Lipid Emulsion Therapy for Verapamil Intoxication—A Case Report

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Abstract

Intravenous lipid emulsion therapy is the administration of a lipid emulsion as a new method for treatment of toxicity from excessive dose of certain medications including local anesthetics, beta-blockers, calcium channel blockers, and tricyclic antidepressant drugs. This article describes successful treatment of a patient of verapamil overdosage with lipid emulsion treatment.

Keywords
- emulsion
- intoxication
- lipid
- overdose
- verapamil

Introduction

Intravenous fat emulsions are a main component of nutrition, which help to prevent essential fatty acid deficiency and are also used as an alternate energy source to dextrose, avoiding the complications of excessive dextrose administration.[1] Intravenous lipid emulsion therapy (IVLET) is a 205 free fatty acid mixture used to deliver parenteral calories to patients unable to take oral nutrition. IVLET is the administration of a lipid emulsion to reduce the clinical administration of toxicity from excessive dose of certain medications including local anesthetics, beta-blockers, calcium channel blockers (CCBs), and tricyclic antidepressant drugs.[1] Several animal studies have shown efficacy of IVLET in the treatment of severe cardiotoxicity associated with lipophilic drugs in an expanded plasma lipid compartment.

Overdose is uncommon but frequently lethal. The drug is naturally eliminated, while all these interventions support the body simultaneously, rather than directly neutralizing the circulating drug. On the other hand, lipid infusions are supposed to sequester lipophilic drugs like verapamil, therefore, directly lowering their bioavailability in the body.[2] It has been a true bench-to-bedside story, emerging from the theory of sequestering lipophilic drugs to successful animal trials and human case reports. Focus is now moving to the use of lipid emulsions as successful antidotes for the lipophilic drugs, such as verapamil, beta-channel blockers, and tricyclic antidepressants.

The American College of Medical Toxicology has recommended the use of IVLET for poisoned patients with hemodynamic or other instability who are not responding to standard resuscitation measures.

Various adverse effects of standard IVLET include hypertriglyceridemia, fat embolism, infection, local vein irritation, acute pancreatitis, electrolyte disturbances, hypersensitivity and allergic reactions. These adverse reactions are uncommon despite widespread use of IVLET.

Resuscitation through IVLET is an effective treatment modality for toxicity that is induced by lipophilic

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medications and may be useful in treating systemic toxicity for all ages and almost all clinical scenarios, including pregnant patients. The "lipid sink" phenomenon is the most commonly accepted mechanism of action for IVLET, which includes surrounding a lipophilic drug molecule and making it ineffective.[3,4]

Calcium Channel Bolockers (CCB's) directly prevent voltage-gated L-type calcium channel opening and calcium influx into myocardial and vascular smooth muscle cells.

Most of these serious cases and deaths result from the intake of nondihydropyridine CCB. The treatment of suspected cardiogenic shock in beta-blocker and CCB poisoning involves similar principles. Expedient and aggressive administration of charcoal and whole bowel irrigation must be instituted to avoid systemic absorption after a substantial verapamil and diltiazem overdose.

Intoxication usually starts at 1 to 5 hours after intake of the drug, while it might be up to 48 to 72 hours in slow-releasing formulations. In verapamil intoxication, cardiovascular, gastrointestinal, central nervous system-related and metabolic effects can be seen.

Case Report

A 27-year-old female, with a chief complaint of pain on the left side of chest, 7 to 8/10 intensity, burning in nature, with no radiation, presented to the emergency room, shortly after taking 90 tablets of verapamil, few Xanax, and Phenergan. She had a past history of hypertension, bipolar disorder, and heroin abuse. She denied usage of alcohol, drug, or smoking. She had a family history of bipolar disorder. On physical examination, vitals were blood pressure = 96/77, respiratory rate = 23, Oxygen Saturation =99% (on mechanical ventillator). Patient was feeling drowsy but responded to verbal stimuli.

