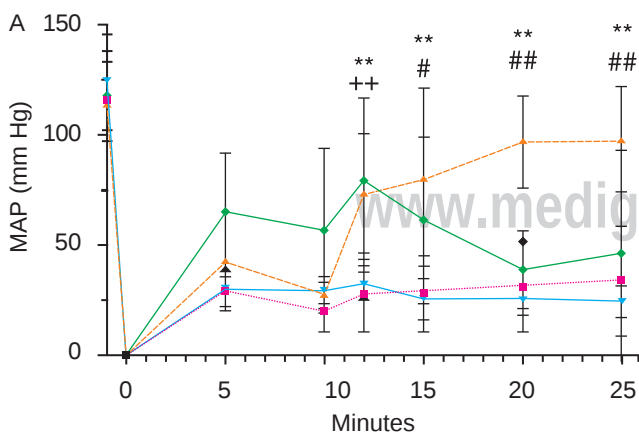
- Compliment activation-related pseudoallergy (CARPA)
 - Hypersensitivity to liposomal preparations
 - Mottling
 - Hypoxemia
- Authors of 16 papers who did studies 1991-2011 contacted
 - 12 replies
 - 3 negative
 - 9 reported mottling
 - Shock state or 2° lipid?
- Are pigs an appropriate model?

Anesth Analg 2012;114:907.

DELAYED RESUSCITATION

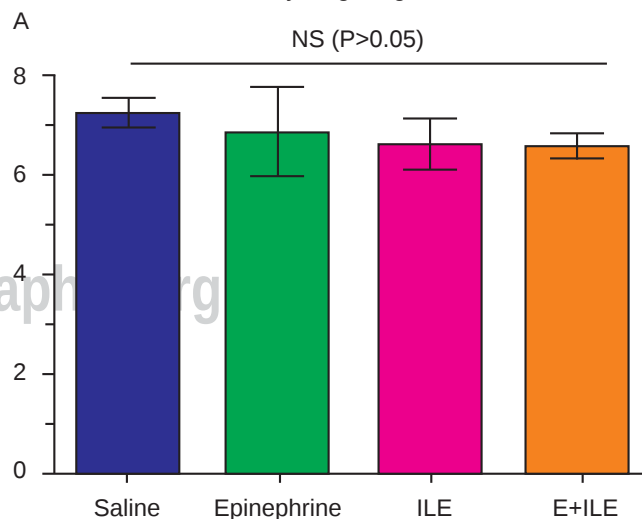
- 32 rats with bupivacaine arrest (30 mg/kg)
- BLS x 10 minutes
- Treatment
 - Saline-1 mL/kg @ 1, 3, 5 min then 5 mL/kg at 10 min and 0.5 mL/kg/min
 - Epi-10 µg/kg @ 1, 3, 5, 10 min then q 3 min to RPP < 20% baseline
 - Lipid-1 mL/kg @ 1, 3, 5 min then 5 mL/kg at 10 min and 0.5 mL/kg/min
 - Lipid+epi-same as lipid but epi 10 µg/kg @ 10 min (12, 15 if needed)
- Results
 - Lipid+epi had marked improvement in hemodynamics to lipid at 25 min
 - CPP higher
 - Myocardial bupivacaine content lower
 - Lipid alone (3/8 survived)
 - Higher PO₂
 - Less severe acidosis

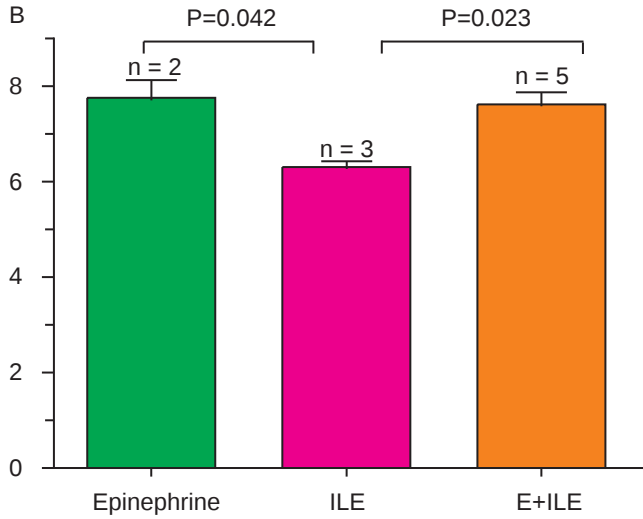
Li. BJA 2012;108:857.



