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Lipid Emulsion for Local Anesthesia Reversal (LAR) after Prolonged Spinal/Epidural Anesthesia

Joseph Eldor[1]*
Tuan Anh Nguyen[2]

[1]*Theoretical Medicine Institute, Jerusalem, Israel*
[2]*Department of Anesthesiology and Pain Medicine, University Medical Center, Hochiminh City, Vietnam*

Abstract

A 71-year-old woman was scheduled for total knee replacement on left side. Combined Spinal Epidural Anesthesia (CSEA) was performed at L3-4 and L2-3 separately and was technically uneventful. Epidural Anesthesia (EA) with levobupivacaine 0.1%+fentanyl (2mcg/ml) was effective at 5 ml/h for postoperative analgesia. Eight hours post-op, she complained of having lost all feeling on the non-operative leg. On examination, she had diminished both touch sensory and motor power on the non-operative leg, but intact on the operative side with VAS at 2/10. Epidural catheter was receded 2 cm and the dose was lowered and paused. Despite of these adjustments after 4 hours, her experience was not improved. It was decided to use lipid emulsion as a challenging therapy. After completion of the lipid therapy, the sensory and movement of the non-operative leg regained normal after 60 min. The severe pain recurred which needed IV morphine titration. The EA of 2-5ml/h was recontinued and effective for pain control for 3 days without no incident.

It is the first time in the medical literature that Lipid Emulsion is used for the purpose of LAR (Local Anesthesia Reversal) not connected to LAST (Local Anesthetic Systemic Toxicity).

Keywords: Intralipid, Lipid emulsion, Fat emulsion, Local anesthesia reversal, Spinal anesthesia, Epidural anesthesia.

Case Report

A 71-year-old woman was scheduled for total knee replacement on left side. Past medical history was hypertension, type 2 diabetes, bilateral degenerative knee pain. Combined Spinal Epidural Anesthesia (CSEA) was performed at L3-4 and L2-3 separately and was technically uneventful. Spinal Anesthesia (SA) with 10 mg bupivacaine 0.5% heavy+20mcg fentanyl was effective for surgery. Epidural Anesthesia (EA) with levobupivacaine 0.1%+fentanyl (2mcg/ml) was effective at 5ml/h for postoperative analgesia. She was sent back to ward after free movement of both knees. Eight hours post-op, she complained of having lost all feeling on the non-operative leg. On examination, she had diminished both touch sensory and motor power on the non-operative leg, but intact on the operative side with VAS at 2/10. After Local Anesthetic Systemic Toxicity (LAST) was ruled out, epidural catheter was receded 2cm and the dose was lowered and paused. Despite of these adjustments after 4 hours, her experience was not improved.

It was decided to use lipid emulsion as a challenging therapy. A vial of 250ml of Lipidem 20% (B. Braun) was infused over 30 min as regimen in ASRA's checklist for treatment of LAST. After completion of the lipid therapy, the sensory and movement of the non-operative leg regained normal after 60min. The severe pain recurred which needed IV morphine titration. The EA of 2-5ml/h was recontinued and effective for pain control for 3 days without no incident.

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***Corresponding author:** Dr. Joseph Eldor, Theoretical Medicine Institute, Jerusalem, Israel. Tel: +972-2-5835528; Email: csen_international(at)csen.com

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Discussion

LAST

On April 1998 Weinberg GL et al. published in Anesthesiology journal the following article: Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats [1]. This article started the Intralipid (lipid infusion) LAST (Local Anesthetic Systemic Toxicity) treatment by Intralipid.

The article conclusion was that "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".

On February 2018 Neal JM et al. published in Regional Anesthesia Pain Medicine journal the following article: The Third American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Local Anesthetic Systemic Toxicity: Executive Summary 2017 [2].

The article conclusion was: "This interim update summarizes recent scientific findings that have enhanced our understanding of the mechanisms that lead to lipid emulsion reversal of LAST, including rapid partitioning, direct inotropy, and post-conditioning. Since the previous practice advisory, epidemiological data have emerged that suggest a lower frequency of LAST as reported by single institutions and some registries, nevertheless a considerable number of events still occur within the general community. Contemporary case reports suggest a trend toward delayed presentation, which may mirror the increased use of ultrasound guidance (fewer intravascular injections), local infiltration techniques (slower systemic uptake), and continuous local anesthetic infusions. Small patient size and sarcopenia are additional factors that increase potential risk for LAST. An increasing number of reported events occur outside of the traditional hospital setting and involve non-anesthesiologists".

