Lipid Therapy for Central Nervous System Symptoms of Prilocaine Toxicity

Prilokain Toksisitesine Bağlı Santral Sinir Sistemi Semptomlarında Lipid Tedavisi

Prilokain Toksisitesinde Lipid Tedavisi / Lipid Treatment for Prilocaine Toxicity

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Özet

Lokal anestezikler; çok sayıda cerrahi işlemin gerçekleştirilmesinde anestezi ve analjezi sağlamak amacıyla sık olarak kullanılmaktadır. Anestezistlere ek olarak cerrahlar tarafından da lokal anesteziklerle bir çok minör cerrahi girişim ameliyathane dışında monitorizasyon ve resüsitasyon olanaklarının yetersiz olduğu koşullarda gerçekleştirilmektedir. Lokal anesteziklerin basit lokalize reaksiyonlara ek olarak, erken veya geç sistemik toksisiteden kardiyovasküler kollapsa kadar uzayabilen ciddi yan etkiler oluşturabileceği bilinmektedir. Lipid emülsiyonları bupivakain gibi lipofilik lokal anesteziklerin neden olduğu sistemik lokal anestezik toksisitesinin tedavisinde sık olarak kullanılmaktadır. Bu yazıda devam eden operasyon ağrısı nedeniyle insizyon bölgesine yüksek doz prilokain infiltrasyonu uygulanan bir hastada gelişen sistemik lokal anestezik toksisitesinin erken tanısı ve intravenöz lipid emülsiyonu ile hızlı ve başarılı tedavisini sunuyoruz.

Anahtar Kelimeler

Sistemik Lokal Anestezik Toksisitesi; Prilokain; Lipid Emülsiyonu

Abstract

Local anesthetics are frequently used to induce anesthesia and analgesia during a wide range of surgical procedures. In addition to anesthesiologists, surgeons also use local anesthetics to perform a large number of minor surgical interventions outside the operation rooms, where monitoring and resuscitation resources are limited. In addition to simple localized reactions, local anesthetics are known to cause serious side effects ranging from early or late systemic toxicity to cardiovascular collapse. Lipid emulsions are commonly used to treat systemic local anesthetic toxicity caused by lipophilic local anesthetics, such as bupivacaine. In this manuscript, we present the early diagnosis of local anesthetic toxicity and its rapid, successful treatment with intravenous lipid emulsion in a patient whom was administered high dose of prilocaine to the incision site due to persistent surgical pain.

Keywords

Systemic Local Anesthetic Toxicity; Prilocaine; Lipid Emulsion

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Introduction

Local anesthetics are frequently used for induction of anesthesia and analgesia in a wide range of surgical interventions. The environment outside the operating room may not always be adequate for such procedures. In addition to simple local reactions, local anesthetics may also cause severe side effects including early and late systemic toxicity or cardiovascular collapse.

Local anesthetic systemic toxicity (LAST) is a serious clinical condition with considerable morbidity and mortality, which may threaten cardiovascular system (CVS) and central nervous system (CNS)[1]. The severity of LAST is determined by personal risk factors, the block technique, the application site, and total local anesthetic dose.

Recent studies reporting successful treatment of LAST with intravenous (IV) lipid emulsions have heralded a new treatment option[2]. IV lipid emulsions were first recommended for treatment of cardiotoxicity associated with local anesthetic toxicity of high lipid soluble agents, which is unresponsive to standard resuscitative techniques. However, it has been recently recommended to use them upon recognition of early signs of potential local anesthetic toxicity and prolonged CNS symptoms.[3] In this case report, we aimed to discuss for the first time in the literature, successful lipid emulsion therapy in a systemic toxicity of prilocaine that has low lipid solubility in which signs of CNS toxicity predominated while signs of cardiac toxicity just began to emerge.

