Review of Local Anaesthetic Systemic Toxicity for Physicians and Surgeons in the Ambulatory Care Setting

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Abstract

Upon review of the literature, we found it to be concerning that there was minimal literature regarding the resuscitation from local anesthetic systemic toxicity in an ambulatory care setting. On a daily basis surgeons and physicians (MD, DO, DPM, DDS, DMD) administer local anesthetic and should be aware of the checklists and steps to resuscitate a patient that may have toxicity. There have been major developments with administrating 20% lipid emulsion to reverse the toxicity one may have from local anesthetics. It is strongly recommended that physicians be BCLS and ACLS certified, perform a good physical diagnosis, and have lipid emulsion therapy readily available in every clinical/hospital/ambulatory surgical setting. In this journal review article, we have provided checklists/steps to follow in case a patient has signs and symptoms of local anesthetic systemic toxicity. The majority of local anesthetic toxicities do occur with upper extremity and neuraxial blockade however there is still a reduced risk of lower extremity local anesthetic systematic toxicity.

Key words: Local Anesthetics, Lipid Emulsion, LASTH.

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We found there to be minimal information regarding resuscitation from local anesthetic systemic toxicity (LAST). We found this to be concerning in the situation of a physician and/or surgeon (MD, DO, DPM, DDS, DMD) knowing how to quickly resuscitate a patient. Approximately 83% of procedures performed in-office/hospital/ambulatory surgical center (ASC) requires local anesthetic and the remaining 17% of procedures require general anesthesia. According to the American Society of Regional Anesthesia (ASRA), there is a checklist that is helpful to us and is useful during times of stress when a patient unexpectedly shows signs of severe local anesthetic toxicity. Overdose of intravascular injection of local anesthetics is associated with cardiac toxicity according to the Anesthesia Patient Safety Foundation (APSF). Primary systemic toxicity usually occurs in the central nervous system (CNS), which will initially cause tremors/convulsions. The cardiac toxicity is characterized by atrioventricular conduction delay, hypotension, with ultimately cardiovascular failure. There have been major developments in understanding treatments for LAST including early administration of lipid emulsion therapy. All physicians and medical professionals should be familiar with signs and treatment of local anesthetic toxicity.

The typical adverse effects due to local anesthetic systemic toxicity most often involves the central nervous system, cardiovascular system (CVS), and haematological system (5). Indicators of LAST usually show around 1 to 5 minutes after anesthetic injection. There may be a delayed manifestations of last which may appear 60 minutes after injection. In Table 1, according to the article based off Local Anesthetic Systemic Toxicity there is a list of signs and symptoms that associate with the systems being affected (3). Below in Table 1, The Regional Anesthesia Pain Medicine journal states the initial presentation of CVS symptoms only is about 24%, CNS symptoms only is 43%, and CNS + CVS together is 33%.

Onset of local anesthetic toxicity is very rapid and potentially fatal, which is most commonly associated with the administration of therapeutic error. There are several types of factors that are associated with administration and the type of drug being used. To achieve the anticipated duration and range of anesthesia, the local anesthetic should be given at the lowest dose that can achieve these two goals. The serum concentration is induced by the dose, method of administration and the site. Local anesthetics may be injected, inhaled, administrated endotracheal tube, or applied topically to skin. The two critical factors for the administration for local anesthetic that should be known is the patient's weight and the concentration of the local anesthetic that is being administered. Table 2 is a reference for the maximum recommended dosages with and without epinephrine for local anesthetic administration (3).

Most adverse effects usually occur within 1 minute of administration of the local anesthetic. However, there can be a delayed onset of greater than 1 hour after the administration of the local anesthetic demonstrating toxicity. Some situations there can be a delayed onset greater than 1 hour. Another variable that can increase the chances

Table 1 Manifestations of the CNS, CVS, and Hematologic systems due to Local Anesthetic Systemic Toxicity.

Central Nervous System (CNS)	Cardiovascular (CVS)	Haematological
• Disorientation	• Chest pain	• Cyanosis
• Drowsiness	• Diaphoresis	• Tachypnea
• Metallic taste	• Shortness of breath	• Dizziness and syncope
• Convulsions	• Palpitations	• Weakness
• Muscle twitching	• Bradycardia	• Fatigue
• Coma	• AV Block	
• Respiratory depression and arrest	• Hypotension	
• Agitation	• Cardiac arrest	
	• Tachyarrhythmias	

Table 2 Suggested recommendations for commonly used local anesthetic agents.