The LAST was the subject regarding Intralipid and nothing else in all these 20 years of research. Eldor defined this Intralipid (fat emulsion containing soybean oil and egg yolk) as a "Magic Bullet" [3].

The case report mentioned in this article is a kind of a Local Anesthesia Reversal (LAR) by Intralipid. It is the first article mentioning this Intralipid – LAR treatment in the medical literature.

AFE

There are other theoretical options for use of intralipid. For example:

Lipid emulsion rescue of amniotic fluid embolism induced cardiac arrest: "As a last resort, IV lipid 20% emulsion (1.5mL/kg) was administered as a bolus [4]. Within 30 to 90 seconds, the patient had return of spontaneous circulation, normal sinus rhythm, and dramatic improvement in left and right ventricular function, shown clearly by TEE. After several minutes, the patient's condition slowly deteriorated once again to asystole, at which time CPR was once again started and a second lipid emulsion bolus (1.5mL/kg) was administered and followed with an infusion at 0.25mL/kg/min. Within 30 to 60 seconds, the patient again had a return of spontaneous circulation with normal sinus rhythm. In addition, she also exhibited spontaneous movements of her extremities".

"Although Eldor et al. were the first to suggest a possible benefit of lipid emulsion therapy in the treatment of AFE, this is the first published instance in which a patient received intravenous lipid emulsion temporally related to the recovery from cardiovascular collapse associated with amniotic fluid embolism [3]. The main limitation is the fact that AFE is a diagnosis of exclusion; however, other differential diagnoses are less likely. There is TEE evidence that shows overall improvement of cardiac function temporally related to administration of lipid emulsion. The patient had return of spontaneous circulation occurring shortly after the administration of lipid emulsion on 2 different occasions after exhausting all other ACLS options, suggesting that lipid emulsion may have been responsible for the successful resuscitation. In addition, after the initial improvement, a relapse occurred, which was treated with a second bolus of lipid emulsion after which the same improvement in clinical and cardiac function occurred. Full neurologic recovery was noted after significantly prolonged cardiovascular collapse with chest compressions (40 min) and exhaustion of other standard ACLS medications. The excellent neurologic recovery emphasizes the importance of high quality and sustained CPR. Furthermore, a possible physiologic mechanism for the cardiopulmonary recovery is presented and is based on scientific models from previous research on the effects of lipid emulsion and its components. This report suggests a possible benefit of lipid emulsion therapy in the treatment of cardiovascular collapse caused by AFE, and further research will be required to elucidate the role of lipid emulsion therapy in the setting of AFE".

Spinal/Epidural Lavage

This study was designed to determine whether epidural motor blockade could be reversed by postoperative injections of crystalloid solutions via the epidural catheter [5]. Twenty-seven patients (ASA physical status I, non-labouring) had epidural anesthesia with 0.75% bupivacaine for elective cesarean delivery. Postoperatively, patients were randomized to receive three 15mL injections (over 30 min) of crystalloid solutions (normal saline or Ringer's lactate) or no treatment (control) via the epidural catheter. Degree of motor and sensory blockade was evaluated with an investigator blinded to treatment group. Rate of resolution of sensory blockade was not different among groups. However, time for resolution of motor blockade was more than twice as long in the control group than in either treatment group (control=178 +/- 70 min vs Ringer's lactate=84 +/- 44 min, normal saline=70 +/- 38 min, P=0.001). The data suggest that unwanted motor blockade due to epidural anesthesia can be reversed by epidural injections of crystalloid solutions [5].

Prolonged motor and sensory block following epidural anesthesia can be associated with extended postoperative

care unit stays and patient dissatisfaction. Previous studies have demonstrated a more rapid motor recovery following the administration of epidural crystalloids in patients who had received plain bupivacaine and lidocaine epidural anesthesia. However, epinephrine is commonly added to local anesthetics to improve the quality and prolong the duration of the epidural block. The objective of this study was to determine the relationship of 0.9% NaCl epidural catheter flush volume (i.e., washout) to the recovery of motor and sensory block in patients undergoing 2% lidocaine with epinephrine epidural anesthesia [6].