LIPID-ONLY RATS HAD LESS INTERSTITIAL PULMONARY EDEMA

Wet-to-dry lung weight ratio





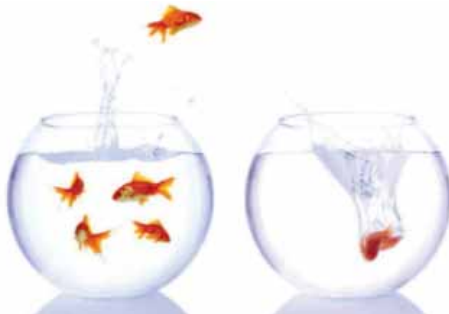
Li. BJA 2012;108:857.

ASRA RECOMMENDS



REDUCING INDIVIDUAL DOSES
OF EPINEPHRINE TO < 1 µG/KG

INTELLECTUAL LEAPS...



AMELIORATION OF LIPID SOLUBLE DRUG TOXIDROMES

TOXICOLOGY CASE REPORT

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

Archib J. Strain, MD
Kevin C. Osterhout, MD
Diane P. Casero, MD
Alicia A. Miller, PhD
Marie R. Wolfhouse, MD
Michael R. Goodkin, MD
Guy L. Weinberg, MD
Fred M. Heavily, MD

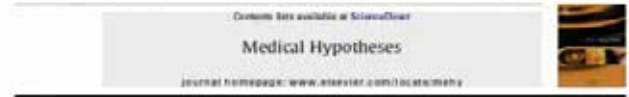
From the Department of Anesthesiology (Strain) and Division of Cardiology (Goodkin), Ridge Memorial Hospital, Modesto, CA; the Department of Pediatrics, University of Pennsylvania School of Medicine and The Children's Hospital of Philadelphia, Philadelphia, PA (Osterhout, Casero, Miller, Wolfhouse, Heavily); the Section of Critical Toxicology, Division of Emergency Medicine, and the Poison Control Center, The Children's Hospital of Philadelphia, Philadelphia, PA (Goodkin); the Department of Anesthesiology, University of Illinois College of Medicine at Chicago, and Jesse Brown VA Medical Center, Chicago, IL (Weinberg).

Intralipid Infusion Ameliorates Propranolol-Induced Hypotension in Rabbits

Martyn G. Harvey, MBChB^a, Grant R. Cave, MBChB^b

^aDepartment of Emergency Medicine, Waikato Hospital, Hamilton, New Zealand

^bEmergency Medical Systems, Australia, Melbourne Australia



Intravenous lipid emulsions combine extracorporeal blood purification: A novel therapeutic strategy for severe organophosphate poisoning

Yanguang Zhou, Chengyao Zhan, Yongsheng Li, Qiang Zhong, Han Pan, Guangrui Yang *

Department of Intensive Care Unit, Fuzhou Hospital, Fuzhou Medical College, Huashan University of Science and Technology, Fujian 350001, China

TOXICOLOGY/ORIGINAL RESEARCH

Intralipid Outperforms Sodium Bicarbonate in a Rabbit Model of Clomipramine Toxicity

Martyn Harvey, BSc, MBChB, FACEM

Grant Cave, BSc, MBChB, FACEM

From the Department of Emergency Medicine, Waikato Hospital, Hamilton, New Zealand (Harvey); and the Department of Intensive Care Medicine, Monash Medical Centre, Melbourne, Australia (Cave).

Hemodynamic Effects of Intravenous Fat Emulsion in an Animal Model of Severe Verapamil Toxicity Resuscitated with Atropine, Calcium, and Saline

Theodore C. Bantz, MD, MS, Jason Cho, MD, Eric Peters, MD, Mark Yu, MD, In-Hui Hahn, MD

OVERDOSE IN THE ED

- 17 yr-old female
- Seizure activity and cardiovascular collapse
 - 7.95 g bupropion (Wellbutrin XL)
 - Dopamine, norepi and serotonin-reuptake inhibitor
 - 4 g lamotrigine (Lamictal)
 - Blocks voltage-dependent sodium channels
- > 10 hours post ingestion cardiovascular collapse
- 100 mL bolus 20% lipid emulsion
- 1 minute later sustainable pulse

Sirianni. Ann Emer Med 2008;51:412.