Patient was very anxious earlier and later started to become unresponsive. Neck examination showed no jugular vein distention, no lymphadenopathy (LAP), and no carotid bruit, on auscultation, bilateral crackles were present. Cardiovascular system (CVS) was found to be normal. Abdomen was soft, non distended (ND) and bowel sounds well present (BS+). Central nervous system signs showed drowsiness and positive response to verbal stimuli. The extremities showed palpable peripheral pulses. Electrocardiogram was advised (►**Fig. 1**). All laboratory investigations except troponin levels were within normal range (0.16–1.78–2.22). Investigation of arterial blood gases (ABG) was found to be 7.33/78/94.7%/38/19.4. Patient was diagnosed with drug overdose (Verapamil/Xanax/Phenergan), non-ST-elevation myocardial infarction and respiratory failure.

Routine management was done for the patient including the use of calcium chloride and glucagon. Airway, breathing, circulation were maintained through mechanical ventilation or intubation. Dopamine drip was given and fluids were restricted following IV lipids, glucagon, and calcium chloride. Heparin protocol, ASA, Plavix, and later catheterization were done for the patient.

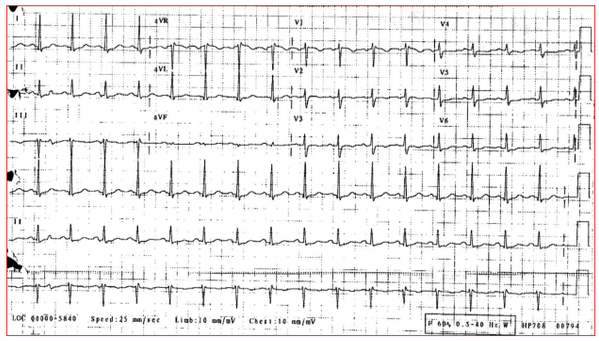

Fig. 1 Electrocardiogram. 7.33/78/94.7%/38/19.4.

The next morning, patient was put off the ventilator that she tolerated well. Her vitals were stable, and chest radiograph looked better than the previous one that showed pulmonary edema. The patient was kept in intensive care unit for 2 days and then was transferred to psychiatry ward for 1 week and was discharged in stable condition.

Discussion

Verapamil, a lipophilic CCB, reduces level of systolic calcium by inhibiting voltage-dependent L-type calcium channels found in the smooth muscles of the myocardium and veins, thus reducing entry of calcium into these cells. Verapamil has the most potent negative ionotropic effects among CCBs. CCBs have four main cardiovascular effects including peripheral vasodilation, negative chronotropy (decreased heart rate), negative inotropy (decreased cardiac contractility), and negative dromotropy (decreased cardiac contraction). Other physiologic responses include suppression of insulin release from the pancreas, decreased free fatty acid utilization by the myocardium and hyperglycemia and lactic acidosis. Most commonly CVS is affected leading to bradycardia, hypotension, and, in fatal cases, cardiac arrest. It may also cause hyperglycemia and altered mental status.

Cardiotoxic effects of verapamil overdose may cause more deaths than all other CCBs. In 2006, the AAPC reported 10,031 exposures to CCBs, resulting in 13 deaths and 316 major outcomes.[5]

Fat emulsion therapy has recently gained vast popularity as an antidote for local anesthetic drug toxicity, emerging from the theory of sequestering lipophilic drugs to successful animal and then human trials. Nowadays, lipid emulsion is successfully used as antidotes for drugs such as verapamil, beta-blockers, and tricyclic antidepressants. Fat emulsion therapy has been successfully used in the treatment of verapamil overdose in various bovine studies done by different authors. Furthermore, human trials have also proven to be successful in this regard.

Drugs like verapamil, bupivacaine, and local anesthetics are lipophilic drugs; therefore, giving IV lipids causes the drugs to bind to lipids and thus decrease the concentration in

free plasma, hence reduces the side effects, mainly cardiac toxicity. The recommended dosage is 20% IV lipid emulsion (1.5 mL/kg bolus dose—maximum 3 and 0.25 mL/kg for 30–60 minutes).[6]

Conclusion

Intravenous lipid therapy is a feasible and effective therapy for enormous CCB overdose, and should be considered early in patients who present with hemodynamic compromise. This case report presents a new method of treatment effectively to generate awareness among all about IV lipids and their role in overdose treatments.

Conflict of Interest
None declared.

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