A prospective, randomized, double-blind study design was utilized. Thirty-three subjects scheduled for elective gynecologic or obstetrical surgical procedures underwent epidural anesthesia using 2% lidocaine with epinephrine (1:200,000). A T4 dermatome level of analgesia, determined by toothpick prick, was maintained intraoperatively. Following surgery, subjects were randomized to 1 of 3 treatment groups. Group 1 (control, n=11) received no epidural 0.9% NaCl (normal saline [NS]) postoperatively.

Group 2 (15 mL NSx1, n=10) received an epidural bolus of 15 mL NS. Group 3 (15 mL NSx2, n=12) received an epidural bolus of 15 mL NS postoperatively and a second 15 mL NS bolus 15 minutes later. Assessment of motor and sensory block was performed at 15-minute intervals until complete motor and sensory recovery.

Times to partial and full motor and sensory recovery were significantly faster in the epidural NS groups than in the control group. Full motor recovery was more rapid in subjects receiving two 15 mL NS epidural NS boluses (30 mL total) compared with those receiving a single 15-mL NS bolus (108 +/- 9 min vs 136 +/- 13 min) and significantly faster than control group subjects (153 +/- 14 min). Both NSx1 and NSx2 epidural bolus groups experienced significantly reduced times to complete sensory recovery when compared with the control group (NSx1=154 +/- 13 min, NSx2=153 +/- 9 min, control 195 +/- 14 min).

A more rapid recovery of motor and sensory block in patients undergoing 2% lidocaine with epinephrine epidural anesthesia can be achieved with the use of 30 mL NS epidural washout [6].

In this case report, we describe the use of cerebrospinal fluid lavage as a successful treatment of an inadvertent intrathecally placed epidural catheter in a 14-yr-old girl who underwent a combination of epidural anesthesia and general anesthesia for orthopedic surgery [7]. In this case, a large amount of local anesthetic was injected (the total possible intrathecal injection was 200 mg of lidocaine and 61 mg of bupivacaine), resulting in apnea and fixed dilated pupils in the patient at the end of surgery. Twenty milliliters of cerebrospinal fluid was replaced with 10 mL of normal saline and 10 mL of lactated Ringer's solution from the "epidural" catheter. Spontaneous respiration returned 5 min later, and the patient was tracheally extubated after 30 min. No signs of neurological deficit or post dural puncture headache were noted after surgery.

Cerebrospinal lavage may be a helpful adjunct to the conventional supportive management of patients in the event of an inadvertent total spinal [7].

Several investigators have described the phenomena of epidural saline washout using bolus injections. This study was designed to determine whether epidural block could be reversed more effectively by infusion of crystalloid solutions via the epidural catheter.

One hundred male patients scheduled for outpatient surgery were enrolled in this study. After 30 min of 2% prilocaine epidural anesthesia, patients were randomly assigned to receive 45 mL of study solution as follows: (1) normal saline bolus (group NSB); (2) Ringer's lactate bolus (group RLB); (3) normal saline infusion (group NSI); (4) Ringer's lactate infusion (group RLI). Patients in the control group received no washout fluid. Motor, sensory blockade and side effects were compared among 5 groups. Ambulation time is defined as the recovery time.

In the control group, ambulation time (139 +/- 15 min) was significantly longer than in the washout groups (NSB 90 +/- 10, RLB 88 +/- 10, NSI 85 +/- 8, RLI 91 +/- 6 minutes) ($P<0.001$). Two-segment sensory regression time in the control group (86 +/- 15 min) was significantly longer than in groups NSB, RLB, NSI and RLI (55 +/- 8, 51 +/- 4, 58 +/- 8, and 53 +/- 10 minutes, respectively) ($P<0.001$).

We concluded that a more rapid recovery of motor and sensory blockade in patients undergoing epidural anesthesia may be achieved by the use of an epidural washout with either bolus or infusion of 45 mL normal saline or Ringer's lactate [8].

High or total spinal anesthesia commonly results from accidental placement of an epidural catheter in the intrathecal space with subsequent injection of excessive volumes of local anesthetic. Cerebrospinal lavage has been shown to be effective at reversing the effects of high/total spinal anesthesia but is rarely considered in obstetric cases. Here, we describe the use of cerebrospinal lavage to prevent potential complications from high/total spinal anesthesia after unintentional placement of an intrathecal catheter in a labouring obstetric patient [9].

