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Chapter

Local Anesthetic Systemic Toxicity

Divya Garg, Shikha Soni and Rakesh Karnawat

Abstract

Local anesthetics are used very often in medicine and dentistry. They have few adverse effects, but the increased use of these drugs has resulted in a higher incidence of local and systemic anesthetic toxicity (LAST). From the initial symptoms to the deleterious effects on cardiac and the central nervous system, LAST is an important consequence of which we should be aware. LAST is known since the introduction and use of local anesthetics; it was originally associated with seizures and respiratory failure. However, in the 1970s, side effects on the heart were also identified, as the fatal cardiac toxicity associated with bupivacaine was discovered in healthy patients. Prevention and safe administration of regional anesthesia remains primary factors in the avoidance of the toxicity of these drugs. When a patient has LAST, treatment should be started immediately to reduce seizures. If there is cardiac arrest, follow ACLS guidelines. Intravenous lipids improve cardiac conduction, contractility and coronary perfusion by removing liposoluble local anesthetic from cardiac tissue.

Keywords: local anesthetic, toxicity, mechanism of action, prevention, management, lipid emulsion

1. Introduction

Systemic toxicity due to local anesthetics (LAST) is a nightmare for each anesthesiologist. It can have catastrophic outcome in an otherwise simple procedure, such as a regional dental anesthesia, local anesthesia, nerve block either peripheral, intravenous or peridural. The clinical phenomenon of LAST has been known for more than 100 years. Historically, the introduction of cocaine as the first local anesthetic (LA) in late nineteenth century was soon accompanied by reports of its systemic toxicity. The symptoms of systemic toxicity were frequently described as seizures or respiratory failure, but some cases also included reports of adverse cardiac effects [1]. These reasons demanded medical and pharmaceutical industries to search for new less toxic LA.

At first, manipulation of existing molecular structures after analyzing natural products lead to development of few drugs. It became clear that the development of more LA of ester group did not return the desired results. The main concern was short duration of action due to instability of ester bonds. The drugs were prepared in an oily formulation to increase the duration (which proved neurotoxic locally, or by enhancing the lipophilicity of the molecule which made it more toxic to central nervous system (CNS) as well as cardiovascular system (CVS)). Lidocaine, synthesized in 1944 was the first amide LA drug to be used clinically. It gave a dependable block, but unfortunately was short acting. In search of an LA with a longer duration of action than lidocaine, a family of N-alkylpiperidines 2,6 xylidides was introduced

in 1950s. It was shown that increasing N-alkyl carbon chain length (to max at C4 or C5) increased lipophilicity, which increases duration of action, but unfortunately also increased systemic toxicity. Derivatives developed for clinical use included mepivacaine, bupivacaine, ropivacaine, levobupivacaine, etc. But in subsequent year's cases of lethal LAST were documented.

Accidental intravascular injection during regional anesthesia is the most common cause of LAST. Some comorbidities may increase the risk of LAST; liver failure, heart disease, pregnancy and metabolic syndromes. In addition, patients at extreme ages have an increased risk factor of toxicity, due to the reduction in anesthetic clearance. Children under 4 months of age have low plasma concentrations of acid glycoprotein, which may result in a lower intrinsic clearance of bupivacaine [2, 3].

The incidence of LAST is extremely variable from zero events after more than 12,000 nerve blocks to 25 per 10,000 nerve blocks. One study reported seizures in 79 of 10,000 brachial plexus block procedures. This complication was due to toxicity of the CNS as a result of intravascular LA injection. Although the published data are inconsistent, the prevailing goal is to prevent LAST, and when it manifests, it must be treated quickly and effectively [4–6].

Cardiac toxicity is the most important component of LAST since, unlike the CNS toxicity, it can end in cardiac arrest and death. It is often due to an intravascular injection not noticed during nerve block. LA bind and inhibit voltage dependent sodium channels. It leads to conduction disorders, contractile dysfunction and ventricular arrhythmias. The incidence of cardiac toxicity increases with bupivacaine due to its affinity for inactive sodium channels during the cardiac action potential at a concentration of 0.2 μg/mL. This is done in a fast/slow manner, which means that bupivacaine binds very rapidly to a large proportion of sodium channels during the potential for cardiac action, but is slowly released from the channels during diastole, which results in a large proportion of medication that accumulates at 60–150 beats per minute. Lidocaine at 5–10 μg/mL will also result in a substantial blockage of sodium channels during a potential for cardiac action. However, in contrast to bupivacaine, lidocaine follows the principle of rapid entry/exit, which means that it is rapidly released from sodium channels during diastole. This allows faster recovery and a lower incidence of cardiac toxicity compared to bupivacaine.

