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Upper Arm Local Anesthesia Reversal (LAR) Using Lipofundin (3 Case Reports)

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Abstract

Local anesthesia reversal(LAR) is a new idea based on the history of Local Anesthetic Systemic Toxicity (LAST). If Intralipid and other specific Lipid emulsions can reverse the cardiac toxicity, why it cannot reverse other features connected to the local anesthesia toxicity?It is a very logical idea. The illogical issue is why it took almost 20 years from the first article on Intralipid and bupivacaine to invent it…?

In our 3 cases the first patient "after finishing the lipofundin bolus injection after 4 mins (137 min after the brachial plexus block), she could move slightly her right finger.The patient could move her hand at 34 mins after the lipofundin bolus injection (166 mins after the brachial plexus block), and she could move her forearm 102 mins after the lipofundin bolus injection".

In the 2nd case "after 80-84 mins of the LE bolus injection (180 min after the brachial plexus block) the patient could move slightly his left thumb.After 184 mins since the lipid emulsion bolus injection (290 mins after the brachial block) the patient could move his hand and arm easily".

In the 3rd case "85-87 mins after the LE bolus injection (220 min after the brachial plexus block), the patient could move slightly his arm. 128 mins after the lipid emulsion bolus injection (261 mins after the brachial plexus block), the patient could move his hand easily".

In all the 3 cases the reversal of the sensory and motor blocks were much faster than in the non-LAR cases as described in the medical literature. In that regards the LAR by Intralipid, Lipofundin and other similar lipid emulsions is a new method for postoperative care of patients after brachial plexus block.

Keywords: Brachial plexus block, Supraclavicular block,Lipofundin, Intralipid, Lipid emulsion, Local anesthetic systemic toxicity, LAST, Local anesthesia reversal, LAR

Case Report 1

A 37 years old female was diagnosed an ununion radial bone. She performed a radial bone surgery on 1st March 2018 at Military Hospital 103,Vietnam Military Medical University:http://www.csen.com/upper4.JPG

Patient was anesthetized by ultrasound guided brachial plexus block, upper clavicular approach with lidocaine 4 mg/kg combined with ropivacaine 1mg/kg and epinephrine 1/200.000 in a total volume of 30 ml.

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Onset time: 8 mins

Duration of surgery: 100 mins

Anesthesia effect was very good for surgery.Sensory and motor functions of the right hand were assessed before Lipofundin injection and were absent completely after surgery.

Lipid emulsion bolus injection was started at 137 mins after brachial plexus block over 3 mins with the dose of 1.5 mg/kg (patient's weight 65 kg, 158 cm), total -97 ml. Then, continuous infusion with the dose of 0.25ml/kg/min (162ml) over 10 mins was done. Patient was monitored closely.

After finishing the lipofundin bolus injection after 4 mins (137 min after the brachial plexus block), the patient could move slightly her right finger.The patient could move her hand at 34 mins after the lipofundin bolus injection (166 mins after the brachial plexus block),and could move her forearm 102 mins after the lipofundin bolus injection.She completely recovered her movement and sensory 127 mins after the lipofundin bolus injection. Vital signs were stable after the lipofundin injections(Table 1).

Videos:

Starting lipofundin bolus injection: https://youtu.be/rTtDOQiih1U

Continuous lipofundin infusion: https://youtu.be/lF4bP5zU4Kg

4 mins after finishing lipofundin bolus injection: https://youtu.be/--TREW5jeTs

13 mins after finishing lipofundin bolus injection: https://youtu.be/HE80oYqxFjc

15 mins after finishing lipofundin bolus injection: https://youtu.be/LcPoQrzwxQM

26 mins after finishing lipofundin bolus injection: https://youtu.be/C2-SOngdgWc

34 mins after finishing lipofundin bolus injection: https://youtu.be/xCwbVNuEZ9U

57 mins after finishing lipofundin bolus injection: https://youtu.be/r1fbMnQNLlM

63 mins after finishing lipofundin bolus injection: https://youtu.be/a6JILCUZQSY

67 mins after finishing lipofundin bolus injection: https://youtu.be/j0ALXiaafzc

72 mins after finishing lipofundin bolus injection: https://youtu.be/91cDOiS3rc4

81 mins after finishing lipofundin bolus injection: https://youtu.be/vUS_GJiRjmk

94 mins after finishing lipofundin bolus injection: https://youtu.be/j0zhtChUsBs

104 mins after finishing lipofundin bolus injection: https://youtu.be/ImSV0dmVpg4

