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Review Article

Local Anaesthetic Systemic Toxicity- Management and Prevention a Narrative Review and Recent Updates

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Abstract

Local anaesthetic systemic toxicity (LAST) is a life-threatening complication caused by either inadvertent intravascular injection (IV) or systemic absorption of injected local anaestheitc (LA) to a toxic level. The diagnosis of LAST may be difficult and often unrecognized or misdiagnosed. LAST is a serious adverse effect that can occur with all local anaesthetics irrespective of routes of administration. Primary affected organs are central nervous system and cardiovascular system and can be often fatal. Clinical presentation of toxicity is highly variable and unpredictable, a high degree of suspicion of LAST should be done whenever any unexplained physiological changes are noticed after administration of LA. Risk factors for LAST include the dose and type of LA, site of injection, the plasma level of LA and patient's physiological status and co-morbidities. The standard treatment guideline for LAST emerged after 2010 when Americal society of regional anesthesia and pain medicine (ASRA) first published the evidence-based treatment guideline for LAST using modified Advanced cardiac Life support (ACLS) and intravenous lipid emulsion therapy. The sequence of management as per the priority include- addressing the airway and breathing to prevent hypoxia and acidosis, control of seizure activity and cardiopulmonary resuscitation and timely administration of intravenous lipid emulsion infusion. The article highlighted the importance of preventive measures to avert LAST and continuous vigilance and timely management of LAST. The article is also intended to provide the recent changes and recent updated guidelines in the prevention and management of LAST.

Keywords: local anaesthetics; local anaesthetic systemic toxicity; regional anaesthesia; lipid emulsion; cardiopulmonary resuscitation

Introduction

Local anaesthetic systemic toxicity (LAST) is a life-threatening complication caused by either inadvertent intravascular injection (IV) or systemic absorption of injected local anaesthetic (LA) to a toxic level. [1,2] LAST is a relatively rare event and lack of awareness about this can lead to delayed diagnosis or the opportunity to treat can be easily missed. The diagnosis of LAST may be difficult and often unrecognized or misdiagnosed. Among the different causes of LAST, the majority of reported cases of LAST have occurred after accidental or inadvertent IV injection of Local anaesthetic. However, injected local anaesthetic may be sufficiently absorbed in systemic circulation to a toxic level and can also cause a delayed, gradual onset of symptoms and signs of LAST. Continuous LA infusion via epidural or other regional analgesia may also cause LAST by either intravascular migration of the catheter or systemic absorption, the onset may vary from hours to days after initial catheter placement. [3-7] Inadvertent placement of the catheter in an epidural vein or migration of catheter after successful placement and subsequent injection of a large dose of local anaesthetic can cause LAST. With the advancement of ultrasound knowledge and widespread use of bilateral filed blocks like transversus abdominis plane (TAP), and quadratus lumborum block (QLB) which require a relatively large volume of LA predisposing them at risk of LAST. The occurrence of LAST may not be preventable in all cases and despite best clinical practice it can still happen but early recognition of LAST and appropriate management is essential for uneventful recovery.[2] The article highlighted the importance of preventive measures to avert LAST and continuous vigilance and timely management of LAST. The article is also intended to provide the recent changes and updated guidelines in the management of LAST especially during pregnancy.

Incidence of Last:

LAST is a serious adverse effect that can occur with all local anaesthetics irrespective of routes of administration. The primary affected organs are the central nervous system and cardiovascular system and can be often fatal. The true incidence of LAST is difficult to ascertain as this is generally reported sparingly and most of the data are from retrospective reviews or regional anaesthetic registries or isolated case reports based on a small number of events that arise from a vast number of regional anaesthetics. Based on these reports' incidence of major LAST ranges from 0.04-1.8/1000 regional anesthesia. [8-13] However, the major incidence of LAST has markedly decreased over the last [3-4] decades due to increased awareness and greater vigilance and incorporation of preventive measures into routine clinical practice. [14,15] Incidence of major LAST may be somewhat less with an epidural than the other peripheral nerve block. [13-17] Minor events of LAST may be more frequent than major and often goes unrecognized, misdiagnosed or unreported.[16] All the available LA can trigger LAST when the plasma concentration reached the toxic level for that particular LA. However, the threshold limit and organ affinity vary among the agents. Cardiotoxicity generally is proportional to the anaesthetic potency for neural block, the more potent a LA, the higher the cardiotoxic risk, bupivacaine, and ropivacaine being more potent are more cardiotoxic as compared to lidocaine. [18]