CNS toxicity is another important consequence of LAST. Although it is composed of many initial prodromal features, it is most often manifested as seizures. A mechanistic theory focuses on acid-sensitive K^+ channels. These pH-sensitive channels generate neuronal currents of leakage of potassium. LA inhibition causes membrane depolarization and increased neuronal excitability. As these channels are expressed throughout the brain, this is the suggested mechanism for seizures in this context. Consequently, it became mandatory to understand the mechanism of LAST, so that it could be prevented and managed efficiently.

This chapter reviews the mechanisms, frequency, clinical characteristics, prevention and treatment of LAST.

2. LAST mechanisms

LA agents are classic sodium channel inhibitors. LAST hypotheses are based primarily on the binding site, ion channels, signaling pathway or enzymes involved in the CNS and cardiac toxicity or its treatment. LA inhibit some components of the oxidative phosphorylation pathway, which affects the myocardium and the CNS that are poorly tolerant of anaerobic metabolism. These deleterious effects differ quantitatively between LA, doses and administration routes. It is appropriate to first review the ion channels implicated in LAST [7–9].

2.1 Sodium channel blockade

LA are sodium channel blocking acting on inactivated sodium channel state and blocking it. They affect the initial depolarization phase and slow it down, leading to slow cardiac conduction. The antiarrhythmic property of lidocaine is related to this slowed conduction as it causes fast blockade of the channels. In contrast, bupivacaine and ropivacaine cannot be used as anti-arrhythmic drugs though they have fast blockade, but slow release of sodium channel (lasting longer than 1 s in contrast to lidocaine which lasts 0.15 s) [10]. Slowed conduction leads to widening the QRS complex, prolongation of the PR interval, AV block and, eventually, ventricular fibrillation due to the unidirectional blockade and re-entry phenomenon.

2.2 Potassium channel blockade

Out of three known organized potassium channels, two groups are of interest where LA toxicity is concerned. Out of these, one group of channels are known as the inward, outward and transient rectifier potassium channels, thus plays an important role in the potassium efflux during phases 2 and 3 of the cardiac muscle action potential [11]. If these channels are blocked, it will lead to prolongation of action potential; i.e. phase 2, delay in repolarization; i.e. phase and shift the resting membrane potential more positive (phase 4) to increase automaticity [12]. The second group of potassium channels of interest are K2p. Previously known as the delayed rectifier channels, these channels are believed to be responsible for the background or leak potassium currents. In this setting, they control the resting membrane potential. A blockade of these channels shifts the resting membrane potential towards spontaneous depolarization. K2p channels are extensively spread in the body. In the CNS they are mainly located in the thalamo-cortical and striatal neurons, where blockade leads to increased neuroexitability [13]. They are also present in high concentrations in the cerebral blood vessels, where blockade leads to vasoconstriction and decreased cerebral blood flow. K2p channels are also present in neurons of the auditory system, where blockade leads to tinnitus. LA agents are also known to have K2p mediated stimulating effect on ventilation [14]. They are located in the brainstem and carotid body, where they regulate the respiratory response to carbon dioxide via sensing the changes of pH and expressed in the oxygen-sensing cells of the glomus body respectively. K2p channels are sensitive to changes in oxygen tension and extracellular pH and are potentiated by volatile anesthetic [13]. In the CVS K2p channel blockade predisposes the patient to re-entry dysrhythmias. It is well known that hyperkalemia exacerbates LAST, and that K^+ATP openers (which effectively lowers intracellular K^+ levels) attenuate the toxic effects of bupivacaine [15].

2.3 Ca^{2+} channel blockade

All voltage-gated Ca^{2+} channels are comprised of two subunits according to the latest research: α and β subunit. The α subunit has fairly constant chemical structure for all voltage gated Ca^{2+} channels and is the main pore- forming element of the channel. The β subunit has highly variable structure that depends on the location and function of the channel for e.g. in cardiac conduction tissue β1 subunit completes the ion channel structure. The role of the β1 subunit seems to be the modulation of channel opening and membrane ion trafficking [16]. In terms of their physiological effect, the heart has two distinct types of channels namely the T-type (transient) that are low voltage activated channels (LVA), and L-type (long lasting). On the other hand, are high voltage activated channels (HVA).