Case Report

A 23-year-old, 58 kg woman, presented to our general surgery clinic with ongoing pain in the incisional site after an inguinal hernia operation performed 6 months ago. Physical examination revealed refractory pain in the right lower quadrant, for which the general surgeon applied 700 mg of prilocaine (Citanest® 2% vial, AstraZeneca, Istanbul-Turkey) to the incision site. Thirty minutes later, the patient developed restlessness, numbness in tongue and scalp, and tinnitus. Following the anesthesiology consultation, she was taken to the postoperative care unit. In the initial examination, she was able to respond to verbal stimuli and cooperate; however, she had muscle weakness and speech disturbance. 100% oxygen was applied via a face mask at a rate of 5 lt/min. During physical examination; it was noticed that her responses to verbal stimuli gradually faded away, her speech became incomprehensible, and she became confused. Two peripheral lines (16 and 18 Gauge) were established and 0.9% NaCl was begun. The patient was rapidly monitored (ECG, SpO2, and non-invasive blood pressure) and necessary preparations were made for cardiopulmonary resuscitation. Meanwhile, she had a blood pressure of 155/90 mmHg, pulse rate of 122 bpm, and oxygen saturation of 97%. Her clinical condition was consistent with LAST. A treatment plan including a rapid application of lipid emulsion was made to prevent deterioration of the patient's status. Initially, she had a normal sinus rhythm on ECG whereas she later developed sinus bradycardia and frequent ventricular extrasystoles. While 0.9% NaCl infusion was continued from a peripheral line, 100 ml lipid emulsion (Intralipid 20% ® 250 ml solution, Fresenius Kabi, Istanbul-Turkey) was administered as a bolus injection via other peripheral line (16G) within 1 minute. Her clinical condition began to improve and she regained consciousness 3 minutes after the bolus dose. She was administered an additional 150 ml of lipid emulsion via an infusion pump in 10 minutes. IV furosemide, 2 mg/kg (Lasix® 20 mg/2 ml ampoule, Sanofi Aventis, Istanbul-Turkey) and a total of 2000 ml 0.9% NaCl were infused. Furosemide was administered due to rapid, bolus injection of the lipid emulsion and 0.9 % NaCl that can cause cardiac failure. Lipid infusion was stopped after hemodynamic stabilization was achieved. No side effects of lipid emulsion, such as allergic reaction or phlebitis were observed.

The patient recovered clinically and was monitored at the postoperative care unit. She was then sent to the intensive care unit with stable vital signs. Her intensive care stay was uneventful and she was transferred to inpatient ward next day. She was discharged with complete cure and called for a follow-up visit 1 week later. No side effects related to lipid therapy were noticed at that time.

Discussion

Local anesthetics are widely used both in and out of operation room. Although rare, some side effects during the use of local anesthetics may be observed. While mild symptoms do not cause major morbidity, LAST characterized by CNS and CVS symptoms is a serious condition that may have a lethal course if it is left untreated. While this complication may occur with intravascular injection, it may also be encountered as a result of rapid absorption from a highly vascularized site or with use of higher doses of local anesthetics[3]. It has been considered that high blood levels of local anesthetics lead to an impaired cellular activity as a result of disrupted sodium, potassium, and calcium channels as well as impaired fatty acid transfer and enzymatic activity necessary for adenosine triphosphate production in mitochondria of brain, heart, and skeletal muscle cells[4]. In the treatment of LAST, the priority should be given to establish the airway patency, ventilation and circulation[3]. It is currently possible to mention that IV lipid emulsion therapy among primary treatment steps in addition to symptomatic therapies directed at CNS and CVS symptoms for LAST. Currently, American Society of Regional Anesthesia (ASRA) and the Association of Anesthetists of Great Britain and Ireland recommend lipid emulsion as the first line therapy in management of LAST[1]. Based on this information, the proposed treatment model for LAST includes; establishment of airway patency, control of ventilation, support of circulation, and IV infusion of lipid emulsion as soon as possible. In our case, the decision to continue treatment with lipid emulsion was rapidly made at a time, when CNS signs predominated and the signs of cardiac toxicity just began to emerge. We believe that timely diagnosis and rapid intervention were the components of life-saving therapy in our case.

