Derleme - Review

Klinik Tıp Bilimleri Dergisi
Cilt: 5 Sayı: 1 Ocak 2017

Lidokain Toksisitesinin Lipid Emülsiyonu ile Başarılı Tedavisi

Successful Treatment of Lidocaine Toxicity with Lipid Emulsion

Uzm. Dr. Demet SERGİN,
Doç. Dr. Esra YÜKSEL,
Prof. Dr. Fatma Zekiye AŞKAR
Ege Üniversitesi Tıp Fakültesi Anesteziyoloji ve Reanimasyon AD.

Yazışma Adresleri /Address for Correspondence:
Uzm. Dr. Demet SERGİN
Ege Üniversitesi Tıp Fakültesi Anesteziyoloji ve Reanimasyon AD., 35100, Bornova, İzmir

Tel/phone: *+90 532 626 11 64*
E-mail:*dsergin@hotmail.com*

Anahtar Kelimeler:
Lidokain; İlaç toksisitesi; Yağ emülsiyonları

Keywords:
Lidocaine; Drug Toxicity; Fat Emulsions

Öz

Bu bildiride, port katater takılması için yüksek doz ve volümde lidokain infiltrasyonu uygulaması sonrasında ani toksisite bulguları gösteren 28 yaşındaki ASA II kadın hasta sunulmaktadır. Literatürdeki olgulardan farklı olarak, lidokain toksisitesi santral veya periferik blok tekniği uygulamadan gelişti. Sistemik toksisite nedeniyle bilinci kapanan ve ventriküler taşikardi gelişen hasta olası bir kardiyak arrest meydana gelmeden acil lipid emulsiyonu başlanmasıyla başarıyla tedavi edildi. Lipid tedavisi sonrasında bilinci açılan hasta nefes almakta güçlük çektiğini bildirdi. Çekilen akciğer grafisi sonrasında kateter takma işlemi sırasında komplikasyon geliştiği fark edildi ve hastaya pnömotoraks tanısı konuldu.

Lokal anestezik toksisitesi gelişen olguların resüsitasyonunda lipid tedavisinin hayat kurtarıcı öneminin olduğu ve ameliyathane, yoğun bakım ve acil serviste resüsitasyon gereçlerinin yanında lipid infüzyonu için kullanılacak preparatların hazır bulundurulmasının gerektiği kanısındayız.

Abstract

This presentation reports a 28 year-old, female ASA II patient showing signs of sudden toxicity following a high-dose and large-volume of lidocaine infiltration for port catheter insertion. Unlike other cases in literature, lidocaine toxicity occurred without performing a central or peripheral nerve block. The patient who lost her consciousness due to systemic toxicity and developed ventricular tachycardia was successfully treated by immediately starting lipid emulsion and a potential cardiac arrest was avoided. Following lipid treatment, the patient regained consciousness and stated that she was having difficulty breathing. An x-ray of the lungs was taken and it was noticed that a complication occurred during the catheter insertion procedure, and the patient was diagnosed with pneumothorax.

We believe that lipid therapy has lifesaving significance in resuscitation of patients who develop local anesthetic toxicity, and alongside resuscitation equipments, preparations to be used for lipid infusion should be made available in operating rooms, intensive care units and emergency departments.

Geliş Tarihi - Received
27/09/2016
Kabul Tarihi - Accepted
15/10/2016

Introduction

Local anesthetics (LAs) in high volume and concentration are known to be associated with toxicity risk.1 The first animal study regarding the use of lipid emulsions (LEs) for the treatment of toxicity caused by LAs was published in 1998.2 LEs were used in 2006 for the first time, for the treatment of cardiac arrest that developed in a patient due to local anesthetic toxicity (3,4).

There are numerous publications and especially those on central nervous system (CNS) and cardiovascular system (CVS) toxicity regarding systemic toxic reactions from peripheral and central blocks induced by LAs.1,5 Cardiac toxicity significantly correlates with the lipophilicity of LAs. The more lipophilicity of LAs, the more cardiac toxic effect occurs (e.g., bupivacaine >ropivacaine > mepivacaine) (1,5).

