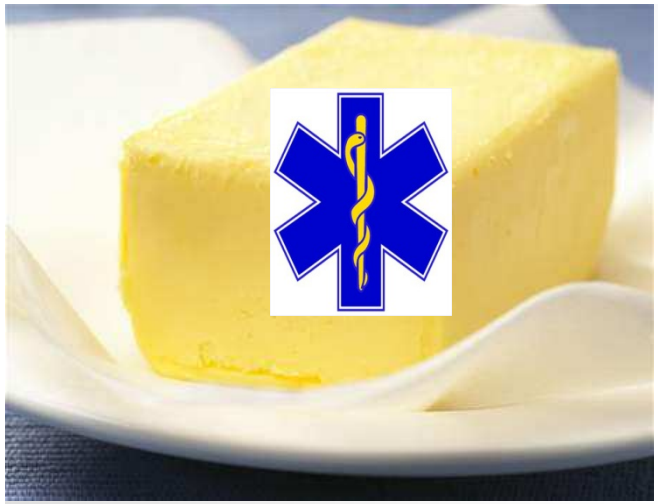

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Lipid rescue

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Toxická reakce na LA

- Metody regionální anestezie – regionální blokády (0,075–0,1%), epidurální anestezie (0,01%)[1]
- **Množství LA (volné frakce) v cévním systému** (koncentrace x objem)

Nesprávná dávka

- Bupivacain>2-2,5mg/kg
- Levobupivacain>2mg/kg
- Ropivacain>3mg/kg
- Lidokain>3mg/kg
  (+adrenalin 5mg/kg)
- Mepivacain>5-6mg/kg
- Prilocain>5mg/kg
  (+adrenalin 7mg/kg)
- Articain>7mg/kg
- Procain>7mg/kg

Nesprávné místo

- Místní perfuze: [2]

1. Pleurální analgezie
2. Interkostální blokáda
3. Kaudální blokáda
4. Epidurální
5. Plexus brachialis
6. N.femoralis
7. N.ischiadicus
8. Infiltrační
9. Subarachnoideální

Toxická reakce na LA

- Toxicita = volná frakce LA v plasmě
- Vazba na bílkovinu – α1–glykoprotein, albumin
- Toxicita : tetrakain>bupivakain >levobupivakain >etidokain >lidokain >mepivakain >prilokain >prokain >chlorprokain [2]
- Více ohroženi pacienti s onemocněním jater, ledvin, srdce, plic, těhotné

Toxická reakce

Neurotoxicita

- Blokáda inhibičních neuronů a nerv.dráh
- Kovová chuť v ústech, parestézie jazyk, rty
- Tinitus, nystagmus
- Poruchy vizu
- Křeče
- Tonicko-klonické křeče typu grand mal
- Porucha vědomí
- Centrální apnoe

Kardiotoxicita

- Negativně inotropní, dromotropní
- Hypertenze, hypotenze
- Bradykardie, raménkové blokády, A-V blokáda, asystolie
- Reentry – tachykardie, FIKO
- Snižuje se amplituda QRS a prodlužují intervaly EKG

Neurotixicita může být 1.příznak toxicity – nemusí být pravidlem

Postup při toxické reakci

- Každé pracoviště kde je praktikována reg.anestezie/analgezie – doporučený postup pro léčbu toxické reakce
- Používat LA s nejnižším stupněm toxicity?! (cost vs benefit, cena, délka učinku u single shot,…)
- **Doporučený postup ČSARIM –** http://www.csarim.cz/Public/csim/21%20%20DP_lecba_toxicka_reakce_LA_CSARIM_final_approval_140212.pdf
- **Dostupný Intralipid 20% (expirace!!! – 18měsíců)**
- Školený personál

Česká společnost anesteziologie, resuscitace a intenzivní medicíny
ČLS JEP

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DOPORUČENÍ PRO LÉČBU TOXICKÉ REAKCE PO PODÁNÍ LOKÁLNÍCH ANESTETIK

Pracovní skupina

Cvachovec Karel
Černý Vladimír
Doležal David
Herold Ivan
Horáček Michal
Křikava Ivo
Ševčík Pavel

http://www.csarim.cz/Public/csim/21%20%20DP_lecba_toxicka_reakce_LA_CSARIM_final_approval_140212.pdf

Postup při toxické reakci

- Příznaky toxicity = STOP aplikace LA
- Volat pomoc
- ABC
- Křeče – benzodiazepiny, sedace, event relaxace
- Intralipid 20% při zástavě oběhu, neustupující event. zhoršující se známky toxicity
- Arytmie bez zástavy oběhu – antiarytmika (amiodaron), intralipid?!