111 mins after finishing lipofundin bolus injection: https://youtu.be/EmVxlUtgiJU

131 mins after finishing lipofundin bolus injection: https://youtu.be/U8ywvu_Ny2I

136 mins after finishing lipofundin bolus injection: https://youtu.be/X5IcvySgBMg

139 mins after finishing lipofundin bolus injection: https://youtu.be/cX8Ki4uFhd4

Case report 2

A 19 years old male was diagnosed with two bone fractures in the left forearm due to vehicle accident:http://www.csen.com/upper3.JPG

He underwent an elective two bone surgery on 27th February, 2018 at the Military Hospital 103,Vietnam Military Medical University. The patient was anesthetized by ultrasound guided brachial plexus block, upper clavicular approach with lidocaine 4 mg/kg combined with ropivacaine 1mg/kg and epinephrine 1/200.000 in total 30 ml of solution.

Onset time: 7 mins.

Duration of surgery: 80 mins.

Anesthesia effect was very good for surgery.Surgery was accomplished in 83 mins after the brachial plexus block. Sensory and motor functions of the left hand were absent completely after the surgery.

Table 1

	Brachial Plexus block	Duration of surgery	Lipid bolus injection 1.5 ml/kg (97ml) over 3 mins	Continuous infusion in 10 mins	Can move slightly her finger	Can move her hand	Can move her forearm	Can move her upper arm	Move her upper arm easily	Complete Recovery ofmovement and sensory
	8h21minAM	(100 mins)	10h 30 min to 10h 33 min	10h 33 to 10h43 min	10h 37	11h 7	12h25	12h 43	12h47	12h51h
After block (mins)			129		137	166	244	262	266	270
Afterlipofundinbolus injection (mins)			0		4	34	102	120	124	127

Lipid emulsion (Lipofundin) bolus injection was started at point 133 mins after the brachial plexus block over 3 mins with the dose of 1.5 mg/kg (patient's weight is 40kg, 158 cm), total -60 ml. Afterwards a continuous infusion with the dose of 0.25 ml/kg/min (100ml/10 mins) over 10 mins was done. The patient was monitored during the LE infusion until the full recovery of the motor and sensory functions.

After 80-84 mins of the LE bolus injection (180 min after the brachial plexus block) the patient could move slightly his left thumb.After 184 mins since the lipid emulsion bolus injection (290 mins after the brachial block) the patient could move his hand and arm easily.Vital signs were stable during and after the LE bolus and infusion(Table 2).Lipofundin: http://www.csen.com/Lipofundin.JPG

Videos:

Starting Bolus LE injection: https://youtu.be/bSUlLPPOOZQ

10 mins after bolus LE injection: https://youtu.be/6V-kXsLXlsc

46 mins after bolus LE injection: https://youtu.be/B8VgbvF8538

60 mins after bolus LE injection: https://youtu.be/Jc9oCClkHTg

80 mins after bolus LE injection: https://youtu.be/F7mEXJG_Sdk

84 mins after bolus LE injection: https://youtu.be/BukCloqzHnU

100 mins after bolus LE injection: https://youtu.be/VpuUV3A8AcA

102 mins after bolus LE injection: https://youtu.be/p1CGcsTHzCM

194 mins after bolus LE injection: https://youtu.be/wfJKDneDj_g

Case report 3

A 49 years old male was diagnosed of a complicated two bone fractures in the right forearm due to labour accident:http://www.csen.com/upper2.jpg

The patient performed an elective two bones surgery on 26th Feb, 2018 at the Military Hospital 103, Vietnam Military Medical University. The patient was anesthetized by ultrasound guided brachial plexus block, upper clavicular approach with lidocaine 4 mg/kg combined with ropivacaine 1mg/kg and epinephrine 1/200.000 in total 30 ml of solution.

Onset time: 8 mins.

Duration of surgery: 110 mins.