The therapy for LA-induced cardiac arrest is still an interesting clinical problem6. Researchers explain mechanism of action of LEs with the "lipid sink" hypothesis. According to Weinberg et al., the so-called "lipid sink" effect is suggested to be the basic mechanism of this therapeutic approach.7,8 Action mechanism of LE therapy is rarely defined and has been postulated to work both by a so-called lipid sink diminishing circulating supply of drugs to the periphery and via a direct energy supply to the myocardium.9

The article discusses a patient given a high dose and volume of lidocaine infiltration by a physician, not an anesthesiologist. The patient developed symptoms of systemic toxicity following the procedure. However, she was successfully treated by a 20 % LE and a pneumothorax was diagnosed after lipid treatment.

Case Report

The patient who was reported as a case in this manuscript signed the consent document issued by the Anesthesiology and Reanimation Department of our University Hospital. A 28-yr- old female patient (weighing 50 kg, 165 cm tall) diagnosed with breast cancer was inserted a port catheter for chemotherapy at the Department of Cardiovascular Surgery. The patient's heart rate (HR), arterial blood pressure (ABP), electrocardiography (ECG), peripheral oxygen saturation (SpO2) and respiratory rate (RR) were continuously monitored and 0.9% saline infusion was administered after inserting intravenous cannula. The patient's vital signs prior to LA infiltration were as follows: ABP 118/72 mmHg, HR:84 bpm, SpO2:98% and RR:14/min.

Anesthesia consultation was requested by the surgeons due to changed consciousness, convulsions and bilateral pupillary dilation, 10 minutes after LA infiltration to place the port catheter into the right subclavian vein. Anesthesia consultation showed that, Glasgow coma score (GCS) was E1M5V1, light reaction (LR) was bilaterally poor and pupillary dilation had developed. Physical examination indicated decreased respiratory sounds in the upper right lobe, 70/45 mmHg ABP, 145 bpm HR, 26/min RR, 90 % SpO2 and ECG consistent with ventricular tachycardia. Analysis of arterial blood gas was as follows: pH:7.48, pO2:66.7 mmHg, pCO2: 25.7 mmHg and SpO2: 93 %. The surgeons told the anaesthesia team that in placement of the port catheter, a total of 500 mg-lidocain infiltration was used within 10 minutes. The patient was given 5 L/min 100 % O2 using a face mask, and 2 mg midazolam was given via the intravenous route. Within 1 minute, 20% LE (Lipofundin® MCT/LCT 20%, Braun, Germany) was given intravenously as a bolus of 2 mL.kg-1. Three minutes later, an additional dose of 0.5 mL.kg-1 was administered when GCS was E2M5V3, considering LE to be beneficial. After administering a total of 125 mL of 20% LE, GCS was E4M6V5 with ABP:100/60 mmHg, HR: 98 bpm, RR:22/min and SpO2: 92%. The patient's consciousness returned to normal in 6 minutes, reporting a metallic taste in her tongue and difficulty in breathing. The patient reported that she could see more clearly 10 minutes after consciousness returned to normal and metallic taste decreased. A chest X-ray showed a pneumothorax in the upper right lobe which was measured to be at a distance of approximately 1.5 cm from the lateral, in the level of fourth posterior rib.

The patient was transported to the operation room and a right thorax tube and port catheter were inserted into the right lung and right subclavian vein, respectively. This procedure was performed under general anesthesia within 30 minutes. The patient was transported to the intensive care unit in a conscious, cooperative and hemodynamically stable state. In the intensive care unit, the patient reported that the taste of metallicity gradually decreased. Therefore, 20 mL.h-1 of LE infusion was continued and the patient was observed until the metallic taste disappeared at the end of the sixth hour. There were no problems and complications related to lipid treatment and the patient was discharged from intensive care unit on the second postoperative day. The thorax tube was removed on the fifth day of the follow-up and the patient was discharged on the seventh day.