Intralipid 20%

- 500ml obsahuje 100ml sójového oleje
- Pomocné látky: vaječný lecitin, glycerol, aqua pro inj., hydroxid sodný
- pH = 8
- Indikace: parenterální výživa – zdroj esenciálních mastných kyselin a E
- 5ml = 1g triglyceridů (20% Intralipid)

Intralipid 20%

- KI: akutní šokový stav, težká hyperlipidémie, jaterní insuficience, alergie na sojové, vaječné, arašidové bílkoviny
- NÚ: bolesti hlavy, třes, únava, ↑TT, bolesti břicha, nauzea, zvracení, pankreatitis, přechodná elevace JT, tromboflebitis,
- Dle SPC je podání u toxické reakce na LA – OFF LABEL!!!

Proč právě lipid?

- Účinek není vysvětlen

1. **Lipid sink** – lipidová emulze naváže lipofilní látky v plasmě = ↓koncentrace volné frakce LA (vysvětlení proč lipid účinkuje i u jiných intoxikací –bupropion, tricyklické antidepresiva, Ca blokátory, kokain .....) – Lipofilní látky
2. **E substrát**
3. **Přímý pozitivně inotropní efekt**[1]

Lipid poprvé

▼ Original Articles

Lipid Emulsion Infusion Rescues Dogs From Bupivacaine-Induced Cardiac Toxicity

Guy Weinberg, M.D., Richard Ripper, B.A., Douglas L. Feinstein, Ph.D., and William Hoffman, Ph.D.

- Reg Anesth Pain Med. 2003 May-Jun;28(3):198-202.
- 12 psů v celkové anestezii
- Bupivacain 10mg/kg i.v.
- 10min. přímá srdeční masáž
- 4ml/kg 20% Intralipid vs FR + následně 0,5ml/kg/min
- 100% vs 0% přežití

Intralipid poprvé u pacienta

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CASE REPORTS

Anesthesiology 2006; 105:217–8

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.§*

Anaesthesia, 2006, **61**, 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

Department of Anaesthesiology and Intensive Care Medicine, Fetscher Str. 74, University Hospital Dresden, 01307 Dresden, Germany

Summary

Ropivacaine 1% 40 ml was mistakenly injected as part of an axillary plexus block in an 84-year-old woman. After 15 min the patient complained of dizziness and drowsiness and developed a generalised tonic–clonic seizure followed by an asystolic cardiac arrest. After 10 min of unsuccessful cardiopulmonary resuscitation, a bolus of 100 ml of Intralipid 20% (2 ml.kg^{-1}) was administered followed by a continuous infusion of 10 ml.min^{-1}. After a total dose of 200 ml of Intralipid 20% had been given spontaneous electrical activity and cardiac output was restored. The patient recovered completely. We believe the cardiovascular collapse was secondary to ropivacaine absorption following the accidental overdose. This case shows that lipid infusion may have a beneficial role in cases of local anaesthetic toxicity when conventional resuscitation has been unsuccessful.

Dávkování intralipidu

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Okamžitě:

- Počáteční bolus 1,5 ml/kg tělesné hmotnosti (t. hm.) v průběhu 1 minuty,
  tj. asi 100 ml/70 kg t. hm.
- Infuze pokračuje rychlostí 15 ml/kg t. hm./hod, tj. asi 1000 ml/70 kg t. hm./hod
  (u tzv. velmi obézních nutná kalkulace dávky podle ideální, nikoliv skutečné t. hm.)

Po 5 minutách:

- Počáteční bolus opakovat nejvíce dvakrát s odstupem vždy 5 minut, pokud:
  - nebyla obnovena stabilita krevního oběhu, nebo
  - došlo opět ke zhoršení krevního oběhu
- Pokračovat v infuzi stejnou rychlostí 15 ml/kg t. hm./hod, tj. asi 1000 ml/70 kg t.hm./ hod až do obnovení hemodynamické stability a dále ještě alespoň 10 minut.