A 34-yr-old female presented to the labour and delivery unit in active labour. Epidural anesthesia was initiated, and after the first bolus dose, the patient experienced lower extremity motor block and shortness of breath. A high spinal was confirmed, and cerebrospinal lavage was performed. In total, 40 mL of cerebrospinal fluid (CSF) were exchanged for an equal volume of normal saline. The patient's breathing difficulties and motor block resolved quickly, and a new epidural catheter was placed after removal of the spinal catheter. Pain control was effective, and the patient delivered a healthy baby.

We show that exchange of CSF for normal saline can be used successfully to manage a high spinal in an obstetric patient [9]. Our results suggest that CSF lavage could potentially be an important and helpful adjunct to the conventional supportive management of obstetric patients in the event of inadvertent high or total spinal anesthesia [9].

Dental LAR

PM (OraVerse) enables the dentist or dental hygienist (where permitted) to significantly decrease the duration of residual STA in patients where such numbness may prove to be potentially injurious (children, geriatric, and special needs patients), or a negative influence on their quality of life (speaking, eating, negative body image). (Note: As of August 3, 2009, dental hygienists are permitted to administer PM in the following states: Alaska, Arkansas, Hawaii, Idaho, Iowa, Louisiana, Montana, Nevada, New York, North Dakota, Oklahoma, Rhode Island, Tennessee, Utah, and Wisconsin) [10].

This study sought to identify and quantify complications with local anesthetic administration and reversal on consecutive patients seen for comprehensive dental care in a school-based, portable dental clinic, and includes data on the patients seen by the participating portable dental providers. In 923 dental visits where local anesthetic was administered, a standardized form was used to gain further information and identify any complications; this was accompanied by a questionnaire for the student's teacher, in order to quantify the student's distraction and disruption ratings following the dental visit. After statistical analysis of the 923 consecutive cases, the overall complication rate was 5.3%. All of the complications were considered to be mild or moderate, and there were no severe event reports. The complications encountered most frequently (n=49) were associated with self-inflicted soft tissue injury. The results of this study indicate that comprehensive care with local anesthesia delivered by a school-based portable dental clinic has a low risk of complications. Whereas safe administration of dental care is achievable with or without phentolamine mesylate as a local anesthetic reversal agent, its use was determined to improve safety outcomes. Three factors appeared to directly increase the incidence of complications: the administration of an inferior alveolar nerve block, attention deficit disorder, and obesity. Teacher evaluations demonstrated that children receiving care by a portable dental team were able to reorient back to class work and were not disruptive to classmates [11].

Administration of local anesthesia is an integral procedure prior to dental treatments to minimize the associated pain. It is learned that its effect stays more than the time required for the dental procedure to be completed. This prolonged soft tissue anesthesia (STA) can be detrimental, inconvenient, and unnecessary.

Phentolamine mesylate, a Food and Drug Administration-approved drug essentially serves the purpose of faster recovery from numbness at the site of local anesthesia. This article reviews the development of the drug phentolamine mesylate and its indication as a local anesthetic reversal agent [12]. A literature search for phentolamine mesylate as a STA reversal agent was conducted in PubMed using the terms "dental local anesthesia reversal, phentolamine mesylate" up to March 2014. The search was limited to articles published in English. The search revealed 13 PubMed indexed articles stating the development and application of phentolamine mesylate. Phentolamine mesylate is an important step in the progress of developing patient care as well as an aid to the dental clinician [12].

Lipid emulsion for non-local anesthetics toxicity

The use of intravenous lipid emulsion (ILE) therapy for the treatment of lipophilic drug toxicity is increasing. Despite this, the evidence for its effect in non-local anesthetic toxicity remains sparse. Furthermore, many case reports describe ILE use for substances in which no clear efficacy data exists. The American Academy of Clinical Toxicology established a lipid emulsion workgroup. The aim of this group is to review the available evidence regarding the effect of ILE in non-LA drug poisoning and develop consensus-based recommendations on the use of this therapy.

A systematic review of the literature was performed to capture articles through 15 December 2014. Relevant articles were determined based upon a predefined methodology. Articles involving pre-treatment experiments, pharmacokinetic studies not involving toxicity, and studies not addressing antidotal use of ILE met pre-defined exclusion criteria. Agreement of at least two members of the subgroup was required before an article could be excluded.