Anesthesia effect was very good for the surgery.Surgery was accomplished in 120 mins after the brachial plexus block. Sensory and motor functions of the left hand were absent completely after the surgery.

Lipid emulsion (Lipofundin) bolus injection was started at the point of 133 mins after the brachial plexus block over 3 mins with the dose of 1.5 mg/kg (patient's weigh is 60kg, 168 cm), total:90 ml. Then, continuous infusion of Lipofundin with the dose of 0.25 ml/kg/min (150ml) over 10 mins was done. The patient was monitored during the LAR (Local Anesthesia Reversal).

85-87 mins after the LE bolus injection (220 min after the brachial plexus block),the patient could move slightly his arm.128 mins after the lipid emulsion bolus injection (261 mins after the brachial plexus block), the patient could move his hand easily.Vital signs were stable during the LAR procedure(Table 3).

Videos:

Bolus LE. Injection: https://youtu.be/vrStLYycNrI

78 mins after LE bolus injection: https://youtu.be/SV6-FvF2dvo

93 mins after LE bolus injection: https://youtu.be/i4oCviFJdIA

97 mins after LE bolus injection: https://youtu.be/C1DTrW2fZo4

101 mins after LE bolus injection: https://youtu.be/f6dr2sahf9I

104 mins after LE bolus injection: https://youtu.be/vVnJbNlSOkY

Table 2

	Brachial Plexus block	Duration of surgery	Lipid bolus injection 1.5 ml/kg (90ml) over 3 mins	Continuous infusion in 10 mins	Move slightly his arm	Can move his forearm	Move his upper arm easily	Completely recover movement and sensory
	9h21 min	(80 mins)	10h 57 min	11h to 11h 10 min	12h 21	12h 39	14h11	15h (feel pain and need pain medication)
After block (mins)			96	99	180	198	290	339
AfterLE bolus injection (mins)			0		84	102	184	233

Table 3

	Brachial Plexus block	Duration of surgery	Lipid bolus injection 1.5 ml/kg (90ml) over 3 mins	Continuous infusion in 10 mins	Move slightly his arm	Move his forearm easily	Move his upper arm easily	Completely recover movement and sensory
	8h46 min	(10h56) 110 mins	11h 7 min	11h10 min to 11h20min	12h 15	12h 25	12h40	13h15
After block (mins)			131	144	199	209	226	261
After LE bolus injection (mins)			0	0	68	78	93	128

Discussion

Lipofundin

Composition 1000 ml emulsion contain:

Lipofundin® MCT/LCT 20%

Soybean oil: 100.0 g

Medium Chain Triglycerides: 100.0 g

Linoleic acid: 48-58 g/L

a-Linoleic acid: 5-11 g/L

Glycerol: 25.0 g

Egg yolk phospholipids*: 12.0 g

Sodium Oleate, α-Tocopherol*, Water for injections

Megajoules/l (approx.): 7.99 (1908 kcal)

Milliosmols/l (approx.):380

pH:6.5-8.5

Lipid emulsions have been used to treat various drug toxicities and for total parenteral nutrition therapy. Their usefulness has also been confirmed in patients with local anesthetic-induced cardiac toxicity. The purpose of this study was to measure the hemodynamic and composition effects of lipid emulsions and to elucidate the mechanism associated with changes in intracellular calcium levels in myocardiocytes[1].

We measured hemodynamic effects using a digital analysis system after Intralipid® and Lipofundin® MCT/LCT were infused into hearts hanging in a Langendorff perfusion system[1]. We measured the effects of the lipid emulsions on intracellular calcium levels in H9c2 cells by confocal microscopy.

Infusion of Lipofundin® MCT/LCT 20% (1 ml/kg) resulted in a significant increase in left ventricular systolic pressure compared to that after infusing modified Krebs-Henseleit solution (1 ml/kg) (P=0.003, 95% confidence interval [CI], 2.4-12.5). Lipofundin® MCT/LCT 20% had a more positive inotropic effect than that of Intralipid® 20% (P=0.009, 95% CI, 1.4-11.6). Both lipid emulsion treatments increased intracellular calcium levels. Lipofundin® MCT/LCT (0.01%) increased intracellular calcium level more than that of 0.01% Intralipid® (P<0.05, 95% CI, 0.0-1.9).