Discussion

Local anaesthetic infiltration is a widely used method to prevent pain during catheter placement.10 However, toxicity risk exists due to LA in high volume and concentration.1 In the present case report, systemic toxicity developed from lidocaine in high dose and volume. The patient was

successfully treated by immediate initiation of lipid emulsion (20% LE as a 125 mL IV bolus and an infusion of 0.4 mL. kg-1. h-1 for six hours) without cardiac arrest developing. In this patient, a pneumothorax was diagnosed as a complication of port catheter insertion via the central venous route.It is important to routinely perform chest radiography after central venous catheter insertion to exclude such complications.

Initial studies regarding the use of intravenous lipid in case of asystole due to local anesthetic toxicity have started in the 90's as animal studies. In 1998, Weinberg et al. reported treating bupivacaine related cardiac toxicity using lipid emulsion in rats2, after which they repeated the same procedure in dogs in 200311.

Recent case reports have indicated that patients without any responses to standard cardiopulmonary resuscitation in LA-induced cardiac arrest required LEs for treatment. 3,4 The difference of our case from others reported in literature is the observation of sudden toxicity signs upon high dose and volume of lidocaine infiltration without the administration of any regional anesthetic techniques, and the early initiation of lipid emulsion treatment before the development of a cardiac arrest. The similarities and differences of our case from others reported in literature are given in Table 1.

The present case report describes local anesthetic induced toxicity from a single agent, but in the literature there are reports of local anesthetic toxicity due to multipl agents (3,12,13,14).

The effectiveness of LEs in the treatment of ventricular arrhythmia from lidocaine toxicity, as well as bupivacaine and ropivacaine was reported (8,9).

In 2008, Ludot et al (12) have administered a posterior lumbar plexus block using 10 mL of 1% lidocaine with epinephrine and 10 mL of 0.75% ropivacaine to a 13 year old female patient (58 kg) under general anesthesia. Upon the formation of ventricular tachycardia (150/min) with wide QRS complex in the ECG of the patient and a decrease of SpO2 to 92, 15 minutes after the administration of the local anesthetic, a toxicity related to local anesthetics was considered and 150 mL (3 mL. kg-1) of IV 20% lipid solution was administered. Approximately two minutes after the treatment, QRS complex was observed to have returned to normal on the ECG and SpO2 was 97. The authors reported that lipid emulsions were effective in the treatment of ventricular arrhythmia that developed following ropivacaine and lidocaine toxicity.

In the present case, the patient's ventricular tachycar-

Table 1. Lipid solutions and application methods used in the treatment of local anesthetic toxicity.

Year	Researchers	Local anesthetic agen	Anesthesia method	Treatment	
				Lipid Solution	Application method
2006	Rosenblatt et al.[3]	0.5% Bupivacaine + 1.5% Mepivacaine	Interscalene block	20% Intralipid	Bolus:100 mL Infusion: 0.5 mL.kg-1.min-1 (2 hour)
2006	Litz et al. [4]	1% Ropivacaine	Brachial plexus block	20% Intralipid	Bolus:100 mL Infusion: 10 mL .min-1 (10 min)
2007	Foxall et al.[18]	0.5% Levobupivacaine	Lumbar pleksus block	20% Intralipid	Bolus:100 mL
2008	Warren et al.[13]	1.5% Mepivacaine + 0.5% Bupivacaine	Brachial plexus block	20% Liposyn III	Infusion: 250 mL within 30 min
2008	Ludot et al.[12]	1% Lidocaine with epinephrine + 0.75% Ropivacaine	Lumbar pleksus block	20% Medialipid	Infusion:150 mL (3 mL.kg-1)
2008	Litz et al.[14]	1% Mepivacaine + 1% Procaine	Brachial plexus block	20% Intralipid	Bolus: 1 mL.kg-1 Infusion: 0.25 mL.kg-1.min-1 Total dose: 200 mL
2009	Markowitz et al.[19]	0.5% Bupivacaine	Femoral nerve block	%20 Intralipid	8 mL.kg-1 Total dose: 500 mL
2009	Sansino et al.[20]	0.75% Ropivacaine	Brachial plexus block	Kabiven 2000	Bolus: 50 mL
2009	Charbonneau et al.[21]	2% Mepivacaine	Brachial plexus block	20% Medialipide	Bolus:100 mL
2009	Gnaho et al.[22]	0.5% Ropivacaine	Sciatic nerve block	20% Intralipid	Bolus: 70 mL

dia reverted to normal sinus rhythm approximately 6 minutes after the initiation of LE treatment. The patient's HR dropped from 145 to 98 bpm without needing any additional drugs. However, ventricular tachycardia reverted to normal sinus rhythm following the administration of oxygen, midazolam and LE.