The final analysis included 203 articles: 141 for humans and 62 for animals. These include 40 animal experiments and 22 case reports involving animal toxicity. There were three human randomized control trials (RCT): one RCT examined ILE in TCA overdose, one RCT examined ILE in various overdoses, and one study examined ILE in reversal of sedation after therapeutic administration of inhaled anesthesia. One observational study examined ILE in glyphosate overdose. In addition, 137 human case reports or case series were identified. Intravenous lipid emulsion therapy was used in the management of overdose with 65 unique substances.

Despite the use of ILE for multiple substances in the treatment of patients with poisoning and overdose, the effect of ILE in various non-local anesthetic poisonings is heterogenous, and the quality of evidence remains low to very low [13].

IRE (Intralipid Rescue Evidence)

The quality of "evidence" related to case reports cannot be "low to very low" unless there is "evidence" that the authors fabricated the facts of the case.

We do not think that anyone in any Practice Advisory in any Executive Summary has any proof to delete any evidence from any case report.

This is what makes Intralipid (or any other fat emulsion with soybean oil and egg yolk) a "magic bullet": "Intravenous lipid emulsion therapy was used in the management of overdose with 65 unique substances".

Does anyone know of another substance that can reverse the toxicity of 65 unique substances? and this is only the beginning.

Conclusion

It is the first time in the medical literature that Lipid emulsion is used for the purpose of LAR (Local Anesthesia

Reversal) not connected to LAST (Local Anesthetic Systemic Toxicity).

References

1. Weinberg GL, VadeBoncouer T, Ramaraju GA, Garcia-Amaro MF, Cwik MJ (1998) Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats. Anesthesiology 88: 1071-1075.
2. Neal JM, Barrington MJ, Fettiplace MR, Gitman M, Memtsoudis SG, et al. (2018) The third american society of regional anesthesia and pain medicine practice advisory on local anesthetic systemic toxicity: executive summary 2017. Reg Anesth Pain Med 43: 113-123.
3. Joseph Eldor (2017) Intalipid–A Magic Bullet?
4. Windrik Lynch MD, Russell K, Jack F, William C, Culp Jr (2017) Lipid Emulsion Rescue of Amniotic Fluid Embolism Induced Cardiac Arrest: A Case Report. A&A Case Reports 8: 64-66.
5. Johnson MD, Burger GA, Mushlin PS, Arthur GR, Data S (1990) Reversal of bupivacaine epidural anesthesia by intermittent epidural injections of crystalloid solutions. Anesth Analg 70: 395-399.
6. Sitzman BT, DiFazio CA, Playfair PA, Stevens RA, Hanes CF, et al. (2001) Reversal of lidocaine with epinephrine epidural anesthesia using epidural saline washout. Reg Anesth Pain Med 26: 246-251.
7. Tsui BC, Malherbe S, Koller J, Aronyk K (2004) Reversal of an unintentional spinal anesthetic by cerebrospinal lavage. Anesth Analg 98: 434-436.
8. Katircioglu K, Ozkalkanli MY, Kalfaoglu H, Sannav S, Ozgurbuz U, et al. (2007) Reversal of prilocaine epidural anesthesia using epidural saline or ringer's lactate washout. Reg Anesth Pain Med 32: 389-392.
9. Ting HY, Tsui BC (2014) Reversal of high spinal anesthesia with cerebrospinal lavage after inadvertent intrathecal injection of local anesthetic in an obstetric patient. Can J Anaesth 61: 1004-1007.
10. Malamed SF (2010) Local anesthesia reversal. Dent Today 29: 65-66.
11. Boynes SG, Riley AE, Milbee S, Bastin MR, Price ME, et al. (2013) Evaluating complications of local anesthesia administration and reversal with phentolamine mesylate in a portable pediatric dental clinic. Gen Dent 61: 70-76.
12. Grover HS, Gupta A, Saksena N1, Saini N (2015) Phentolamine mesylate: It's role as a reversal agent for unwarranted prolonged local analgesia. J Indian Soc Pedod Prev Dent 33: 265-268.
13. Levine M, Hoffman RS, Lavergne V, Stork CM, Graudins A, et al. (2016) Lipid Emulsion Workgroup. Systematic review of the effect of intravenous lipid emulsion therapy for non-local anesthetics toxicity. Clin Toxicol (Phila) 54: 194-221.

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