Time	Age	Sex	Weight	Height	Temp	HR	BP	SpO2	Glucose	ECG	ABG	UO	Other
11:15	17	F	50	160	36.5	110	110/70	98	100	Normal			
11:20	17	F	50	160	36.5	110	110/70	98	100	Normal			
11:25	17	F	50	160	36.5	110	110/70	98	100	Normal			
11:30	17	F	50	160	36.5	110	110/70	98	100	Normal			
11:35	17	F	50	160	36.5	110	110/70	98	100	Normal			
11:40	17	F	50	160	36.5	110	110/70	98	100	Normal			
11:45	17	F	50	160	36.5	110	110/70	98	100	Normal			
11:50	17	F	50	160	36.5	110	110/70	98	100	Normal			
11:55	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:00	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:05	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:10	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:15	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:20	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:25	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:30	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:35	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:40	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:45	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:50	17	F	50	160	36.5	110	110/70	98	100	Normal			
12:55	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:00	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:05	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:10	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:15	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:20	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:25	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:30	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:35	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:40	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:45	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:50	17	F	50	160	36.5	110	110/70	98	100	Normal			
13:55	17	F	50	160	36.5	110	110/70	98	100	Normal			
14:00	17	F	50	160	36.5	110	110/70	98	100	Normal			

WHERE ARE WE NOW?

Other Therapies

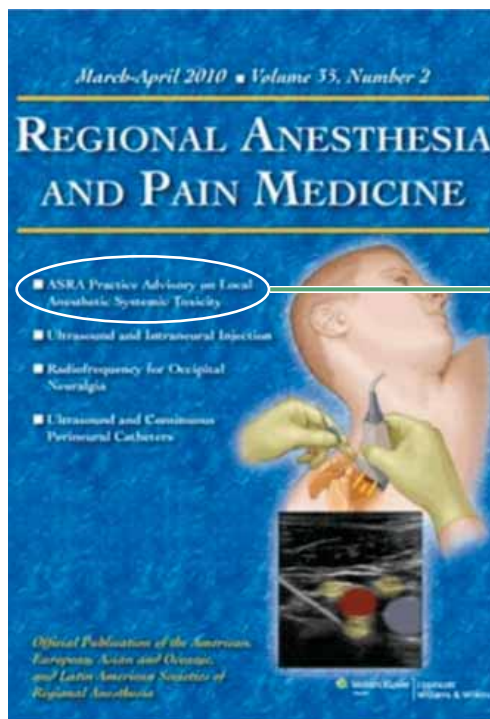
Case reports have suggested that in patients who remain critically hypotensive despite maximal vasopressor therapy, specific interventions using intra-aortic balloon counterpulsation, ventricular assist devices, and extracorporeal membrane oxygenation or other extra corporeal life support (ECLS) devices may be lifesaving.²⁷²⁻²⁷⁴ While evidence remains weak, at least two human case reports indicate a possible benefit from lipid emulsion infusion for overdose by β -blockers.^{275,276} Animal studies are mixed.²⁷⁷⁻²⁸⁰ Because this area of therapy is rapidly evolving,²⁸¹⁻²⁸³ prompt consultation with a medical toxicologist or other specialists with up-to-date knowledge is recommended when managing treatment-refractory hypotension from β -blocker overdose.

Local Anesthetic Toxicity

Inadvertent intravascular administration of local anesthetics, such as bupivacaine, mepivacaine, or lidocaine, can produce refractory seizures and rapid cardiovascular collapse leading to cardiac arrest. Clinical case reports³⁵¹⁻³⁵⁵ and controlled animal studies³⁵⁶⁻³⁶⁰ have suggested that rapid IV infusion of lipids may reverse this toxicity either by redistributing the local anesthetic away from its site of action or by augmenting metabolic pathways within the cardiac myocyte.

Case reports have shown return of spontaneous circulation in patients with prolonged cardiac arrest unresponsive to standard ACLS measures,^{361,362} suggesting a role for administration of IV lipids during cardiac arrest. Although ideal dosing has not been determined, because dosage varied across all studies, it may be reasonable to consider 1.5 mL/kg of 20% long-chain fatty acid emulsion as an initial bolus, repeated every 5 minutes until cardiovascular stability is restored (Class IIb, LOE C).³⁶³ After the patient is stabilized, some papers suggest a maintenance infusion of 0.25 mL/kg per minute for at least 30 to 60 minutes. A maximum cumulative dose of 12 mL/kg has been proposed.³⁶³

Some animal data suggest that lipid infusion alone may be more effective than standard doses of epinephrine or vasopressin.^{357,360} Although there is limited evidence to change routine care for severe cardiotoxicity, several professional societies advocate protocolized clinical use.³⁶⁴⁻³⁶⁶ Because this is a rapidly evolving clinical area,^{367,368} prompt consultation with a medical toxicologist, anesthesiologist, or other specialist with up-to-date knowledge is strongly recommended.