Kdykoliv po 5 minutách a později:

- Zvýšit rychlost infuze na 30 ml/kg t. hm./hod, tj. asi 2000 ml/70 kg t. hm./hod, pokud:
  - nebyla obnovena stabilita krevního oběhu
  - stabilita oběhu se znovu zhoršuje

http://www.csarim.cz/Public/csim/21%20%20DP_lecba_toxicka_reakce_LA_CSARIM_final_approval_140212.pdf

American Society of Regional Anesthesia and Pain Medicine

Checklist for Treatment of Local Anesthetic Systemic Toxicity

The Pharmacologic Treatment of Local Anesthetic Systemic Toxicity (LAST) Is Different from Other Cardiac Arrest Scenarios

- ❑ Get Help
- ❑ Initial Focus:
  - ❑ Airway management: ventilate with 100% oxygen
  - ❑ Seizures suppression: benzodiazepines are preferred; AVOID propofol in patients having signs of cardiovascular instability
  - ❑ Alert the nearest facility having cardiopulmonary bypass capability
- ❑ Management of Cardiac Arrhythmias
  - ❑ Basic and Advanced Cardiac Life Support (ACLS) will require adjustment of medications and perhaps prolonged effort
  - ❑ AVOID vasopressin, calcium channel blockers, beta blockers, or local anesthetic
  - ❑ REDUCE individual epinephrine doses to <1 mcg/kg
- ❑ Lipid Emulsion (20%) Therapy (values in parentheses are for 70kg patient)
  - ❑ Bolus 1.5 mL/kg (lean body mass) intravenously over 1 minute (~100mL)
  - ❑ Continuous infusion 0.25 mL/kg/min (~18 mL/min; adjust by roller clamp)
  - ❑ Repeat bolus once or twice for persistent cardiovascular collapse
  - ❑ Double the infusion rate to 0.5 mL/kg/min if blood pressure remains low
  - ❑ Continue infusion for at least10 minutes after attaining circulatory stability
  - ❑ Recommended upper limit: Approximately 10 mL/kg lipid emulsion over the first 30 minutes
- ❑ Post LAST events at www.lipidrescue.org and report use of lipid to www.lipidregistry.org

http://www.lipidrescue.org

BE PREPARED

- We strongly advise that those using local anesthetics (LA) in doses sufficient to produce local anesthetic systemic toxicity (LAST) establish a plan for managing this complication. Making a *Local Anesthetic Toxicity Kit* and posting instructions for its use are encouraged.

RISK REDUCTION (*BE SENSIBLE*)

- Use the least dose of LA necessary to achieve the desired extent and duration of block.
- Local anesthetic blood levels are influenced by site of injection and dose. Factors that can increase the likelihood of LAST include: advanced age, heart failure, ischemic heart disease, conduction abnormalities, metabolic (e.g., mitochondrial) disease, liver disease, low plasma protein concentration, metabolic or respiratory acidosis, medications that inhibit sodium channels. Patients with severe cardiac dysfunction, particularly very low ejection fraction, are more sensitive to LAST and also more prone to 'stacked' injections (with resulting elevated LA tissue concentrations) due to slowed circulation time.
- Consider using a pharmacologic marker and/or test dose, e.g. epinephrine 5 mcg/mL of LA. Know the expected response, onset, duration, and limitations of "test dose" in identifying intravascular injection.
- Aspirate the syringe prior to each injection while observing for blood.
- Inject incrementally, while observing for signs and querying for symptoms of toxicity between each injection.

DETECTION (*BE VIGILANT*)

- Use standard American Society of Anesthesiologists (ASA) monitors.
- Monitor the patient during and after completing injection as clinical toxicity can be delayed up to 30 minutes.
- Communicate frequently with the patient to query for symptoms of toxicity.
- Consider LAST in any patient with altered mental status, neurological symptoms or cardiovascular instability after a regional anesthetic.
- Central nervous system signs (may be subtle or absent)
  - *Excitation* (agitation, confusion, muscle twitching, seizure)
  - *Depression* (drowsiness, obtundation, coma or apnea)
  - *Non-specific* (metallic taste, circumoral numbness, diplopia, tinnitus, dizziness)
- Cardiovascular signs (often the only manifestation of severe LAST)
  - *Initially may be hyperdynamic* (hypertension, tachycardia, ventricular arrhythmias), then
  - *Progressive hypotension*
  - *Conduction block, bradycardia or asystole*
  - *Ventricular arrhythmia* (ventricular tachycardia, Torsades de Pointes, ventricular fibrillation)
- Sedative hypnotic drugs reduce seizure risk but even light sedation may abolish the patient's ability to recognize or report symptoms of rising LA concentrations.