Local anesthetic	Plain		With epinephrine	
	Maximum dose	Maximum dose	Maximum dose	Maximum dose
Bupivacaine	2 mg-kg^{-1}	175 mg	3 mg-kg^{-1}	225 mg
Levobupivacaine	2 mg-kg^{-1}	200 mg	3 mg-kg^{-1}	225 mg
Lidocaine		350 mg	7 mg-kg^{-1}	500 mg
Mepivacaine	5 mg-kg^{-1}	350 mg	7 mg-kg^{-1}	500 mg
Ropivacaine	3 mg-kg^{-1}	200 mg	3 mg-kg^{-1}	250 mg
Prilocaine	6 mg-kg^{-1}	400 mg	8 mg-kg^{-1}	600 mg

of LAST is dependent on which local anesthetic is used. The more lipophilic of the local anesthetic, the increased chances of toxicity. According to the choices of drugs in Table 3, for example, bupivacaine is more lipid soluble than mepivacaine. The dosage of administration is substantially less due to it being more potent, which can result in an amplified occurrence of local toxicity. Lastly, according to the American Heart Association (AHA), epinephrine is typically added to low doses of local anesthetic solution to reduce the systemic absorption and maximum local anesthetic plasma concentrations.

Table 3 Relative Potencies of Local Anesthetics .

Agent	Relative Clinical Potency
Procaine	Low
Lidocaine	Moderate
Mepivacaine	Moderate
Levobupivacaine	High
Bupivacaine	High
Ropivacaine	High

Most anesthetics are administered through peripheral nerve blocks, spinal/neuroaxial anesthesia, and combined spinal epidural (CSE). Peripheral nerve blocks are the most common route of administration of local anesthetics in a clinical setting. Physicians are urged to be equipped and prepared for LAST treatment. Advanced cardiac life support and administration of 20% lipid emulsion are the mainstay treatment remedies for LAST. According to intravenous lipid emulsion in clinical toxicology journal, they state that 20% Intralipid formula consists of 20% soybean oil, 1.2% egg yolk phospholipids, 2.25% glycerin, water, and sodium hydroxide (1). For example, Henry Schein, sells a case of 12 of 20% Lipid Emulsion 500mL for the price of $222.17. The shelf life for lipid emulsion is 24 months. This treatment choice is recommended for physicians to have readily available for emergency use in clinical setting. The 20% lipid emulsion offered by Henry Schein is less expensive than paying attorney fees for a malpractice claim. The American Society of Regional Anesthesia (ASRA), Figure 1, (near here) has developed a procedure checklist to be followed for the stabilization of a patient undergoing local anesthetic systemic toxicity (6).

There are multiple theories describing how local anesthetic systemic toxicity affect the body, but one major affect is the mitochondrial oxidative-phosphorylation pathway. Essentially the local anesthetic toxicity disables cells from regenerating ATP for energy. Without the energy production of ATP for major organs such as the heart, lungs, and brain, normal conduction is disrupted & then we see the symptoms of LAST-induced arrest. This is when one would administer the 20% lipid emulsion which has a mechanism of action by a protein type lipid mechanism that acts like a sink that draws in local anesthetic and binds it up. Local anesthetics for example, bupivacaine, are very lipophilic meaning they are able to dissolve or combine with lipids and/or fats. When a patient undergoes toxicity, the lipid emulsion is administered which begins to make a lipid compartment in the blood stream called a "lipid sink" or lipid reservoir (1). The local anesthetics are then drawn away from areas with high plasma concentrations/ high perfusion tissues such as the heart, lungs, and brain to the lipid reservoir compartment. Once the local anesthetic is drawn to the lipid reservoir, it is then reallocated to liver for detoxification and muscle for storage (4). The lipid compartment works rapidly and has been indicated to improve the cardiac output and blood pressure.

The Anesthesia Patient Safety Foundation (APSF) and the AHA suggest the use of cardiac arrest drugs such as high-dose epinephrine can be counterproductive in treatment of LAST (6). Therefore, the AHA and APSF recommends using the lowest dose of epinephrine in local anesthetic solution, because epinephrine could be used later in higher doses if one were to have LAST reaction (2). After the patient is successfully resuscitated and stabilized from local anesthetic toxicity, the patient should be admitted to the intensive care setting for 24 hours of monitoring and re-evaluated. Cardiology, Nephrology, and Neurology and other medical specialties as needed should be consulted to check so there are no residual cardiac, renal, or neurological dysfunctions, etc.