Mechanism:

All LA acts by primarily blocking voltage-gated sodium channels which prevent sodium influx and subsequently prevent depolarization and generation of action potential and neural conduction of pain signals. (19,20) Toxicity occurs the LA block the cardiac cells or thalamocortical pathway in the central nervous system. (5,20,21) In addition to the blockade of the sodium channel, LA has other wide range of effects including the blockade of potassium and calcium channels, interaction with N-methyl D aspartate (NMDA) or cholinergic receptors, also interaction with the cellular metabolic process (oxidation, cyclic adenosine monophosphate production, free fatty acid utilization etc). Both cardiac and neuronal cells in the brain cannot sustain inhibition of oxidative phosphorylation and anaerobic metabolism, resulting in depletion of tissue adenosine triphosphate (ATP) that could be the most important underlying cellular mechanism in severe LAST, this might also explain why traditional haemodynamic treatments (e.g., vasopressors and inotropes) are only marginally effective. Such effects may explain some of the manifestations of LAST and its reversal with lipid emulsion which directly reduces the tissue LA concentration. [16]

Clinincal presentation

Clinical presentation of toxicity is highly variable and unpredictable, a high degree of suspicion of LAST should be done whenever any unexplained physiological changes are noticed after administration of LA. The onset of toxic manifestation and its presentation and speed of progression depends on the route of administration, type of LA, the plasma concentration of LA and patients' characteristics. The classical description of LAST includes CNS excitation followed by depression, cardiovascular excitation followed by inhibition and in extreme cases cardiac arrest and death. (Table 1) The classic presentation may not be evident in 40% of cases, [22] the onset may also be highly variable ranging from instantaneous to 60 min after administration of LA. [7,16,23] The CNS manifestation is more frequent than the cardiac component. The presentation varies from simple peri-oral tingling, and numbness to frank seizure followed by CNS depression manifested as unconsciousness, respiratory depressant and arrest.[24] Cardiotoxicity by far is the more serious and important component of LAST as, unlike CNS toxicity, it can lead to cardiac arrest and death. Cardiac toxicity manifests various arrhythmias due to conduction disorder, contractile dysfunction and cardiac arrest. [16-23].

However, these phases are described separately, progression from early to late phases may not be well delineated in individual clinical cases and the manifestation may not follow the classic description, it may be limited or may include prodromal symptoms like perioral numbness, twitching, frank CNS symptoms in the form of seizure, combined CNC and cardiac symptoms or isolated cardiac symptoms. [16]. Inadvertent injection into systemic circulation may results in LAST almost immediately even with a relatively small volume of LA, injection into the highly vascular area may cause rapid absorption resulting in LAST within an hour and usually results in relatively high-volume LA especially in the presence of other risk factors, whereas continuous infusion of LA may cause delay onset presentation over hours to days. Macfarlane et al in a recent review of the 36 published cases from 2017 to 2020, the onset of LAST was within 10 minutes of injection in 53% of cases, in 19% of cases it was within the first hour and in 16% occurred in 1 to 12 hours or more. [16]

	Central nervous symptoms	Cardiovascular symptoms
Early or excitatory phase	Restlessness agitation dizziness confusion circumoral numbness sensory changes (auditory, visual, taste) muscle twitching lightheadedness seizures	Tachycardia hypertension palpitations escape beats arrhythmias
Late or depressive phase	decreased consciousness loss of consciousness coma respiratory arrest	hypotension bradycardia heart block ventricular ectopy cardiovascular collapse cardiac arrest

