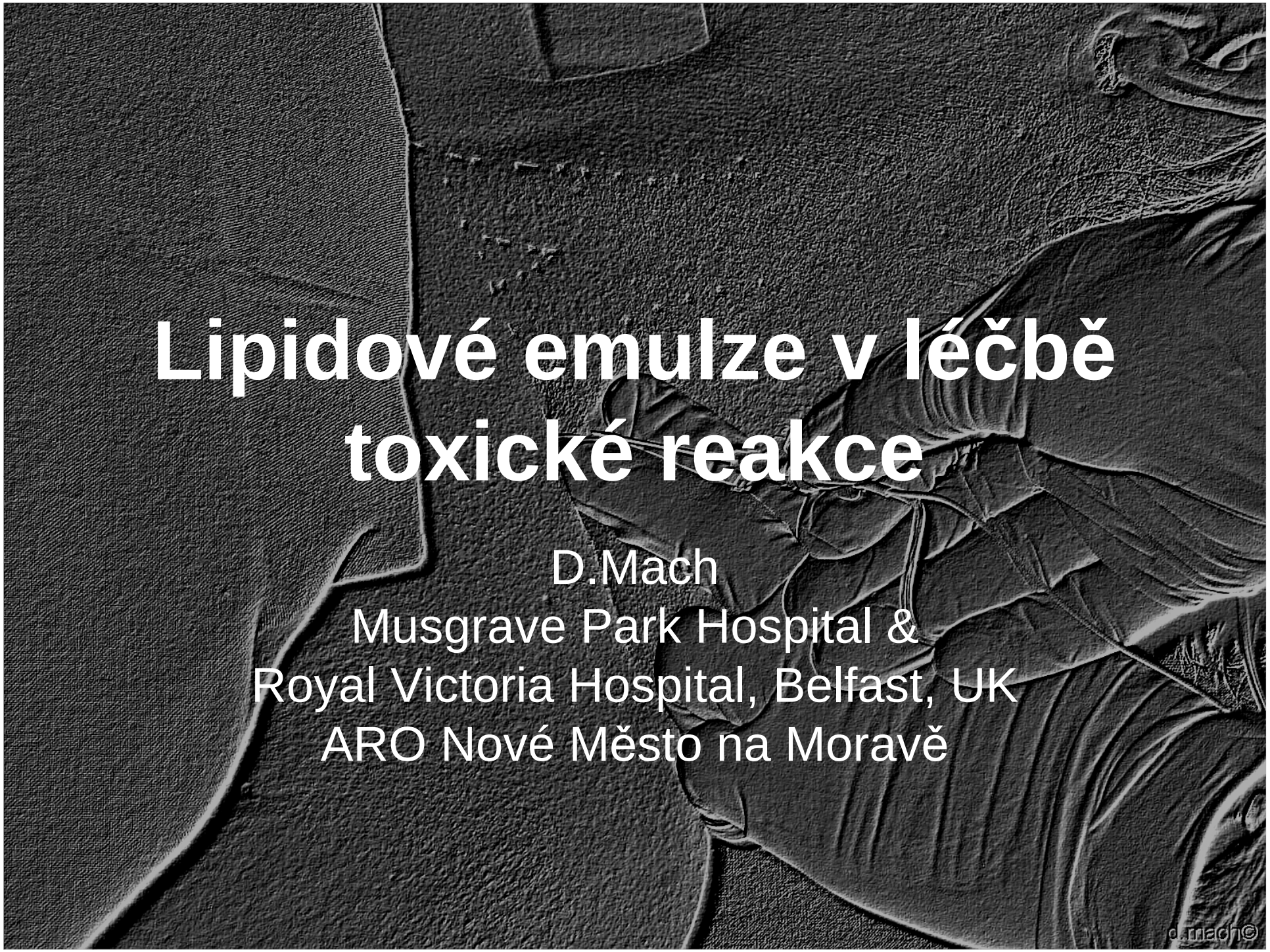

Lipidové emulze v léčbě toxické reakce

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ARO Nové Město na Moravě

Nejužívanější farmaka v rukou anesteziologa

- I.v. anestetika ?
- Inhalační anest.?
- Kurarimimetika?
- Opioidní analgetika?
- Antibiotika?
- Antiemetika?
- Lokální anestetika?