The T-type channels are mainly located in the pacemaker cells of the sinoatrial node, and the opening of these channels completes the prepotential required for the pacemaker potential. L-type channels are present on the surface of the myocytes of both atrium and ventricle, and are closely associated with the T-tubules. The plateau phase (phase 2) of cardiac muscle action potential is produced by opening of these L-type channels. LA bind to these channels and predispose them to an inactivated state. The consequence of this is prolongation of the action potential (phase 2) and depressed contractility [9].

3. LAST risk factors

Risk factors to develop LA toxicity are related to kind of LA used, the type of nerve block, and the patient.

3.1 LA related

The most important and most studied factors in the development of LAST are undoubtedly the type and dose of LA.

3.1.1 Type of LA

The kind of LA injection influence toxicity risk. Animal studies showed that [17] more levobupivacaine than bupivacaine was required to induce cardiac arrest and levobupivacaine caused fewer convulsions and arrhythmias than bupivacaine, at similar doses [18]. Ropivacaine may cause less motor block, but whether it is clinically significantly less toxic is unknown. Other property differentiating the toxicity of LA is their intrinsic effect on vessels, where levobupivacaine and ropivacaine have intrinsic vasoconstrictors properties (that may prolong duration of action and slow systemic absorption), whereas bupivacaine is an intrinsic vasodilator. The clinical significance of this difference remains unclear. Another important concept in the study of LAST is the ratio of the dose required to produce cardiovascular collapse to that required to induce seizures, the so called CC/CNS ratio (ratio of dose causing cardiovascular collapse to the dose causing seizures). Bupivacaine has a CC/CNS ratio of 2.0 compared with 7.1 for lidocaine. Therefore, progression from CNS signs and symptoms to cardiovascular collapse can occur more readily with bupivacaine than with lidocaine.

3.1.2 Dose of LA

Determining the optimal dose of LA to use is complex and always a topic of debate. Using the lowest effective dose is always prudent and advisable practice along with consideration of patient characteristics and site of administration. Some may argue that the recommended doses provide a rough guide for clinical use. The maximum weight-based doses have lost rationale in others view as such dosing does not correlate to the resulting blood level and does not take into account relevant patient factors or the site of injection. Other factors that question the maximum weight based doses are variation between different texts and countries, no recommendation whether dose calculation is based on actual body weight or ideal body weight and such hard and fast dosing rules do not take into account the complete clinical context [19]. As a result, if dosing is calculated on actual body weight, the obese, pregnant, or both patients may receive a dangerously high dose.

3.2 Block-related

Inadvertent intravenous injection of LA can occur during any regional anesthetic technique, but tends in becoming LAST only if larger volumes (5–10 mL) are injected, or small doses during face and neck procedures. Symptoms usually occur within 3–5 min and can be severe if appropriate measures are not taken. LAST resulting from the gradual systemic absorption of LA is characterized by a late presentation (20–30 min or more after a bolus injection), and usually occurs when a relatively high dose of LA has been administered in the presence of another risk factor. Local anesthetic systemic toxicity may also occur in the context of continuous LA infusion, in which case the onset may be hours to days after starting the infusion. The symptoms last until the drug metabolism reduces concentrations plasma levels below the toxic threshold. Prolonged monitoring and supportive therapy are essential.

3.2.1 Site of block

Blocking site is important since rate of absorption, chances of direct intravascular injections and thus chances of toxicity depends on the anatomical location. For example, interscalene block, stellate ganglion block, intercostal nerve block have a higher risk of direct intravascular injection and other blocks like scalp, bronchial mucosa, inter pleural cavity carry an increased risk of rapid absorption and toxicity due to the injection being in a highly vascularized area. The classic order of sites propensities to lead to toxicity, in order from lowest to highest: subcutaneous injection, brachial plexus, epidural, caudal, and finally intercostal blocks and topical mucosal anesthesia.

3.2.2 Conduct of the block

Performing the block in a safer way decreases the chances of toxicity by manifolds. The practice of giving the dose of LA in incremental injections, after frequent aspiration, adding test dose and most important is using ultrasound-guided needle placement to give the LA reduces the risk of toxicity.

