

Lipid resuscitation

A new treatment approach?

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Poisoning & therapeutic options

- Supportive therapy
- Reducing absorption
 - Vomiting – gastric emptying
 - Gastric lavage – whole bowel irrigation
 - Activated charcoal
- Increasing elimination
 - Repeated activated charcoal
 - Forced diuresis – extracorporeal drug removal
- Antidotes
- Psychosocial therapy

Poisoning & therapeutic options

- Limited evidence - Limited studies
- Options for acute life threatening poisonings?
 - ECMO
 - Changing pharmacokinetics / dynamics?

Sixth therapeutic cornerstone?



LET: Lipid Emulsion Therapy

postulated mechanisms



- « lipid sink » = new pharmacokinetic equilibrium
 - Sequester lipophilic drugs in IV lipid compartment
 - Dose response relationship
- Clearance promotion = hepatic delivery of chylomicrons
- Stimulation of insulin secretion
- Facilitation of calcium influx

Arroyo AM & Kao LW. Calcium channel blocker toxicity. *Pediatr Emer Care* 25: 532-541, 2009
Cave G & Harvey M. Intravenous lipid emulsion as antidote beyond local anesthetic toxicity: a systematic review. *ACAD EMERG MED* 16(9): 815-824, 2009

Lipid resuscitation

- Known phenomenon: lipids & phenytoine
- Weinberg in 1989: local anesthetic toxicity
 - No systematic studies
 - Based on case reports & animal – in vitro studies
- Other poisonings?



Leski U & Weinberg GL. Lipid resuscitation for local anesthetic toxicity: is it really lifesaving? *Curr Opin Anaesthesiol* 22: 667-671, 2009
Cave G & Harvey M. Intravenous lipid emulsion as antidote beyond local anesthetic toxicity: a systematic review. *ACAD EMERG MED* 16(9): 815-824, 2009
Felice KL & Schumann HM. Intravenous lipid emulsion for local anesthetic toxicity: a review of the literature. *Journal of Medical Toxicology* 4(3): 184-191, 2009

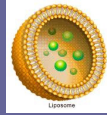
Lipid resuscitation

- TCA – SSRI – haldol
- Verapamil – propranolol / atenolol
- Thiopentone
- Organophosphates
- ...

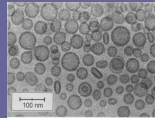


Cave G & Harvey M. Intravenous lipid emulsion as antidote beyond local anesthetic toxicity: a systematic review. *ACAD EMERG MED* 16(9): 815-824, 2009
Howell BA, Chaudhri A. Binding of imipramine, desipramine, and citalopram to liposomes for overdose treatment. *Journal of Pharmaceutical Sciences* 98(10): 3718-3729, 2009
Arroyo AM & Kao LW. Calcium channel blocker toxicity. *Pediatr Emer Care* 25: 532-541, 2009
Zhou Y, Zhan C, Li Y, Zhong Q, Pan H, Yang G. Intravenous lipid emulsions combine extracorporeal blood purification: a novel therapeutic strategy for severe organophosphate poisoning. *Medical Hypotheses* 74: 309-311, 2010
Sirianni AJ, Osterhoudt KC, Calello DP, Muller AA, Waterhouse MR, Goodkin MB, Weinberg GL & Henretig F. Use of lipid emulsion in the resuscitation of a patient with prolonged cardiovascular collapse after overdose of bupropion and lamotrigine. *Ann Emerg Med* 51: 412-415, 2008

Lipid resuscitation



- Different therapeutic protocols
 - Bolus of 20 % lipid: 1.5 ml/kg
 - 0.25 ml/kg/min for 20 min
- Up to...800 ml
- Adverse events – risks?



Lipid resuscitation

- **Adverse effects** = fat overload
 - Allergic reactions - Pyrogenic reaction (chills, nausea, ...)
 - Thrombocytopenia – hypercoagulability
 - Pancreatitis - Elevated liver enzyme levels
 - Fat embolism
- **Additional risks**
 - Increase enteric absorption after oral ingestion??
 - Delayed toxicity after metabolism of lipid emulsion?
 - Interaction with other lipophilic drugs (amiodarone – insulin)?
- **Interference with diagnostic tests**

Lipid resuscitation indication

Life threatening poisoning of lipid soluble
drug(s)
Before ECMO?

Sirianni AJ, Osterhoudt KC, Caelelo DP, Muller AA, Waterhouse MR, Goodkin MB, Weinberg GL & Henretig F. Use of lipid emulsion in the resuscitation of a patient with prolonged cardiovascular collapse after overdose of bupropion and lamotrigine. *Ann Emerg Med* 51: 412-415, 2008

Lipid resuscitation Future

- Different nanoparticulates
- Anionic loading
- Polymer shielded
- Proteins?
- Sugars?

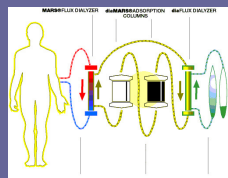
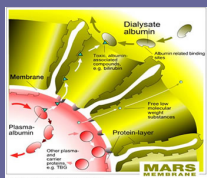
Howell B, Chauhan A. Amitriptyline overdose treatment by pegylated anionic liposomes. *Journal of Colloid and Interface Science* 324: 61-70, 2008

Howell BA, Chauhan A. Binding of imipramine, dosulepin, and opipramol to liposomes for overdose treatment. *Journal of Pharmaceutical Sciences* 98(10): 3716-3729, 2009

Protein resuscitation?



- MARS (molecular adsorbent recirculating system)

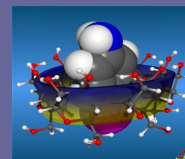


De Pont A-C. Extracorporeal treatment of intoxications. *Curr Opin Crit Care* 13: 668-673, 2007

Churchwell MD, Pasko DA, Smoyer WE & Mueller BA. Enhanced clearance of highly protein-bound drugs by albumin-supplemented dialysate during modeled continuous hemodialysis. *Nephrol Dial Transplant* 24: 231-238, 2009

Sugar resuscitation? cyclodextrins

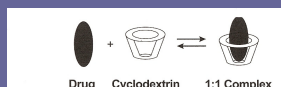
- Derived from starch containing 6 (alpha), 7 (beta), 8 (gamma), 9 (delta), 10 (epsilon) dextrose molecules



Brewster ME & Loftsson T. Cyclodextrins as pharmaceutical solubilizers. *Advanced Drug Delivery Reviews* 59: 645-666, 2007

Sugar resuscitation? *cyclodextrins*

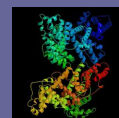
- Bridion 2 mg/kg
 - Vecuronium bromide
 - Rocuronium bromide



Yang LPH & Keam SJ. Suggammadex. A review of its use in anaesthetic practice. Drugs 69(7), 919-942, 2009

Conclusions

- **Lipid resuscitation**
 - = therapy for local anesthetic overdose
 - = therapeutic option for life threatening poisonings with lipophilic drugs
- **Pharmacokinetic manipulation** becomes a reality
 - Liposomes
 - Albumin
 - cyclodextrins



The European Society for Emergency Medicine (EuSEM) and The American Academy of Emergency Medicine (AAEM), along with the Hellenic Society for Emergency Medicine (HeSEM)

have the pleasure to announce

The Sixth Mediterranean Emergency Medicine Congress (MEMC VI)