Warren et al (13) reported in 2008 that unsuccessful defibrillations were performed 11 times in row in the case with ventricular fibrillation from local anesthetic toxicity. The patient was returned to normal sinus rhythm after LE given in the 15th minute after unsuccessful defibrillations.

We consider that IV bolus dose LE should be administered before cardioversion in cases with disturbances in CVS and associated arhythmia due to local anesthetic toxicity. In patients with local anesthetic toxicity, the success of cardioversion may be low as the toxic dose may be affecting the CVS. We also believe that in patients with local anesthetic toxicity, cardioversion applied without LE treatment is less likely to return arhythmias to normal sinus rhythm.

According to current guidelines, it is clear that lipid solutions play an important role in the treatment of toxicity induced by LA's and are a vital part of resuscitation of cardiac arrest due to LA toxicity (15, 16).

Recent laboratory studies and case reports have indicated that LEs can reduce the morbidity rate from LA toxicity (12,17). However, our case is the first to establish systemic toxicity following local infiltration of only lidocaine, without any other LAs. In the present case, sudden toxicity signs appeared after high dose and volume of lidocaine infiltration, without any central or peripheral block administration. The patient was treated succesfully with early initiation of LE treatment. The patient's GCS was E1M5V1, which became E4M6V5, 6 minutes after starting lipofundin treatment. Her consciousness returned sufficiently to complain about respiratory difficulties, which facilitated diagnosis of pneumothorax. Consequently, lipid treatment both prevented development of cardiac arrest and enabled us to diagnose the pneumothorax.

The present case showed LA toxicity occuring when non-anesthesiology residents performed local anesthesia. In this regard, it is important to inform non-anesthesiology colleagues about the risks and management of LA overdose. All physicians to use LAs should consider their dose, maximum dose, side effects, toxicity symptoms and treatments.

Literature shows differences in loading dose and infusion rate of LEs to treat LA toxicity. However, the common approach is to start the treatment early without a cardiac arrest developing (15). We believe that cardiac arrest was prevented in our case by the immediate administration of 20% LE as an IV bolus and its continuation at a rate of 0.4 mL.kg-1. h-1 until all signs of systemic toxicity disappeared (6 hours). It is also important to attend to patient's symptoms, as we were able to diagnose the pneumothorax after the patient complained of dyspnea.

Finally, lipid treatment should be remembered to be an important part of resuscitation in LA toxicity. Despite varying loading doses and infusion rates, similarities in the success of treatments for local anaesthetic toxicity suggest that a certain amount of IV LE be administered immediately.

It is clear that cases suspected of LA toxicity require urgent LE treatment. Consequently, we believe that the presence of preparatory items for lipid infusion as well as resuscitation materials proves lifesaving in operation rooms, intensive care units and emergency services.