- Předávk., anafyl.
- MH, předávkování
- Anafyl, MH, rez. blok
- Dechová deprese
- Anafylaxe
- QT interval
- Toxická r., anafylaxe

Bezpečnost lokálních anestetik

ANAFYLAXE

- Raritní, (0,25% všech anafylaxí v anestézii)
- Častěji estery než amidy
- PABA a parabeny jsou nejčastější spouštěč

TOXICKÁ REAKCE

- Periferní blok 0,075-0.1% (interkostální blok ...)
- Epidurální blok 0,01%

Neurotoxicita

- Zmatenost , excitace
- Setřelá řeč
- Poruchy vidění
- Kovová pachuť na jazyku
- Parestézie
- Bezvědomí
- Tonicko klonické křeče

Kardiotoxicita

- Negativně chromotropní efekt (HCN kanál)
- Negativně inotropní efekt (Ca)
- Negativně dromotropní efekt (Na kanál)
- Metabolický efekt (blokáda CACT)

Kardiotoxicita

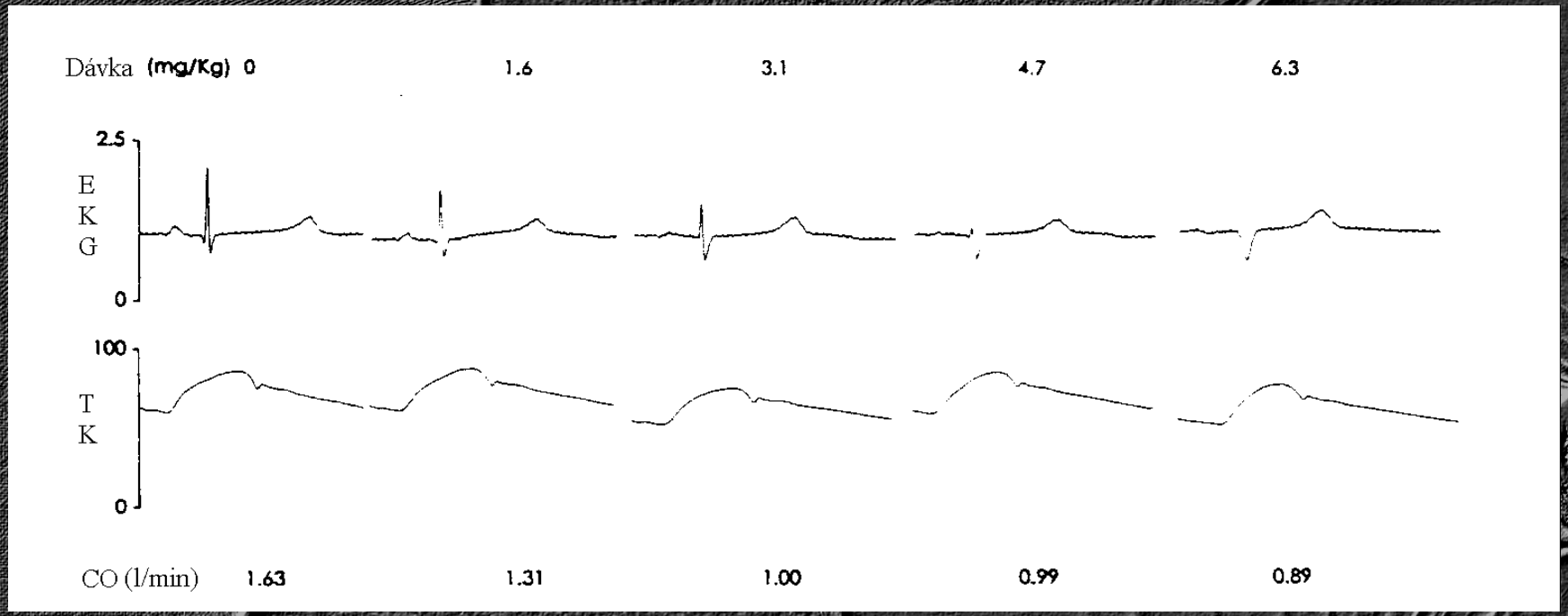
EKG ZMĚNY

- Snižování amplitudy QRS,T
- Prodlužování převodních časů, QT
- Blokády, rozšiřování QRS
- Asystolie, VF