3.3 Patient-related factors

3.3.1 General principles

Various factors are related to toxicity of LA. Most common being the free peak plasma concentration, perfusion at the site of injection, co-morbidities (renal, liver, metabolic, and cardiac diseases). As already discussed earlier, more the perfusion at the site of injection, more will be the peak plasma concentration as systemic absorption is accelerated. A low α1-acid glycoprotein (AAG) titer results in a higher concentration of free LA.

In patients with severe renal impairment there may be slightly increased risk of toxicity as these patients typically have a reduced clearance of LA, hyper dynamic circulation but increased AAG. So, it is prudent to reduce the initial dose by 10–20% according to severity of renal impairment.

In patients with liver disease, single dose blocks are unaffected, but the doses for repeat boluses and continuous infusions should be reduced. Such patients may also have renal or cardiac disease. AAG is synthesized in patients with end-stage liver disease, offering some protection against LAST. Patients with severe cardiac failure are particularly susceptible to LA-induced myocardial depression and arrhythmias.

Further, lower liver and renal perfusion slows metabolism and elimination, so safe initial and maintenance doses of LA are correspondingly lower too. On the other hand, poor perfusion at the injection site may decrease peak plasma concentrations.

3.3.2 Age related factors

Extremes of age have different physiological changes making them different from young and adolescent age group. In elderly patients; there is a safety benefit in dose reduction without altering the clinical efficacy. In the geriatric patient's nerves appears to be more sensitive to LA due to various factors like altered nerve morphology, there is less fat tissue surrounding the nerves, and axonal function is also reduced. Moreover, this age group has multiple co-morbidities and decreased muscle mass; blood flow to organs is reduced, decreased clearance and organ function. In patients older than 65 years' involuntary overdoses being responsible for some cases of LAST. When considering the use of LA in geriatric patients, it is mandatory to pay special attention to the presence of systemic disease and muscle wasting [20].

In neonates and infants, the risk of accumulation of LA with continuous infusions is more than in adults as AAG levels are reduced (about half that of adult at birth). Children have an increased elimination half-life of LA, which in neonates is increased to 2–3 times that of an adult. Bupivacaine accumulates with continuous infusion and 2-chloroprocaine can be used as an alternative. LAST has the highest incidence in infants less than 6 months of age and is associated with bolus dosing and penile nerve blocks [21].

3.3.3 Pregnant patients

Pregnancy is one of several clinical settings in which LAST can be potentiated. Pregnant patients are at an increased risk of toxicity as they have increased perfusion as well as decreased AAG levels; thus high peak free plasma concentration of LA. Some of the earliest anecdotal reports of LAST-related fatal cardiac arrests involved pregnant women [1]. Notably, several of the original anecdotal reports of LAST-related fatal cardiac arrests involved pregnant women. It has since been proven that pregnancy increases the risk for LAST, and subsequent guidelines preclude use of 0.75% bupivacaine in late gestation because this concentration was involved in cases of fatal toxicity in parturients [22–24].

4. Clinical presentation of LAST

Most of the LAST events happen a few minutes after the LA injection and present with signs of the CNS, which may or may not be accompanied by changes in the CVS (**Figure 1**). Sometimes, the manifestations are atypical in terms of time and clinical picture. The onset of symptoms may be delayed up to 60 min after a bolus injection, and signs of CVS toxicity may appear in the absence of any CNS characteristics. This last scenario may be more common in patients who are very sedated or under general anesthesia. High plasma concentrations during LAST can occur in three circumstances: inadvertent intra-arterial injection, intravenous injection or systemic absorption, each of which has a characteristic temporal course. LAST associated with intra-arterial injection occurs classically during nerve blockages in the head and neck (stellate ganglion, interscalene or deep cervical plexus blocks) in which there is an involuntary injection of LA in an artery that supplies the brain. The symptoms of the CNS, usually seizures, occur almost immediately. When the injected dose is small, progression to CVS collapse is uncommon. Recovery