ASRA recommends 1.5 ml/kg bolus dose of 20% lipid emulsion as the initial treatment after the first signs and symptoms of LAST appears. It is also recommended that the bolus dose should be given over approximately 1 minute, followed by infusion (0.25 ml/kg/min) for 10 minutes; the bolus dose should be repeated and the infusion rate doubled (0.5ml/kg/min) if no clinical improvement becomes evident[3]. First the neurological signs of our case improved following a bolus dose of approxi-

mately 100 ml (1.5 ml/kg), followed by achievement of hemodynamic stability with infusion of 150 ml lipid emulsion at a rate of 0.25 ml/kg/min for 10 minutes. No additional doses were required.

Despite it is not very clear how the lipid therapy exerts its effects in the management of LAST, it has been believed that it confines circulating local anesthetics by forming a lipid phase in plasma and reduces their plasma and tissue levels by precipitating them in the emulsion. This is called as "lipid sink theory" and has been supported by many clinical studies[1]. It is also considered that intravenous lipid emulsion increases intracellular myocardial fatty acid content, enhances mitochondrial fatty acid metabolism and adenosine triphosphate depots, and exerts a direct inotropic effect by raising the intracellular calcium concentration of myocardial cells[5].

The most common side effect of lipid therapy is thrombophlebitis due to venous irritation. Thus, the intravenous line should rather be placed in a large vein. We therefore employed the emulsion via a peripheral route of 16 Gauge intravenous line established in the antecubital veins. Less commonly, allergic reactions, dyspnea, cyanosis, nausea, vomiting, chest pain, diaphoresis, and hypercoagulability may occur. Hepatomegaly, jaundice due to cholestasis, splenomegaly, thrombocytopenia, transient rise in liver enzymes, and pancreatitis may also rarely develop as late side effects. In fact, we did not expect any late side effects due to small and safe dose of lipid emulsion. As the maximum dose, ASRA recommends 10 ml/kg of 20% lipid emulsion [3]. Although we administered approximately 4.3 ml/kg as the total dose, 1 week later blood was drawn to measure, serum triglycerides, amylase, urea, creatinine, alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), serum phosphorus levels. All laboratory values were within normal limits. Also there were no signs of thrombophlebitis on physical examination. So that we did not observe any early or late side effect associated with lipid therapy in our case. Because that we did not meet any advice of more than one week follow in the literature, late investigations were not needed.

Lipid solubility is the primary determinant of anesthetic potential and is expressed as lipid/water partition coefficient. Studies and case reports with lipid therapy included agents with high lipid solubility and potency, such as bupivacaine, ropivacaine, and levobupivacaine whereas case reports with agents having low lipid solubility, such as mepivacaine, lidocaine, and prilocaine are sparse[6,7]. However, recent clinical approach has favored use of lipid emulsion even in the treatment of toxicity due to less lipophilic local anesthetics[1,8]. Prilocaine is a moderately lipophilic local anesthetic agent. This property of prilocaine is similar to lidocaine but it is less lipophilic than bupivacaine. In this case we employed IV lipid emulsion for the first time after high dose prilocaine infiltration. By this way, we successfully treated signs of CVS and CNS toxicities and prevented a potential cardiovascular collapse with timely diagnosis and rapid treatment after sole prilocaine injection.

Local anesthetics are used not only by anesthesiologists, but also frequently by surgical teams outside of operating rooms for a number of minor surgical procedures. Therefore, resuscitation medications and equipment including also lipid emulsions should be readily available in medical settings where local anesthetics are administered.

In conclusion, we suggest to take necessary measures against emergency complications in medical settings where local anesthetics are used, and to use lipid emulsions as the first-line treatment of toxicity associated not only with local anesthetics with high lipid solubility, but also those having low lipid solubility, including prilocaine.

Competing interests

The authors declare that they have no competing interests.

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