TREATMENT

- Timing of lipid infusion in LAST is controversial. The most conservative approach, waiting until after ACLS has proven unsuccessful, is unreasonable because early treatment can prevent cardiovascular collapse. Infusing lipid at the earliest sign of LAST can result in unnecessary treatment since only a fraction of patients will progress to severe toxicity. The most reasonable approach is to implement lipid therapy on the basis of clinical severity and rate of progression of LAST.
- There is laboratory evidence that epinephrine can impair resuscitation from LAST and reduce the efficacy of lipid rescue. Therefore it is recommended to avoid high doses of epinephrine and use smaller doses, e.g., <1mcg/kg, for treating hypotension.
- Propofol *should not be used* when there are signs of cardiovascular instability. Propofol is a cardiovascular depressant with lipid content too low to provide benefit. Its use is discouraged when there is a risk of progression to cardiovascular collapse.
- Prolonged monitoring (> 12 hours) is recommended after any signs of systemic LA toxicity, since cardiovascular depression due to local anesthetics can persist or recur after treatment.

The ASRA Practice Advisory on Local Anesthetic Toxicity is published in the society's official publication *Regional Anesthesia and Pain Medicine*, and can be downloaded from the journal Web site at www.rapm.org.

Neal JM, Bernards CM, Butterworth JF, Di Gregorio G, Drasner K, Hejtmanek MR, Mulroy MF, Rosenquist RW, Weinberg GL. ASRA practice advisory on local anesthetic systemic toxicity. *Reg Anesth Pain Med* 2010;35:152-161.

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Anesthesiology 2009; 111:498–505

Epinephrine Impairs Lipid Resuscitation from Bupivacaine Overdose

A Threshold Effect

David B. Hiller, M.D., Guido Di Gregorio, M.D.,† Richard Ripper, C.V.T.,‡ Kemba Kelly, M.S.,‡ Malek Massad, M.D.,§ Lucas Edelman, B.S.,‖ Guy Edelman, M.D.,# Douglas L. Feinstein, Ph.D.,** Guy L. Weinberg, M.D.††*

Results: Epinephrine improved initial return of spontaneous circulation (rate-pressure product > 30% baseline) but only 3 of 5 rats at 10 mcg/kg and 1 of 5 rats at 25 mcg/kg sustained return of spontaneous circulation by 15 min. Lipid alone resulted in slower but more sustained recovery. Epinephrine doses above a threshold near 10 mcg/kg increased lactate, worsened acidosis, and resulted in poor recovery at 15 min, as compared with lipid controls. There was tight correlation of epinephrine dose to serum lactate at 15 min.

Conclusions: Epinephrine over a threshold dose near 10 mcg/kg impairs lipid resuscitation from bupivacaine overdose, possibly by inducing hyperlactatemia.

Maximální dávka Intralipidu

- ČSARIM – max.dávka Intralipid 20% – 12ml/kg
- ASRA – 10ml/kg
- SPC – 20ml/kg/den

- **Safety of High Volume Lipid Emulsion Infusion: A First Approximation of LD50 in Rats**
- **Hiller, David B. MD*; Di Gregorio et al.**
- Regional Anesthesia & Pain Medicine:
- March/April 2010 - Volume 35 - Issue 2 - pp 140–144
- Results: **The maximum likelihood estimate for LD_{50} was 67.72 (SE, 10.69) mL/kg.** Histologic diagnosis of myocardium, brain, pancreas, and kidneys was normal at all doses. **Microscopic abnormalities in lung and liver were observed at 60 and 80 mL/kg**; histopathology in the lung and liver was worse at 1 hr than at 4 and 24 hrs.

Lipidrescue.org

- Podání lipidů na podkladě animálních experimentálních studií z konce 90.-tych let
- *První podání Intralipidu u pacienta – 2006*
- ***Registr podání Intralipidu*** – klinické případy (poslední únor 2012) – není už toxicity? :D
- Možnost vložit kazuistiku

Intralipid intraoseálně

- Intraoseální aplikace lipidové emulze:efektivní alternativa k i.v. podání v urgentních případech (animální model)
- Michael Robert Fettiplace, Richard Ripper, Kinga Lis et al.
- Subjekty léčeny intraoseální aplikací lipidové emulze vykazovali signifikantně rychlejší normalizaci sledovaných hemodynamických parametrů ve srovnání se skupinou i.v. FR a kontrolní skupinou, nicméně srovnatelné se skupinou i.v. lipidové emulze.
- Crit Care Med 2013; 42:00-00
- http://www.akutne.cz/index.php?pg=aktuality&aid=425

Děkuji za pozornost

Lipid Rescue :D

Literatura

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4. http://www.lipidrescue.org/