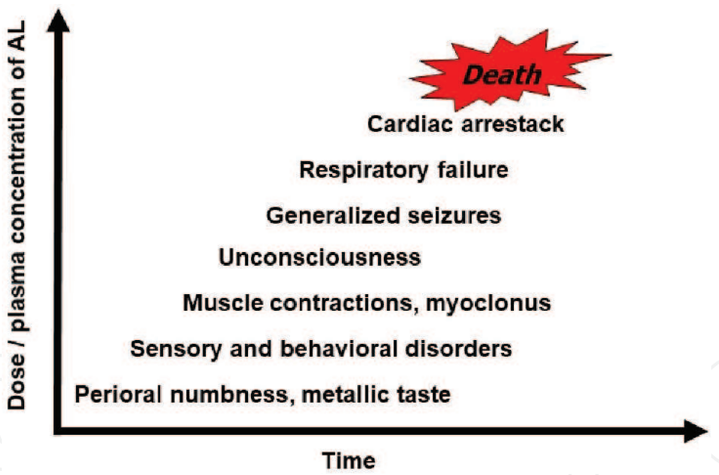

Figure 1.
Scheme showing the most important clinical manifestations of LAST.

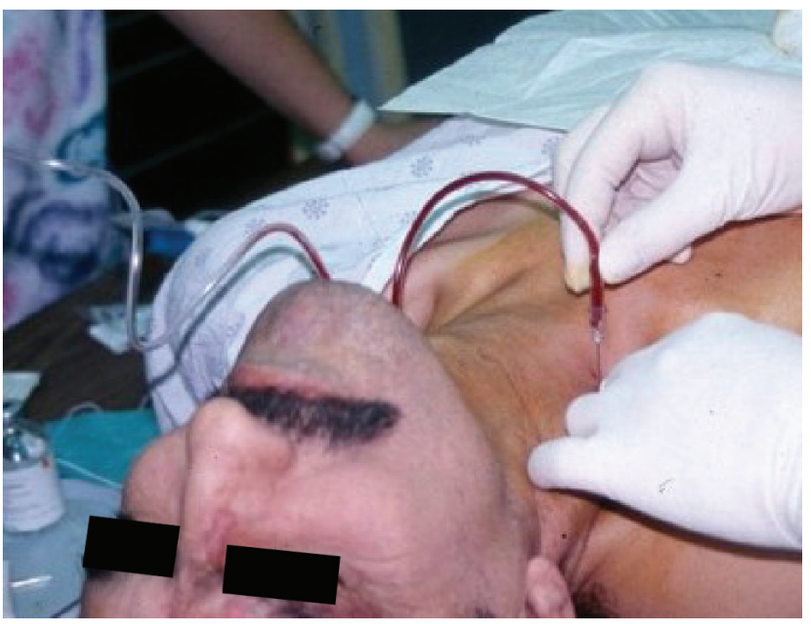

Figure 2.
Accidental arterial puncture during a stellate ganglion block in a patient with postherpetic neuropathy.

is equally rapid since LA quickly redistributes from the cerebral circulation [25]. **Figure 2** shows an intra-arterial puncture detected during the blockage of the stellate ganglion in a patient with herpes zoster neuropathy.

4.1 Central nervous system toxicity

Central nervous system toxicity could be presumed as a two-stage process in which initial blockade of Na^+ channels occurs in the inhibitory neurons thus allowing excitatory neurons to act unopposed which culminates in generalized convulsions. Higher concentrations of LA agent affect all neurons, leading to global CNS depression, which is clinically seen as coma and evident on EEG as slowing and ultimately silent EEG. In most cases, convulsions, although an impressive clinical entity, can be handled safely without permanent brain damage. Clinical manifestations of the systemic neurotoxicity of LA usually occur in stages; in the initial phase there is perioral numbness, confusion, tinnitus followed by an exciting phase that shows seizures and, finally, a depressive phase where there is loss of consciousness and respiratory depression.

4.2 Cardiovascular system toxicity

Both the direct and indirect effects of the LA drugs on myocardium are involved in the mechanism of cardiovascular toxicity [26].

Clinical presentation includes hypertension and tachycardia in initial phase (during CNS excitatory phase), followed by intermediate phase showing myocardial depression, decreased cardiac output and thus hypotension, followed by sinus bradycardia, peripheral vasodilatation, conduction defects and dysrhythmias in terminal phase.