HEMODYNAMIKA

- MAP se drží v normě často při EKG vyjádřených známkách toxicity
- Postupně progredující hypotenze do úplného KV zhroucení

Kardiotoxicita



Léčba toxické reakce

- Začít dle platných resuscitačních postupů (ABC)
- Zajištění průchodnosti DC, přiměřená ventilace (odstranit hypoxii a hyperkapnii, ale vyhnout se hypokapnii)
- Při křečích antikonvulziva (benzodiazepiny, TP), pokud křeče neustupují - sedace, svalová relaxace

Léčba toxické reakce

- Kardiotoxicita – léčba dle platných resuscitačních doporučení (amiodaron jako antiarytmikum)
- úprava hypovolemie, acidózy,iontových poruch
- ……

Neresuscitovatelná zástava?

- Dlouhodobé setrvání lokálního anestetika v Na kanálech
- Jeho kumulace v těchto kanálech při narůstající srdeční frekvenci
- Potenciální zhoršení metabolické situace po podání adrenalinu

Mechanismus působení lipidů

- Zvýšení dostupnosti MK v mitochondriích (odblokování karnitin-acylkarnitin-translokázy)
- „lipid sink“ - absorbce lipofilních látek v tomto tukovém krevním depu a jejich stahování z tkání (léčba některých dalších intoxikací)
- Přímý pozitivně inotropní efekt na srde

Table 2. Applying Classification of Recommendations and Level of Evidence

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT →			
	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	**CLASS IIa** *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	**CLASS IIb** *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	**CLASS III** *Risk ≥ Benefit* Procedure/Treatment should **NOT** be performed/administered **SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL**
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations†	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

Lipid Registry

Welcome

'Lipid Rescue Resuscitation' is a term coined by Guy Weinberg MD denoting the use of intravenous lipid emulsion (ILE) preparations as antidote. Since initial discovery a decade ago ILE have been reported to reverse central nervous system, and cardiotoxicity from overdose with lipophilic local anaesthetics. More recently ILE has been reported to ameliorate neurologic and cardiovascular manifestations of *non* local anaesthetic lipophilic-drug poisonings in animal models and anecdotal human cases.

Systemic evaluation of ILE in human cases of overdose is however limited by ethical constraints associated with the infrequent and catastrophic nature of such presentations. In the absence of randomized clinical trials of ILE, a prospective registry of ILE use is required to collate clinical experience of efficacy, and adverse events, associated with ILE use.

The LIPAEMIC (**L**ipid **I**njection for the **P**urpose of **A**ntidotal **E**ffect in lipophilic **M**edicine **I**ntoxi**C**ation) Study Group is an international collaborative of clinician investigators formed with the aim of compiling a prospective dataset of uses of ILE as antidote. LIPID REGISTRY is a project of the LIPAEMIC Study Group.

A companion website to LipidRescue

THE ASSOCIATION OF ANAESTHETISTS

of Great Britain & Ireland

Guidelines for the Management of Severe Local Anaesthetic Toxicity

Signs of severe toxicity:

- Sudden loss of consciousness, with or without tonic-clonic convulsions
- Cardiovascular collapse: sinus bradycardia, conduction blocks, asystole and ventricular tachyarrhythmias may all occur
- Local anaesthetic (LA) toxicity may occur some time after the initial injection

Immediate management:

- Stop injecting the LA
- **Call for help**
- Maintain the airway and, if necessary, secure it with a tracheal tube
- Give 100% oxygen and ensure adequate lung ventilation (hyperventilation may help by increasing pH in the presence of metabolic acidosis)
- Confirm or establish intravenous access
- Control seizures: give a benzodiazepine, thiopental or propofol in small incremental doses
- Assess cardiovascular status throughout

Management of cardiac arrest associated with LA injection:

- Start cardiopulmonary resuscitation (CPR) using standard protocols
- Manage arrhythmias using the same protocols, recognising that they may be very refractory to treatment
- Prolonged resuscitation may be necessary; it may be appropriate to consider other options:
  - Consider the use of cardiopulmonary bypass if available
  - Consider treatment with lipid emulsion