Kaynaklar

1. *Schroeder H. [Temporary bilateral blindness after acute lidocaine toxicity]. Anesth Analg 2002; 95(1): 224-226.*
2. *Weinberg GL, VadeBoncouer T, Ramaraju GA, Garcia-Amaro MF, Cwik MJ. [Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats]. Anesthesiology 1998; 88 (4):1071–1075 .*
3. *Rosenblatt MA, Abel M, Fischer GW, Itzkovich CJ, Eisenkraft JB. [Successful use of a 20% lipid emulsion to resuscitate a patient after a presumed bupivacaine-related cardiac arrest]. Anesthesiology 2006; 105(1):217–218.*
4. *Litz RJ, Popp M, Stehr SN, Koch T. [Successful resuscitation of a patient with ropivacaineinduced asystole after axillary plexus block using lipid infusion]. Anaesthesia 2006; 61(8):800–801.*
5. *Sharma R, Goel N, Kumar A, Panda A. [Central nervous system toxicity with a 1 mL lidocaine injection in the aberrant carotid artery overlying the trachea]. Acta Anaesthesiol Scand 2008;52(10):1436.*
6. *Zausig YA, Zink W, Keil M, Siner B, Barwing J, Wiese CHR et al. [Lipid emulsion improves recovery from bupivacaine-induced cardiac arrest, but not from ropivacaine- or mepivacaine-induced cardiac arrest]. Regional Anesthesia 2009; 109(4):1323–1326.*
7. *Weinberg GL. [Lipid infusion therapy: translation to clinical practice]. Anesth Analg 2008;106 (5):1340–1342.*
8. *Weinberg GL, Di Gregorio G, Ripper R, Kelly K, Massad M, Edelman L et al. [Resuscitation with lipid versus epinephrine in a rat model of bupivacaine overdose]. Anesthesiology 2008;108 (5):907–913.*
9. *Satsumae T, Tanaka M, Saito S, Inomata S. [Convulsions after ropivacaine 300 mg for brachial plexus block]. Br J Anaesth 2008;101(6):860-862.*
10. *Özyuvacı E, Kutlu F. [Totally implantable venous access devices via subclavian vein: a retrospective study of 368 oncology patients]. Adv Ther 2006; 23(4):574-581.*
11. *Weinberg G, Ripper R, Feinstein DL, Hoffman W. [Lipid emulsion infusion rescues dogs from bupivacaine-induced cardiac toxicity]. Reg Anesth Pain Med 2003, 28(3):198-202.*

12. *Ludot H, Tharin JY, Belouadah M, Mazoit JX, Malinovsky JM. [Successful resuscitation after ropivacaine and lidocaine-induced ventricular arrhythmia following posterior lumbar plexus block in a child]. Anesth Analg 2008;106(5):1572-1574.*
13. *Warren J, Thoma RB, Georgescu A, Saurin S. [Intravenous lipid infusion in the successful resuscitation of local anesthetic-induced cardiovascular collapse after supraclavicular brachial plexus block]. Anesth Analg. 2008; 106(5):1578–1580.*
14. *Litz RJ, Roessel T, Heller AR, Stehr SN. [Reversal of central nervous system and cardiac toxicity afterlocal anesthetic intoxication by lipid emulsion injection]. Anesth Analg 2008; 106(5):1575-1577.*
15. *Picard J, Ward SC, Zumpe R, Meek T, Barlow J, Harrop-Griffiths W. [Guidelines and the adoption of 'lipid rescue' therapy for local anaesthetic toxicity]. Anaesthesia. 2009; 64(2):122-125.*
16. *Neal JM, Bernards CM, Butterworth JF 4th, Di Gregorio G, Drasner K, Hejtmanek MR et al. [ASRA practice advisory on local anesthetic systemic toxicity]. Reg Anesth Pain Med. 2010; 35(2):152-161.*
17. *Leskiw U, Weinberg GL. [Lipid resuscitation for local anesthetic toxicity: is it really lifesaving?]. Curr Opin Anaesthesiol. 2009; 22(5): 667-671.*
18. *Foxall G, McCahon R, Lamb J, Hardman JG, Bedforth NM. [Levobupivacaine-induced seizures and cardiovascular collapse treated with Intralipid]. Anaesthesia 2007; 62(5): 516-518.*
19. *Markowitz S, Neal JM. [Immediate lipid emulsion therapy in the successful treatment of bupivacaine systemic toxicity]. Reg Anesth Pain Med 2009; 34(3):276.*
20. *Sonsino DH, Fischler M. [Immediate intravenous lipid infusion in the successful resuscitation of ropivacaine-induced cardiac arrest after infraclavicular brachial plexus block]. Reg Anesth Pain Med 2009;34(3):276-277.*
21. *Charbonneau H, Marcou TA, Mazoit JX, Zetlaoui PJ, Benhamou D. [Early use of lipid emulsion to treat incipient mepivacaine intoxication]. Reg Anesth Pain Med 2009; 34(3):277-278.*
22. *Gnaho A, Eyrieux S, Gentili M. [Cardiac arrest during an ultrasound-guided sciatic nerve block combined with nerve stimulation]. Reg Anesth Pain Med 2009; 34(3):278.*