5. Management of LAST

All medical and paramedical personnel working in operating theaters and hospital locations where LA are used should be prepared to recognize, diagnose and treat patients with signs and symptoms of LAST in a timely manner. The ASRA has published and updated the guidelines recommended by experts for the management of LAST (**Table 1**) [4, 5]. The initial treatment of LAST should focus on keeping the airways permeable with adequate ventilation, circulatory support and the reduction of systemic side effects. Immediate ventilation and oxygenation to prevent hypoxia and acidosis can facilitate resuscitation and reduce the likelihood of progression to seizures or cardiovascular collapse [24, 25].

5.1 Preparation

All patients receiving LA injections in doses potentially to trigger LAST should have oxygen, standard monitoring which is to be continued at least 30 min after completion of injection to detect delayed presentation if any, and intravenous access applied [27, 28]. Immediate access to LAST Management Checklist is advisable, and all medications and resuscitation equipment required should be immediately available, preferably in the form of a "LAST Rescue Kit".

5.2 Immediate management

Immediate management involves the general safety and resuscitation measures that are essential in any emergency. First, stop LA injection and call for help. The immediate priority is to manage the airway, breathing, and circulation. Avoid factors potentiating LAST like hypoxia, hypercarbia, and acidosis (metabolic or respiratory [24, 25, 29]).

5.2.1 Intravenous lipid emulsion therapy

Use of intravenous lipid emulsion as a therapeutic modality comes with several advantages. Theories suggest that it improves cardiac conduction, contractility and coronary perfusion by removing the liposoluble LA from cardiac tissue. Better understanding of the mechanism of action of lipid emulsion with recent advances underlines its importance as therapeutic modality in the management of LAST. First advantage is that lipid emulsion may shuttle any LA agent from high blood flow organs to detoxification organs such as the liver [30]. Secondly, lipid emulsion therapy may also improve the cardiac output and blood pressure. Post conditioning myocardial protection may also occur [31–34]. There is an unavailability of large scale data collection and other prospective studies to demonstrate efficacy of lipid

Checklist for LAST treatment	
The pharmacologic treatment of LAST is different from other cardiac arrest scenarios	
Reduce individual epinephrine boluses to ≤1 mcg/kg	
Avoid vasopressin, calcium channel blockers, beta blockers, or other local anesthetics	
• Stop injecting local anesthetic • Get help ○ Consider lipid emulsion therapy at the first sign of a serious LAST event ○ Call for the LAST rescue kit ○ Alert the nearest cardiopulmonary bypass team – resuscitation may be prolonged • Airway management ○ Ventilate with 100% oxygen / avoid hyperventilation / advanced airway device if necessary • Control seizures ○ Benzodiazepines preferred ○ Avoid large doses of propofol, especially in hemodynamically unstable patients • Treat hypotension and bradycardia—if pulseless, start CPR	
Lipid emulsion 20% (precise volume and flow rate are crucial)	
Greater than 70 kg patient	**Less than 70 kg patient**
Bolus 100 mL lipid emulsion 20% rapidly over 2–3 min	Bolus 1.5 mL/kg lipid emulsion 20% rapidly over 2–3 min
• Lipid emulsion infusion 200–250 mL over 15–20 min	• Lipid emulsion infusion ~0.25 mL/kg/min (ideal body weight)
If patient remains unstable:	
• Re-bolus once or twice at the same dose and double infusion rate; be aware of dosing limit (12 mL/kg) • Total volume of lipid emulsion can approach 1 L in a prolonged resuscitation (e.g., > 30 min) • Continue monitoring ○ At least 4–6 h after a cardiovascular event ○ Or, at least 2 h after a limited CNS event • Do not exceed 12 mL/kg lipid emulsion (particularly important in the small adult or child) ○ Much smaller doses are typically needed for LAST treatment	
With permission from www.anestesia-dolor.org.	

Table 1.
Checklist for LAST treatment [4, 5].

emulsion therapy due to various difficulties [24, 35, 36]; however various animal studies provide strong support for use of lipid emulsion therapy to reduce mortality when used along with resuscitative measures [37]. Early administration of 20% intravenous lipid emulsion therapy should, therefore, be an immediate priority after airway management in any LAST event that is judged to be potentially serious. A bolus of 1.5 mL/kg of 20% lipid emulsion and the subsequent infusion of 0.25 mL/kg per minute should be administered. The infusion should be continued for 10 min after reaching hemodynamic stability. An additional bolus and an infusion rate increase to 0.5 mL/kg per minute can be administered if stability is not achieved. The maximum recommended dose for initial administration is approximately 10 mL/kg for 30 min (**Table 1**) [4, 37, 38]. Lipid emulsion remains first-line therapy (in conjunction with standard resuscitative measures) in LAST. However, more research in humans is necessary to establish its real usefulness [36].