Table 1: Summary of progression of symptoms and signs in LAST

Risk factors:

Risk factors for LAST include the dose and type of LA, the site of injection, the plasma level of LA and the patient's physiological status and co-morbidities. The lipid solubility of LA is directly related to its potency and risk of cardiac toxicity. Higher lipid soluble LA has a higher affinity for cardiac tissue as compared to the brain. The affinity of LA to neural/cardiac tissue and its plasma concentration determined the manifestation of LAST. The ratio of the dose requirement for cardiac arrest to the dose requirement for seizure called as CC/CNC ratio. This ratio is 7.1 for lidocaine as compared to 2.0 for bupivacaine, therefore the progression from CNS symptoms to cardiovascular collapse can occur more rapidly with bupivacaine than with lidocaine. The plasma concentration of LA is determined by the total injected dose, rate of injection, site of injection, the

technique used for administration, and patient's physiological status and presence of comorbid conditions which impact the pharmacokinetics and pharmacodynamic of LA (absorption, distribution, metabolism and excretion). [16]

The optimal dose of LA is a matter of conflict and debate. The weight-based maximum dosing has some drawbacks whether considering the ideal or actual body weight into consideration, especially in patients with morbid obesity, pregnancy or extreme ages and as such wight based dosing roles do not take into account the complete clinical context. The use of a minimal effective dose (ED95 the dose required to achieve the desired effect in 95% of the population) is always prudent, consideration should be given to patient-related factors and the site of administration. [25] Block site or site of LA administration is also an important factor for LAST. The regional block with a higher risk of absorption and subsequent LAST are (in decreasing order) paravertebral, intercostal, caudal and epidural anaesthesia, interfascicular plane block, abdominal wall, psoas compartment block, sciatic block and cervical and brachial plexus block. [26,27] As a general role bilateral interfascicular plane block requiring higher volume and dose of LA may increase the risk of LAST. [27, 28] Contrary to previous reports, recent analyses revealed that epidural, caudal and upper limb blocks constitute a smaller proportion of LAST, whereas LA infiltration and penile blocks accounted for up to 20% of the LAST events. [23] Continuous infusion of LA through the catheter, unsurprisingly, is associated with a higher risk of LAST as compared to single shot injection due to the potential for gradual accumulation over some time, usually manifested hours to days from the start of administration. [5] In our patient the manifestation of seizure was almost immediately after the epidural bolus injection followed by cardiac arrhythmias and arrest, such rapid progression can occur only in inadvertent intravascular injection, although the epidural aspirate was negative for blood, intravascular placement or migration cannot be roll out.

Among the patient-related factors extreme age have a different physiological and biochemical system to metabolize the LA making them susceptible to LAST, impaired kidney and liver function also predisposes patients to LAST as they have a reduced ability to metabolite and eliminate the LA. Patients with existing cardiac disease are also vulnerable as slight changes in cardiac physiology will predispose these patients to myocardial depression and arrhythmias. The following patient group are at increased risk of toxicity [23,24, 29,30]

- Patients with pre-existing cardiac problem
- Extremly frail patient or patients with small muscle mass;
- Extremes of age
- Poor hepatic perfusion and function;
- Reduced plasma α-1 acid glycoprotein levels
- Significant medtabolic or respiratory Acidosis that shifts the binding equilibrium and increases free plasma LA concentration

Pregnancy and LAST:

The physiological changes associated with pregnancy and increased sensitivity to LA during pregnancy put them in a high-risk group for LAST. There may be several reasons for this, increased cardiac output and perfusion and reduced level of albumin and binding protein alpha 1 glycoprotein (AAG) and reduced overall drug clearance, as a result, freer fraction of LA is available in the circulation. Distension of the epidural venous plexus predisposed them to entrapment of LA and intravascular migration of the epidural catheter. The hormonal effects of estrogen and progesterone appear to enhance neural sensitivity lowering the limit of seizure threshold and altering the electro-physiological function of cardiac myocytes predisposing them to neuro and cardiotoxicity with LA. [31-34] Cardiac arrest secondary to LAST after neuraxial analgesia for labour is a serious potential complication despite the use of a lower concentration of LA and increased awareness and vigilance for the toxicity. [32-34] The conversion of epidural analgesia to the surgical level of anaesthesia for cesarean delivery, may have potential medical implications and is strongly associated with life-threatening complications including LAST. [35] In addition to the high-risk factor for LAST, the resuscitation of pregnant women is challenging as attempted resuscitation effort of the pregnant woman is complicated by changes in physiology associated with pregnancy, inherit risk of aortocaval compression by the gravid uterus that reduces venous return and cardiac output, leading to hypotension and further aggravating the pathophysiology of the arrest state. [36]

Management of LAST:

The standard treatment guideline for LAST emerged after 2010 when the American Society of Regional Anaesthesia and pain medicine (ASRA) first published the evidence-based treatment guideline for LAST using modified Advanced Cardiac Life support (ACLS) and intravenous lipid emulsion therapy.[37] Before ASRA guidelines, cardiopulmonary bypass was the only recommended standard therapy for LAST. The ASRA guideline stresses maintenance of the airway, breathing and circulation and timely administration of LA antidote in the form of lipid emulsion. [37,38] Prevention of hypoxia and circulatory support is an immediate priority along with initiation of lipid emulsion, The sequence of management as per the priority includes- addressing the airway and breathing to prevent hypoxia and acidosis, control of seizure activity and cardiopulmonary resuscitation and timely administration of intravenous lipid emulsion infusion. Immediate management includes stopping further injection of LA and calling for help on the slightest suspicion of LAST or development of prodromal symptoms.[38] The respiration must be supported with 100% oxygen, avoiding both hypo or hyperventilation as hypoventilation increases acidosis and potentiate the LA effects as well as increases the cerebral blood flow and more LA diverted to the brain, hyperventilation on the other hand increases the intrathoracic pressure and reduces the venous return and subsequently the cardiac output. [38] For seizure control in LAST, the drug of choice is benzodiazepine as propofol, thiopentone though very effective for seizure control, is a myocardial depressant and can potentiate cardiac toxicity. Neuromuscular blockers may be considered for the treatment of sustained muscle contraction as vigorous muscle contraction leads to hypoxia and acidosis. [16] Conventional therapies are to be used for the treatment of bradycardia, hypotension or other arrhythmias and standard cardiopulmonary resuscitation (CPR) with some modification to commence if cardiac arrest occurs.[38] The pharmacological treatment of cardiac arrest in LAST is differ from the standard Advanced Cardiac Life Support (ACLS) protocol. A high level of LA suppresses cellular activities rendering the standard ACLS drug therapy relatively ineffective or interfering with lipid emulsion therapy. [16] Adrenaline bolus doses are to be reduced to 1mcg/kg as higher adrenaline and vasopressin may cause intense vasoconstriction and increase after-load and affect pulmonary gas exchange by inducing pulmonary oedema.[37,38] Furthermore higher intravenous adrenaline may impair the lipid resuscitation in LAST, possibly by inducing hyperlactemia.[39] Vasopressin, calcium channel blockers, beta blockers and lidocaine to treat arrhythmias are to be avoided as they will further deteriorate the already compromised cardiac function. Amiodarone is the preferred antiarrhythmic for LAST-induced ventricular arrhythmias. [37,38]

Lipid emulsion therapy:

Intravenous infusion of 20% lipid emulsion (intralipid 20%) has become an accepted treatment guideline for both CNS and cardiac toxicity unresponsive to standard therapy. [38,39] The mechanism of action of intralipid for the treatment of LAST is still not clearly understood, in addition to the lipid sink hypothesis whereby lipid emulsion creates a lipid phase that extracts the lipid-soluble molecules of the LA from the aqueous plasma phase. [40-42] Other possible mechanisms of lipid emulsion may be related to its cardiotonic effect involving reversal of sodium channel, [43] fatty acid processing, [44] reversal of mitochondrial dysfunction, [45] inhibition of nitric oxide release. [46] Intralipid can be given immediately on any suspicion of LAST as stated in the guideline in ASRA [38] and the Association of Anaesthetists of Great Britain and Ireland (AAGBI). [47] The

lipid-shink effect of intralipid combined with inotropic support along with chest compressions may improve the coronary blood flow 'washing out' LA, thereby essentially accelerating its redistribution away from the cardiac tissue.[16] Lipid emulsion containing long-chain triglyceride may be superior to medium triglyceride for the management of LAST, medium-chain triglycerides containing lipid emulsion have been shown in the animal model to increase the cardiac afterload through systemic vasoconstriction and reduces ventricular contractility. [46] Dose of intralipid: The optimum dose of intralipid is yet to define clearly. ASRA recommends the intralipid 20% to be given immediately as an intravenous bolus of 100 ml for a patient weighing more than 70 kg and 1.5 ml/kg for a patient weighing less than 70 kg over 2-3 min, followed by continuous infusion of 0.25 ml/kg/min, and repeat bolus of 1.5 ml/kg, doubled the infusion to 0.5 ml/kg/hr as necessary for persistent cardiovascular instability. The lipid emulsion is to be continued for at least 10 min. The dose of intralipid should be based on the ideal body weight and not based on the actual body weight. The maximum recommended limit of intralipid is 12 mg/kg, the use of repeat boluses, rather than continuous infusion may be superior to achieve this maximum limit. [16,38,47]

For liposomal preparation of bupivacaine, a sustain release formulation of bupivacaine, currently there is no recommendation on intralipid dosing for LAST associated with liposomal bupivacaine. Considering its prolonged effects lasting more than 36 hours may require a prolonged infusion of intralipid and extended monitoring in a designated area. Intralipid has also been used successfully in neonates associated with high serum levels of LA with CNS or cardiac symptoms like seizure, bradycardia, heart block or apnea. [48] Lipid emulsions like all other antidotes have its limitation and unfortunately, deaths from LAST continue to occur despite intralipid administration. In the following condition the use of intralipid may be ineffective [16]

- If the local anaesthetic load in the tissue is too high
- The administration of intralipid is too late
- pre-existing coronary occlusion that prevents enough transport of lipid emulsion to the coronary capillary.
- existing poor cardiac function.
- Presence of other significant comorbidities.

Side efects of lipid emulsion:

The safety of High volume intralipid infusion is not precisely known. Given the potential benefit of lipid therapy in LAST, the side effects or adverse effects appear to be minor. Possible side effects associated with intralipid include allergic reaction, interference with certain laboratory testing of blood, hyperamylasemia, bronchospasm, chest pain, deep venous thrombosis, pancreatitis, interference with the filter used for renal replacement therapy, interference with membrane oxygenator and circuit clot in cardiopulmonary bypass. [48-52]

Prevention of LAST:

Despite meticulous technique and best practice, LAST can still occur. Prompt diagnosis and immediate management of LAST are key to a successful outcome, all medical personnel working within the operating room should be aware of the LAST as timely recognition and management are paramount for a successful outcome. Like Malignant Hyperthermia there needs to be a LAST specific plan in place and simulation should be done once in a few months for all team members to be aware. There needs to be a LAST box available with all necessary drugs to treat if such a situation arises. The expiry of lipid emulsion should be checked frequently with a checklist and be replaced if expired. The anaesthesia and theatre team to be aware of where to get the intralipid from when needed in an emergency. the LAST protocol should be available in each theatre for reference in case of emergency.