These two lipid emulsions had different inotropic effects depending on their triglyceride component. The inotropic effect of lipid emulsions could be related with intracellular calcium level[1].

Free fatty acid (FFA) oxidation is depressed in the post ischaemic stunned myocardium and recovers in parallel with the normalization of contractile performance. Assuming a causal role for this metabolic disturbance in the pathogenesis of stunning, we questioned whether exogenous administration of high dose triglycerides during reperfusion of post ischaemic myocardium, could improve its functional recovery[2].

Thirteen dogs were chronically instrumented to measure global and regional haemodynamics and to produce a 10 min episode of regional myocardial ischaemia. In 7 dogs, Intralipid 20% was administered i.v. during the reperfusion phase. Contractile recovery of stunned myocardium was compared with control saline treatments. The series were repeated in another 6 animals, but oxfenicine (CPT I inhibitor) preceded Intralipid during reperfusion.

Contractile recovery of stunned myocardium was faster and more extensive when Intralipid was administered during reperfusion than with saline treatment (wall thickening fraction 86 +/- 6% of pre-ischaemic controls versus 52 +/- 11% at 90 min post-reperfusion; P<0.05). Oxfenicine pretreatment completely abolished this beneficial effect.

Exogenous administration of triglycerides during reperfusion of post ischaemic myocardium improves functional recovery from stunning. This beneficial effect most likely operates through enhanced FFA availability and/or oxidation since it could be abolished by selective inhibition of the carnitine palmitoyl I enzyme[2].

The authors sought to confirm a chance observation that intravenous lipid treatment increases the dose of bupivacaine required to produce asystole in rats. The authors also measured the partitioning of bupivacaine between the lipid and aqueous phases of a plasma-lipid emulsion mixture[3].

Anesthetized Sprague-Dawley rats were used in pretreatment (protocol 1) and resuscitation (protocol 2) experiments. In protocol 1, animals were pretreated with saline or 10%, 20%, or 30% Intralipid (n=6 for all groups), then received 0.75% bupivacaine hydrochloride at a rate of 10 mlx kg x min(-1) to asystole. In protocol 2, mortality was compared over a range of bolus doses of bupivacaine after resuscitation with either saline or 30% Intralipid (n=6 for all groups). The lipid:aqueous partitioning of bupivacaine in a mixture of plasma and Intralipid was measured using radiolabelled bupivacaine.

Median doses of bupivacaine (in milligrams per kilogram) producing asystole in protocol 1 were for 17.7 for saline, 27.6 for 10% Intralipid, 49.7 for 20% Intralipid, and 82.0 for 30% Intralipid ($P<0.001$ for differences between all groups). Differences in mean +/- SE concentrations of bupivacaine in plasma (in micrograms per millilitre) were significant ($P<0.05$) for the difference between saline (93.3 +/- 7.6) and 30% Intralipid (212 +/- 45). In protocol 2, lipid infusion increased the dose of bupivacaine required to cause death in 50% of animals by 48%, from 12.5 to 18.5 mg/kg. The mean lipid:aqueous ratio of concentrations of bupivacaine in a plasma-Intralipid mixture was 11.9 +/- 1.77 (n=3).

Lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats. Partitioning of bupivacaine into the newly created lipid phase may partially explain this effect. These results suggest a potential application for lipid infusion in treating cardiotoxicity resulting from bupivacaine[3].

Local anesthesia drug inhibition of mitochondrial ATPase

The concentrations of n-butanol and tetracaine required for 50% inhibition of the ATPase activity of F1 particles isolated from bovine heart mitochondria were 160 mM and 1.1 mM, respectively. The results are offered as evidence that the physiological effects of these anesthetics may be due to direct interaction with membrane proteins rather than with the lipids[4].