5.2.2 Seizure management

Prompt seizure prevention and termination is crucial to avoid injury and acidosis. Benzodiazepines are first line therapy for management of seizures due to their cardio stable profile. Propofol or thiopental can be used in low doses, although these drugs may worsen the hypotension or cardiac depression associated with LAST. It should be avoided in patients with cardiovascular compromise. Neuromuscular blockade can be considered in cases of ongoing seizures; small doses of succinylcholine should be administered intermittently to stop muscle activity and increased acidosis. Early termination of seizure activity helps to avoid metabolic acidosis and hypoxia that occurs due to repeated muscular contractions [24].

5.2.3 Cardiovascular support

The treatment of LA-induced cardiac arrest focuses on restoring cardiac output, to restore tissue perfusion, prevent and treat underlying acidosis. Chest compressions should be started without delay and to be continued till return of spontaneous circulation (as per ACLS algorithms for cardiopulmonary resuscitation). If epinephrine is used, small initial doses of ≤1 μg/kg are preferred to avoid impaired pulmonary gas exchange and increased afterload [39]. Vasopressin is not recommended, as it can cause pulmonary hemorrhage. If myocardial LA levels is more than the threshold that corresponds to ion channel blocking concentrations, then the ionotropic effect of lipid emulsion therapy remains questionable. Chest compressions ensure the coronary perfusion that is sufficient to reduce tissue LA levels. In the absence of rapid recovery following ACLS measures and intravenous lipid emulsion therapy, early consideration should be given to cardiopulmonary bypass for circulatory support. For other deleterious CVS effects—such as arrhythmias, conduction block, progressive hypotension, and bradycardia – standard ACLS algorithms should be followed with the omission of LA, such as lidocaine and procainamide. Amiodarone is the first-line antiarrhythmic in the event of ventricular dysrhythmia. In addition, calcium channel blockers and B-adrenergic receptor blockers are not recommended.

5.2.4 Post-event management

Report the case of LAST to the registry at www.lipidrescue.org [39]. Monitoring is mandatory for at least 2 h in isolated and recovering CNS event but for 6 h for LAST with CVS features.

6. Prevention

The primary objective of every anesthesiologist is always patient safety. Preanesthetic evaluation, patient preparation, complete monitoring before starting administration of LA, and continuing this monitoring during surgery and the immediate postoperative period are mandatory.

6.1 Pre-procedure

- During preoperative assessment, evaluate the patient for co-morbidities, evaluation of the risks and benefits of regional anesthesia for that individual should be discussed, patient should be explained regarding procedure and appropriate consent to be obtained.

- Preparation includes selection of type of LA, prior calculation of doses, labeling all syringes.

- All monitoring facilities to be available along with LAST rescue kit and resuscitative measures.

6.2 Intra-procedure

- Block to be performed with continuous monitoring attached, with a capable help nearby.

- The method of administration of LA should include the administration of incremental doses with frequent aspiration, ultrasound-guided needle placement, administration of test doses. This can help in the early detection of accidental intravascular placement of the needle or catheter and thus avoid erroneous administration of the LA, avoiding toxic plasma concentrations.

- Continuous communication with the patient to detect early signs of intravascular injection like perioral numbness, tinnitus etc.

6.3 Post-procedure

Clearly label any kind of spinal/epidural catheter or peripheral nerve block catheter; it should be documented well in patient chart also. Drug and dose already administered or to be administered should be well informed in instructions to the medical staff responsible for post-operative care of the patient. Continuous monitoring of vital signs in the postoperative period in suspected case of delayed LAST to be considered.

7. Conclusion

LAST is a serious life-threatening emergency, with protean manifestations, that can happen after administering LA. Anesthesiologists must understand its risks, prevention, and safe management. Promptly recognition and timely management of LAST can dramatically change the clinical course. In addition to the usual advanced cardiac resuscitation maneuvers, the current treatment focuses on the administration of lipid emulsion. While the development of new treatment plans can help limiting the associated morbidity and mortality, prevention remains vitally important. It is mandatory for all the practitioners using LA to understand patho-physiological basis, mechanisms, risk factors, prevention and treatment modalities of LAST.

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