Following general strategies should be used as part of preventive measures for LAST [25]

- Dose of LA- it is unreasonable to perform a nerve block without any dosing or dose-limit guidance. The dose should be minimised to the lowest possible dose (ED95) that is required for the desire extend and duration of the block. The maximum allowable dose that is given in various publications are rough guideline that cannot be generalized for every block and it does not take into account the individual pharmacokinetics and pharmacodynamic variables.
- The maximum allowable LA dose should be based on lean body weight, not on actual body weight.
- The dose of LA should be reduced in the vulnerable patients-pregnant patient, those extremes of age, hepatic or renal impairment or patients with cardiac illness.
- Epinephrine can be added to reduce the rapid absorption of LA when it is injected into a highly vascular bed.
- Aspiration before injection – it should always be aspirated before any LA injection. False negative aspiration is a real possibility, especially with multi-orifice epidural catheters that may be as high as 2% of a labour epidural.[53]
- Slow incremental injection of small boluses over some time and waiting a few minutes in between the injection allow for accidental intravascular injection before the toxic dose is administered. [8]
- Intravascular marker- a small dose of epinephrine (1:200,000 to 1:400,000) along with LA should be used as a test dose to rule out intravascular placement of the catheter. However, it may be unreliable in labouring women, or patients under sedation, anaesthesia or using beta blockers as the resultant tachycardia may be masked or misinterpreted.
- Avoidance of heavy sedation / general anaesthesia -there is no robust evidence that performing blocks in awake patients reduces the risk of LAST as this may mask the early warning sign associated with LAST. It is logical, therefore, that early presentations of LAST may be detected sooner in awake patients, allowing both further injections of a local anaesthetic to be stopped as well as earlier administration of lipid rescue therapy.
- Ultrasound guidance in regional blocks may reduce the risk of LAST nearly four-fold.[54] The use of ultrasound in regional anaesthesia has several advantages like reduce the incidence of vascular puncture and inadvertent intravascular injection, ultrasound being real-time monitoring of the injected drug gives evidence of tissue expansion with LA and not intravascular injection, reducing the requirement of LA as the injection are more precise minimising the dose requirement for a particular block. [16,54-56]
- Knowledge sharing and education of all staff including the surgeon where local anaesthetic is administered regarding the signs and symptoms of LAST to facilitate prompt recognition, and familiarity with LAST treatment guidelines
- Consider stocking a 'local anaesthetic toxicity box'
- Consider including local anaesthetic dosing in the surgical timeout and sign-out form.

Mixting of local anaesthetics

Many clinicians still practice mixing up a long-acting LA with a fast (short) acting LA believing that the short-acting will accelerate the onset time while the long-acting provides the extended duration. However, the mixing of long-acting local anaesthetic (LALA) with short-acting local anaesthetic (SALA) is flawed on pharmacokinetic principles. The driving force for any LA to penetrate the neural tissue is concentration dependent, combining two different local anaesthetics results in the dilution of each component, lowering the concentration gradient of each LA across the neural tissue and

thus limiting its transfer to neural cells. [57]. Moreover, all LA exist in the ionised and non-ionised state depending on the PH of the solution, PK of LA is the PH where it exists equally in both ionised and non-ionised states. It's only the non-ionised LA that can enter a cell membrane, mixing two or more LA results in a change in the PH of the resultant mixture resulting in a change in the efficacy of each or both components. [57,58] Another drawback of combining LALA with SALA is that the SALA first penetrate the neural cell and binds with the available sodium channel leaving behind the free LALA which is absorbed and carried in systemic circulation to be metabolised by the liver resulting in rapid onset and offset of block as compared to sole LALA. [59-61] There is a myth among clinicians that combining two LA within their recommended limit allows them to inject a large volume of LA without increasing the risk of toxicity. On the contrary, by combining two different LA, the risk of systemic toxicity is not reduced as the toxicity is additive and in fact, the risk of LAST may be potentiated by the mixture. This issue is often neglected in routine clinical practice. [62,63] Thus, the idea of combining the advantages of two drugs (SALA and LALA) cannot be supportedin light of modern regional anaesthetic techniques.