ASRA
Practice
Advisory
on Local
Anesthetic
Systemic
Toxicity

ORIGINAL ARTICLE

Clinical Presentation of Local Anesthetic Systemic Toxicity A Review of Published Cases, 1979 to 2009

Guido Di Gregorio, MD,* Joseph M. Neal, MD,† Richard W. Rowenquist, MD,‡ and Guy L. Weinberg, MD§

REVIEW ARTICLE

Treatment of Local Anesthetic Systemic Toxicity (LAST)

Guy L. Weinberg, MD

REVIEW ARTICLE

Prevention of Local Anesthetic Systemic Toxicity

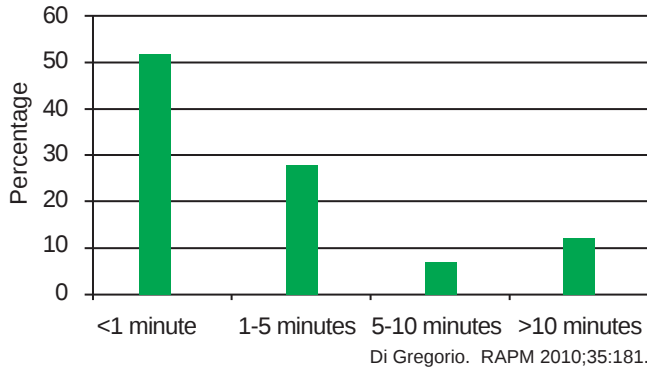
Michael F. Mahoney, MD and Michael R. Hajimaneck, MD

HISTORY ARTICLE

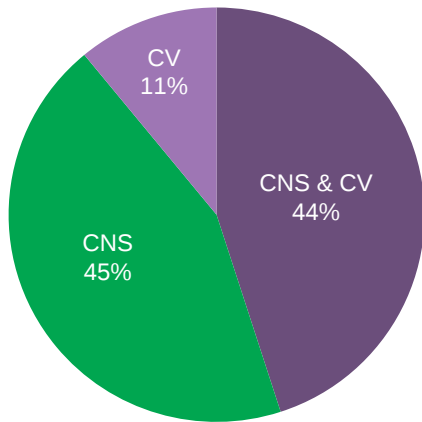
Local Anesthetic Systemic Toxicity A Historical Perspective