Local anesthetics and alcohols were found to inhibit mitochondrial electron transport at several points along the chain. The anesthetics employed were the tertiary amines procaine, tetracaine, dibucaine, and chlorpromazine, and the alcohols were n-butanol, n-pentanol, n-hexanol, and benzyl alcohol. Uncoupled sonic sub mitochondrial particles from beef heart and rat liver were studied. We [5]report the following: (1) All of the anesthetics were found to inhibit each of the segments of the electron transport chain assayed; these included cytochrome c oxidase, durohydroquinone oxidase, succinate oxidase, NADH oxidase, succinate dehydrogenase, succinate-cytochrome c oxidoreductase, and NADH-cytochrome c oxidoreductase. (2) NADH oxidase and NADH-cytochrome c oxidoreductase required the lowest concentration of anesthetic for inhibition, and cytochrome c oxidase required the highest concentrations. (3) We conclude that there are several points along the chain at which inhibition occurs, the most sensitive being in the region of Complex I (NADH dehydrogenase). (4) Beef heart sub mitochondrial particles are less sensitive to inhibition than are rat liver particles. (5) Low concentrations of several of the anesthetics gave enhancement of electron transport activity, whereas higher concentrations of the same agents caused inhibition. (6) The concentrations of anesthetics (alcohol and tertiary amine) which gave 50% inhibition of NADH oxidase were lower than the reported concentrations required for blockage of frog sciatic nerve[5].

The following characteristics are reported for mitochondrial ATPase prepared by the chloroform extraction method: (1) The pH optimum for enzyme activity is at 8.0. (2) The neutral anesthetic benzocaine inhibits the enzyme at all pH values. (3) Reciprocal plots of 1/v versus 1/[ATP] show that inhibition by lidocaine, tetracaine, dibucaine, and chlorpromazine is non-competitive; slope and intercept replot are hyperbolic, showing that the inhibition is partial rather than complete[6].

Supra clavicular brachial plexus anesthesia duration

To compare the efficacy of ropivacaine 7.5 mg x ml(-1) with bupivacaine 5.0 mg x ml(-1) for subclavian perivascular brachial plexus block.

After informed consent, 104 ASA I-III adults participated in a randomized, double-blind, multi-center trial to receive 30 ml of either ropivacaine 7.5 mg x ml(-1) or bupivacaine 5.0 mg x ml(-1) for subclavian perivascular brachial plexus block prior to upper limb surgery. Onset and duration of sensory and motor block in the distribution of the axillary, median, musculo-cutaneous, radial and ulnar nerves were assessed.

Onset times and duration of sensory and motor block were similar between groups. Mean duration of analgesia for the five nerves was between 11.3 and 14.3 hr with ropivacaine and between 10.3 and 17.1 hr with bupivacaine. Quality of muscle relaxation judged as excellent by the investigators was not significantly different (ropivacaine-35/49, bupivacaine-30/49). The median time to first request for analgesia was comparable between the two groups (11-12hr). One patient developed a grand mal seizure shortly after receiving bupivacaine and recovered consciousness within 30 min. There were no serious adverse events in the ropivacaine group.

Thirty ml ropivacaine 7.5 mg x ml(-1) (225 mg) produced effective and well tolerated brachial plexus block of long duration by the subclavian perivascular route. In this study, the results were similar to those of 30 ml bupivacaine 5.0 mg x ml(-1) [7].

We examined the outcomes and levels of patient satisfaction in 202 consecutive cases of ultrasound-guided supraclavicular brachial plexus block (SBPB) in upper limb surgery performed between September 2007 and March 2010[8]. All blocks were performed by orthopaedic surgeons using ultrasound visualisation with a high-frequency linear probe. The probe was placed in the coronal-oblique plane in the supraclavicular fossa, and the puncture was 'in-plane' from lateral to medial. Most of the blocks were performed with 0.75% ropivacaine/1% lidocaine (1:1), with or without

adrenaline in 1:200,000 dilution. In 201 patients (99.5%) the brachial plexus block permitted surgery without conversion to general anaesthesia. The mean procedure time for block was 3.9 min (2 to 12), the mean waiting time for surgery was 34.1 min (10 to 64), the mean surgical time was 75.2 min (6 to 232), and the mean duration of post-anaesthetic analgesia was 437 min (171 to 992). A total of 20 patients (10%) developed a transient Horner's syndrome. No nerve injury, pneumothorax, arterial puncture or systemic anaesthetic toxicity were recorded. Most patients (96.7%) were satisfied with ultrasound-guided SBPB. This study demonstrates the efficacy and safety of ultrasound-guided SBPB for orthopaedic surgery on the upper limb[8].

Localanesthesiareversal (LAR)

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Conclusion

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