Follow-up

All patients recovering from LAST should be observed in a designated area depending on the severity and symptoms of LAST. Patients with cardiac symptoms due to LAST leading to cardiovascular compromise must be observed for a minimum of 6 hrs as there is the possibility of redistribution of LA from the peripheral tissue depot. For isolated CNS symptoms, 2 hrs of observation is recommended. LAST is mild to moderate with a limited duration of symptoms without cardiovascular compromise and the diagnosis of LAST is clear, it may be reasonable to proceed with planned surgery after treatment with intralipid and observation for an additional 30–40 min to assure that LAST does not recur. [16]

Preparation	Stocking a LAST kit Lipid emulsion 500 ml, large syringe, wide bore needle and tubing. LAST checklist and guideline printout.
Prevention	Identify at risk group of patients (extreme of age, freility, pregnant, significant cardiac, renal or hepatic impairement) Appropriate regional anesthetic technique and choice of LA- dosing based on ideal body wight. Ultrasound guidance whenever possible Aspiration before injection, pause between injection, slow increamental injection, epinephrine as additive to reduce absorption in from highly vascular bed, use of intravscular marker (adrenaline) when in doubt Avoid heavy sedation routinely
Detection	Consider LAST whenever sign and symptoms of CNS/CVS instability occur in any patient who received LA. CNS Early warning sign- Restlessness, agitation, dizziness, confusion, circumoral numbness, sensory changes (auditory, visual, taste), muscle twitching, lightheadedness, seizures, Late - decreased consciousness, loss of consciousness, coma, respiratory arrest
	CVS- Early- Tachycardia, hypertension, palpitations, escape beats, arrhythmias Late- hypotension, bradycardia, heart block, ventricular ectopy, cardiovascular collapse, cardiac arrest
Initial management	Stop further injection of LA Call for help and LAST kit Address Airway and breathing- secure airway if threatened, 100% oxygen, maintain normocarbia Confirm/ establish IV assess Lipid emulsion therapy (intralipid 20%) Seizure control- with benzodiazepam Alert for cardiopulmonary bypass team / nearest facility for extracorporeal membrane oxygenation (ECMO) if CVS instability persits.
Treatment	If circulatory arrest occurs, follow modified ACLS algorith for cardiac arrest Maintain Oxygenation, ventilation and cardiac compression Administered intravenous lipid emulsion if not already started Limit individual adrenaline boluses to 1 mcg/kg- preferabbly only after commencement of lipid emulsion. Do not use vasopressin, betablocker, calcium channel blocker or lignocaine Amiodarone can be used for ventricular arrhythmias Consider cardipulmonary bypass if resuscitation is ineffective Lipid emusion therapy –

	1.5 ml /kg IV bolus over 2-3 minimised. Continous infusion 0.25 ml/kg/min-untill patient is stable for 10 min. After 5 min – if CVS instability persist or deteriorates repeat the sme bolus dose Doubled the infusin rate to 0.5 ml/kg/min. Further boluses can be given every 5 min. maximum dose of lipid emulsion 10-12 ml/kg.
Follow up	Transfer to desiganted clinincal are (ICU/HDU) for monitoring for atleast 6 hrs. Regular follow up Watch for side effects from lipid emulsion therapy (DVT, pancreatitis) Report to LAST registry.

summary for prevention and management of last

Conclusion

LAST is a devastating complication of regional anaesthesia and can occur with any regional anaesthesia technique. Despite increasing awareness, education, treatment guideline and advances in ultrasound guidance techniques, with the widespread use of regional anaesthetic techniques, LAST events persist and continue to occur till LA are in clinical use. When prevention is the most important element to avoid morbidity and mortality. The key is to recognize it immediately and start appropriate management. Lipid emulsion has significantly improved the outcome. Incident reporting systems should be used to share experiences with the medical community.

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