Treatment of cardiac arrest with lipid emulsion: (approximate doses are given in red for a 70-kg patient)

- Give an intravenous bolus injection of Intralipid® 20% 1.5 ml.kg^{-1} over 1 min
  - Give a bolus of 100 ml
- Continue CPR
- Start an intravenous infusion of Intralipid® 20% at 0.25 ml.kg^{-1}.min^{-1}
  - Give at a rate of 400 ml over 20 min
- Repeat the bolus injection twice at 5 min intervals if an adequate circulation has not been restored
  - Give two further boluses of 100 ml at 5 min intervals
- After another 5 min, increase the rate to 0.5 ml.kg^{-1}.min^{-1} if an adequate circulation has not been restored
  - Give at a rate of 400 ml over 10 min
- Continue infusion until a stable and adequate circulation has been restored

Remember:

- Continue CPR throughout treatment with lipid emulsion
- Recovery from LA-induced cardiac arrest may take >1 h
- Propofol is not a suitable substitute for Intralipid®
- Replace your supply of Intralipid® 20% after use

Follow-up action:

- Report cases from the United Kingdom to the National Patient Safety Agency (via www.npsa.nhs.uk). Cases from the Republic of Ireland should be reported to the Irish Medicines Board. Whether or not lipid emulsion is administered, please also report cases to the LipidRescue™ site: www.lipidrescue.org.
- If possible, take blood samples into a plain tube and a heparinised tube before and after lipid emulsion administration and at 1 h intervals afterwards. Ask your laboratory to measure LA and triglyceride levels (these have not yet been reported in a human case of LA intoxication treated with lipid).
- Please read the notes overleaf

Your nearest bag of Intralipid® is kept .....

HOME

Resuscitation Council (UK)

Cardiac arrest or cardiovascular collapse caused by local anaesthetic

Introduction

Following some convincing animal studies,[1,2] recent case reports describe the successful use of 20% lipid emulsion to treat cardiovascular collapse,[3] arrhythmias[4] and cardiac arrest[5-7] caused by local anaesthetic. It has been recommended that 20% lipid emulsion should be available wherever patients receive large doses of local anaesthetic (e.g., operating rooms, labour wards, emergency department, radiology suite).[8,9] The following protocol is based on others that have been published previously.[8,10] This treatment is supported by only low-level evidence but in the absence of obvious significant harm it seems reasonable to follow this protocol.

Protocol

1. If a patient develops cardiac arrest that is likely to have been caused by local anaesthetic toxicity give 20% lipid emulsion 1.5 ml kg^{-1} (100 ml in 70 kg patient) intravenously once CPR, following advanced life support guidelines, has been started. This treatment should also be considered if a patient develops severe cardiovascular compromise (hypotension, unstable arrhythmias) that is attributable to local anaesthetic toxicity – thus potentially preventing cardiac arrest.
2. Start an infusion of 20% lipid emulsion at 0.25 ml kg^{-1} min^{-1} (about 20 ml min^{-1} in 70 kg patient) and continue until a stable rhythm and adequate circulation has been restored.
3. Repeat the bolus dose at 5 min intervals until a stable rhythm and adequate circulation is restored.

Notes

- Restoration of spontaneous circulation after local anaesthetic-induced cardiac arrest may take more than 1 hour to achieve.
- Ensure that 500 – 1000 ml 20% lipid emulsion is available for the treatment of severe cardiovascular compromise or cardiac arrest associated with local anaesthetic toxicity in all clinical areas where high doses of local anaesthetics are used.
- Report all cases of suspected local anaesthetic intoxication to the National Patient Safety Agency (www.npsa.nhs.uk).
- The nearest lipid emulsion is stored . . . . . *(for completion locally)*

LipidRescue TM

LÉČBA SRDEČNÍ ZÁSTAVY INDUKOVANÉ PODÁNÍM LOKÁLNÍHO ANESTETIKA

TENTO PROTOKOL, PROSÍM, PŘILOŽIT K VAKU S INTRALIPIDEM

V případě srdeční zástavy způsobené podáním lokálního anestetika, nereagující na standardní terapii srdeční zástavy, současně se standardními postupy kardio-pulmonální resuscitace by měl být podán Intralipid 20% dle následujícího dávkovacího schématu:

- bolus Intralipid 20% 1,5 ml/kg během jedné minuty
- následovaný kontinuálním infusním podáním 0,25ml/kg/min
- pokračující komprese hrudníku (Intralipid musí cirkulovat v oběhu)
- opakovat bolus každé 3-5 minut to celkové dávky 3ml/kg do obnovení krevního oběhu
- pokračovat kontinuální infusní podání do obnovení hemodynamické stability zvýšit dávku na 0.5 ml/kg/min v případě poklesu krevního tlaku
- maximální doporučená celková dávka: 8ml/kg

Praktický příklad resuscitace 70kg dospělého jedince:

- *vezmi vak s 500ml Intralipidu 20% a 50 ml stříkačku*
- *natáhni plně 50ml stříkačku Intralipidem a podej STATIM i.v. 2x*
- *napoj zbylý vak s Intralipidem na set a podej i.v. během následujících 15 minut*
- *nebyl-li dosud obnoven krevní oběh, až dvakrát zopakuj podání původního bolusu*

V případě užití Intralipidu k terapii toxického účinku lokálního anestetika, podejte, prosím, zprávu o tomto případu na www.lipidrescue.org a ověřte, že spotřebovaný vak s Intralipidem byl nahrazen novým.

LipidRescue TM

LÉČBA SRDEČNÍ ZÁSTAVY ZPŮSOBENÉ PODÁNÍM LOKÁLNÍHO ANESTETIKA
TENTO PROTOKOL, PROSÍM, PŘILOŽIT K VAKU S INTRALIPIDEM

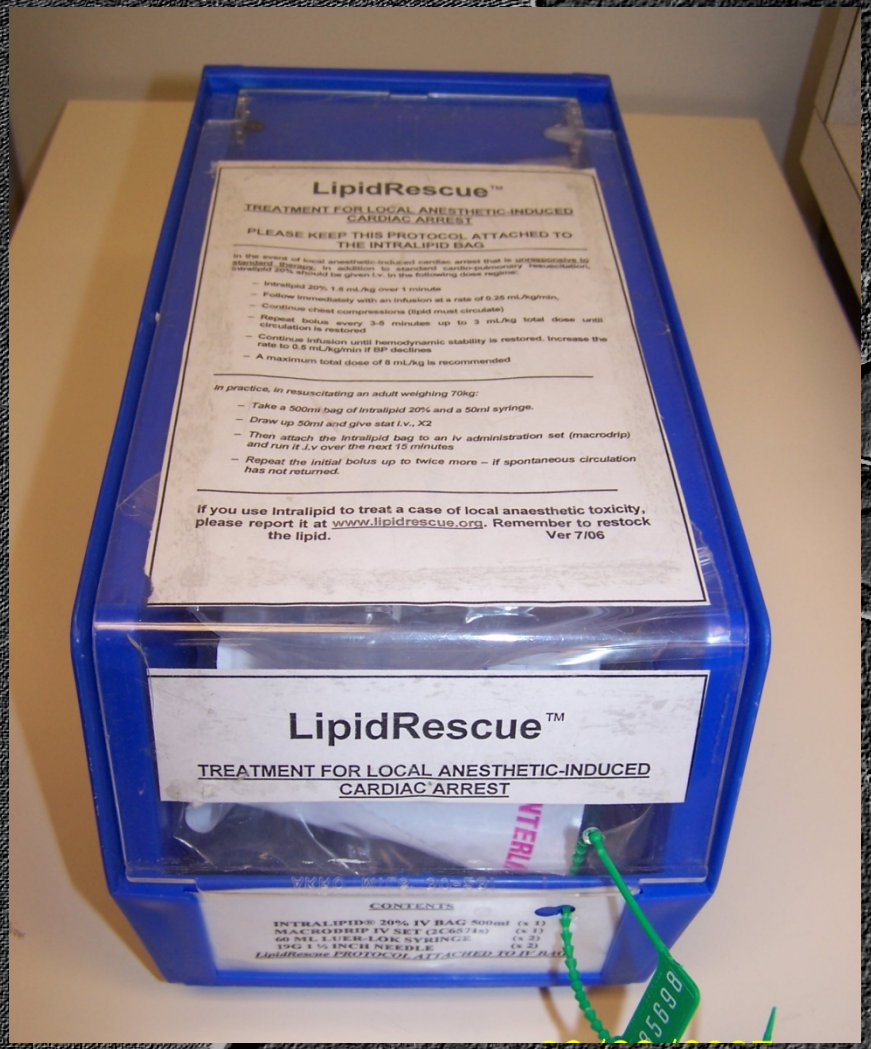
V případě srdeční zástavy způsobené podáním lokálního anestetika a nereagující na standardní terapii srdeční zástavy bysoučasně se standardními postupy kardio-pulmonální resuscitace měl být podán Intralipid 20% i.v. podle následujícího dávkovacího schématu:

- bolus Intralipidu 20% 1,5 ml/kg i.v. během jedné minuty
- následovaný kontinuálním infuzním podáváním 0,25ml/kg/min
- pokračující komprese hrudníku (Intralipid musí cirkulovat v oběhu)
- opakovat bolus každé 3-5 minut do celkové dávky 3ml/kg do obnovení krevního oběhu
- pokračovat kontinuálním infuzním podáváním do obnovení hemodynamické stability
- zvýšit dávku na 0,5 ml/kg/min v případě poklesu krevního tlaku
- maximální doporučená celková dávka: 8ml/kg

Praktický příklad resuscitace 70kg dospělého jedince:

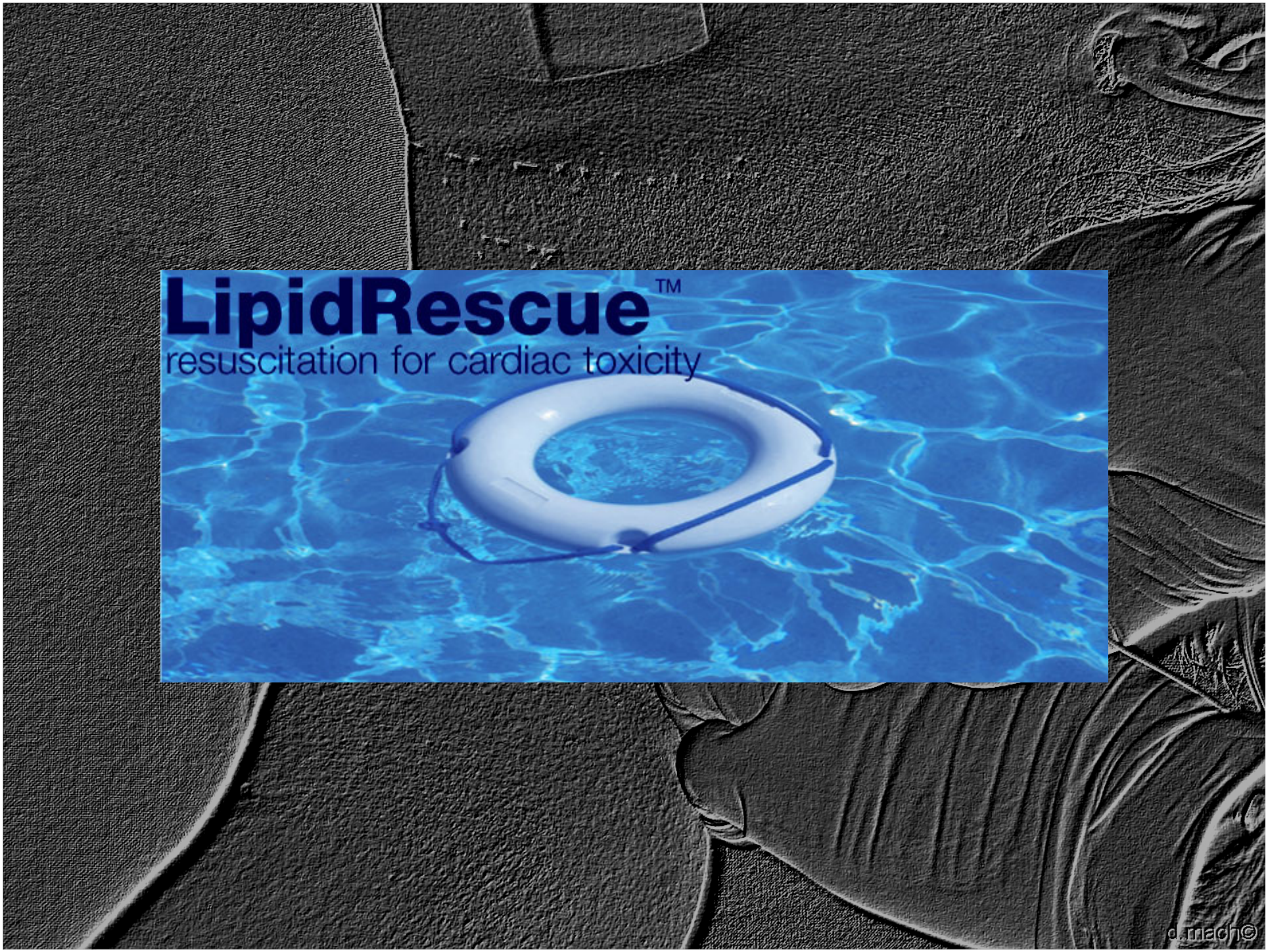
- vezmi vak s 500ml Intralipidu 20% a 50 ml stříkačku
- natáhni plně 50ml stříkačku Intralipidem a podej STATIM i.v. 2x
- připoj infuzní set k vaku se zbývajícím Intralipidem a podej i.v. během následujících 15 minut
- nebyl-li dosud obnoven krevní oběh, až dvakrát zopakuj podání původního bolusu