The best prevention and treatment for local anesthetic toxicity on the market currently today is the immediate availability of 20% of lipid for immediate resuscitation of local anesthetic toxicity (5). These resources are efficient and readily available to every physician. It is strongly recommended for physicians to be BCLS and ACLS certified per facility requirements. BCLS and ACLS trained physician along with readily available 20% lipid emulsion and the low dose administration of the less potent local anesthetics all combined to provide a reasonable margin of safety for the patient (6).

Physicians are urged to perform a good physical diagnosis and patient selection for surgical procedures involving local anesthetics. Physicians and surgeons should be intimately aware that they are treating the whole patient systemically and not just the surgical site. Physicians and surgeons are urged to be aware of local anesthetic toxicity and the treatment modality for the local anesthetic toxicity.

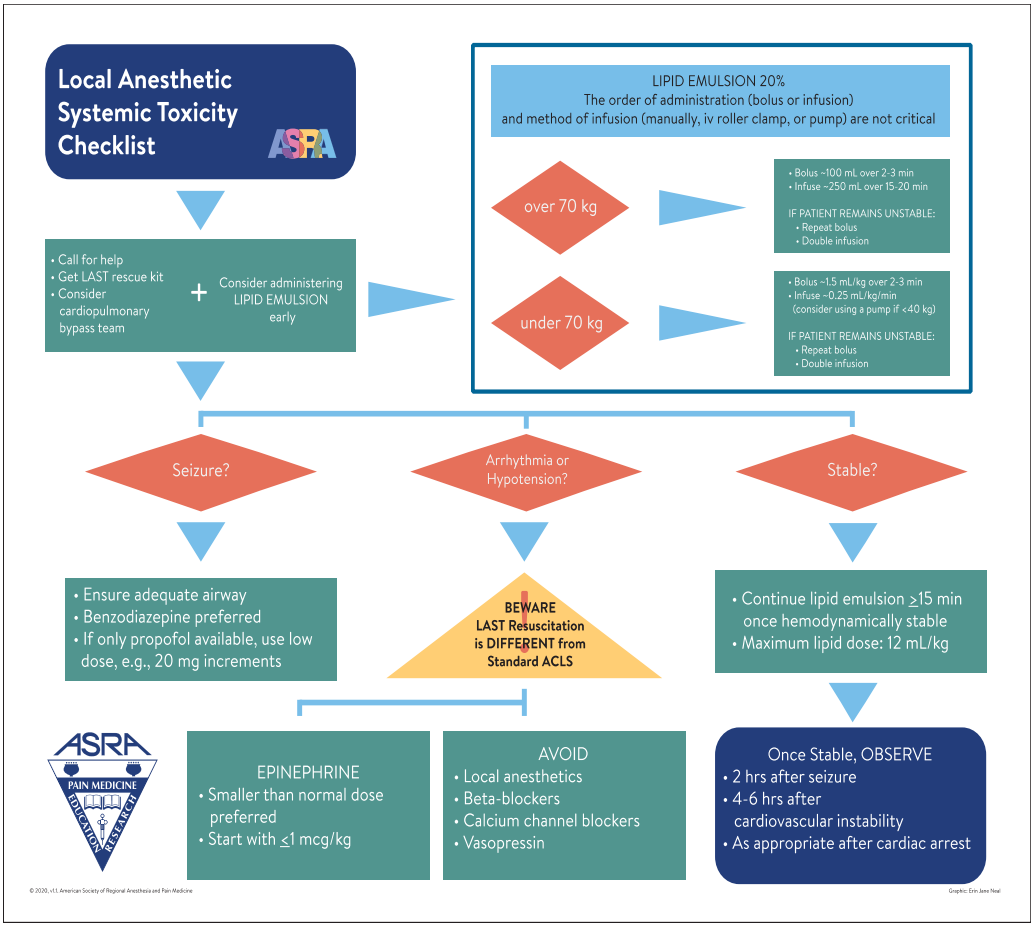

Figure 1 Step by step checklist to treat local anesthetic systemic toxicity.

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