Kenneth Dussner, MD

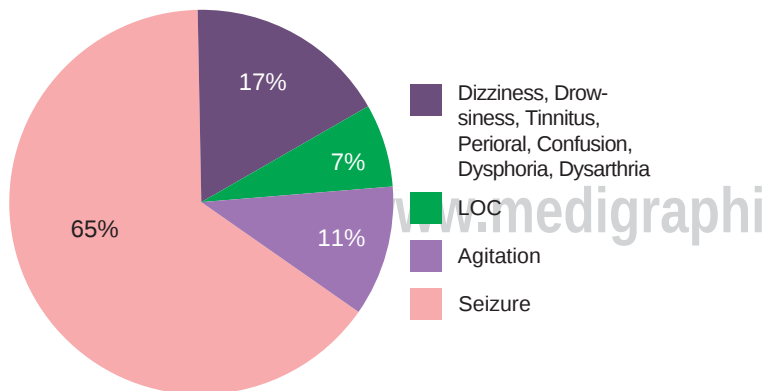
TIMING OF ONSET OF SYMPTOMS, N = 77



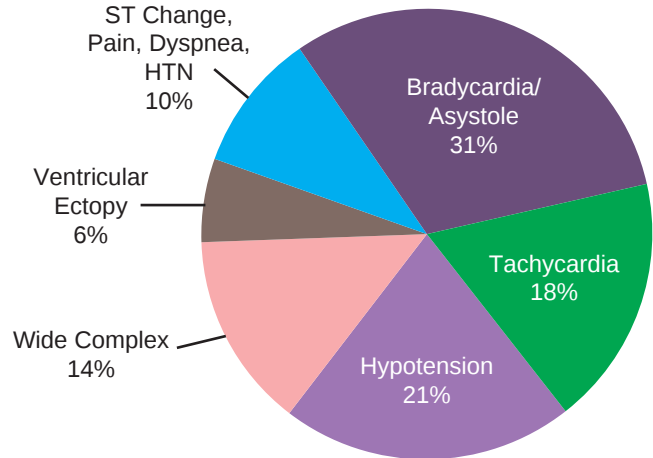
SPECTRUM OF PRESENTING SIGNS, N = 93



SPECTRUM OF CNS SIGNS



SPECTRUM OF CARDIAC SIGNS



RECOMMENDATIONS FOR DIAGNOSING LAST

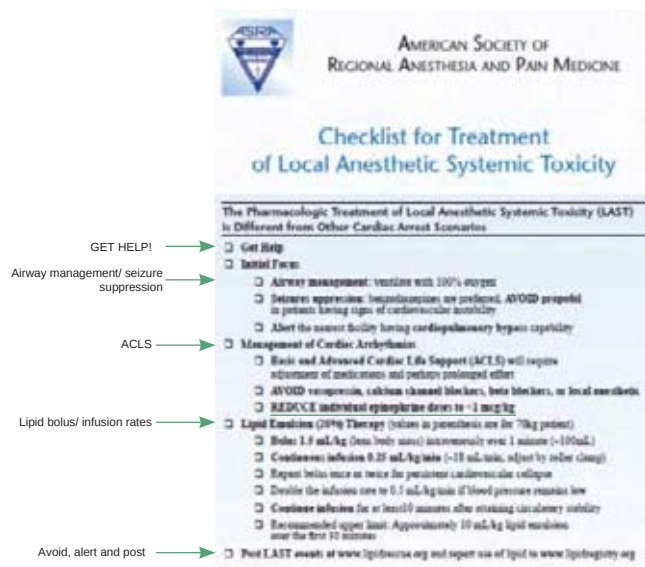
- Progression of subjective symptoms
 - Vigilant
- Timing is variable
 - < 1 minute - IV injection with direct access to brain
 - 1-5 minutes - partial IV injection/slow circ time/delayed absorption
 - > 15 minutes - consider monitoring for 30 min
- Heightened vigilance
 - Underlying disease
 - Extremities of age
- Have LOW threshold for considering dx of LAST with atypical symptoms after receiving more than minimal dose

Di Gregorio. RAPM 2010;35:181

PREVENTION

Use the lowest effective dose of local anesthetic (dose = volume x concentration).
Particularly with fixed needle techniques, incrementally pause 15-30 seconds between injections.
Aspirate before each injection, but recognize that aspiration has a 2% false-negative rate.
Intravascular markers are highly recommended. Only epinephrine (10-15 mcg per test dose) or fentanyl (100 mcg in laboring patients) have been proven effective for this purpose.
Ultrasound guidance reduces the frequency of accidental vascular puncture, but studies are conflicting regarding its ability to actually decrease LAST events. Ultrasound-guidance should not be considered a substitute for other preventative measures.
Patients receiving potentially toxic doses of local anesthetic should be monitored for at least 30 minutes after injection.

Neal. ASA Newsletter. 2012;76:22.



WWW.LIPIDRESCUE.ORG

LipidRescue™ Rescate Lipidico

TRATAMIENTO PARA LA PARADA CARDIACA INDUCIDA POR ANESTESICO LOCAL

POR FAVOR MANTENGA ESTE PROTOCOLO ADJUNTO A LA BOSA DE INTRALIPID

En caso de parada cardiaca precipitada por anestésico local que no responde al tratamiento standard, a parte de la reanimación cardiopulmonar, Intralipid 20% debe ser administrado de acuerdo con el siguiente regimen:

- Intralipid 20% 1.5 mL/kg inyección rápida durante 1 minuto
- Seguido inmediatamente por una infusión a 0.25 mL/kg/min ,
- Continúe el masaje cardiaco (el lipido tiene que circular)
- Repetir una inyección rápida cada 3-5 minutos llegando a los 3 mL/kg dosis total en inyección rápida hasta que la circulación recomience
- Continuar la infusión hasta que se establezca estabilidad hemodinámica. Aumentar la velocidad a 0.5 mL/kg/min si la presión arterial baja
- La dosis total máxima recomendada es 8 mL/kg

En la practica, en la reanimación de un adulto que pesa 70 Kg:

- Coja una bolsa de 500ml de Intralipid 20% y una jeringuilla de 50 ml.
- Prepare 50 ml de Intralipid de la bolsa y adminístrelo en inyección rápida, repita la operación otra vez
- Despues introduzca un gotero en la bolsa de Intralipid y dejelo correr intravenosamente durante los proximos 15 minutos
- Repetir la inyección rápida inicial dos veces mas – si la circulación espontanea no ha vuelto.

Si usa Intralipid para tratar un caso de toxicidad de anestésico local por favor informenos a traves de la pagina web www.lipidrescue.org.

WHAT'S ON THE HORIZON?

- Dissemination of guidelines for the treatment of LAST
- Studies elucidating the role of epinephrine/vasopressors in resuscitation needed with attention to:
 - Experimental design
 - Endpoints
- The development of anionic pegylated particles with increased surface area that may be specific LA antidotes