V případě užití Intralipidu k terapii toxického účinku lokálního anestetika, podejte, prosím, zprávu o tomto případu na www.lipidrescue.org a ověřte, že spotřebovaný vak s Intralipidem byl nahrazen novým.


LipidRescue™
TREATMENT FOR LOCAL ANESTHETIC-INDUCED CARDIAC ARREST
PLEASE KEEP THIS PROTOCOL ATTACHED TO THE INTRALIPID BAG
In the event of local anaesthetic-induced cardiac arrest that is unresponsive to standard therapy, in addition to standard cardio-pulmonary resuscitation, Intralipid 20% should be given I.v. in the following dose regime:
– Intralipid 20% 1.5 mL/kg over 1 minute
– Follow immediately with an infusion at a rate of 0.25 mL/kg/min.
– Continue chest compressions (lipid must circulate)
– Repeat bolus every 3-5 minutes up to 3 mL/kg total dose until circulation is restored
– Continue infusion until hemodynamic stability is restored. Increase the rate to 0.5 mL/kg/min if BP declines
– A maximum total dose of 8 mL/kg is recommended
In practice, in resuscitating an adult weighing 70kg:
– Take a 500ml bag of Intralipid 20% and a 50ml syringe.
– Draw up 50ml and give stat I.v., X2
– Then attach the Intralipid bag to an iv administration set (macrodrip) and run it i.v over the next 15 minutes
– Repeat the initial bolus up to twice more – if spontaneous circulation has not returned.
If you use Intralipid to treat a case of local anaesthetic toxicity, please report it at www.lipidrescue.org. Remember to restock the lipid.
Ver 7/06
LipidRescue™
TREATMENT FOR LOCAL ANESTHETIC-INDUCED CARDIAC ARREST
CONTENTS
INTRALIPID® 20% IV BAG 500ml (x 1)
MACRODRIP IV SET (2C6571) (x 1)
60 ML LUER-LOK SYRINGE (x 2)
19G 1 ½ INCH NEEDLE (x 2)
LipidRescue PROTOCOL ATTACHED TO IV BAG


PLEASE KEEP THIS PROTOCOL ATTACHED TO THE INTRALIPID BAG
Intralipid® 20%
A 20% I.V. Fat Emulsion
Fresenius Kabi
INTERLINK System
Baxter


LipidRescue™
TREATMENT FOR LOCAL ANESTHETIC-INDUCED CARDIAC ARREST
CONTENTS
DRAWER #1
Restraints, Syringes, Needles
DRAWER #3
Suction Tubing, NGT, Suction Catheter Kit
Swing Up
02/22/2007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resuscitation for cardiac toxicity
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