

Local Anesthesia-Induced Coma During Total Knee Arthroplasty.

July 28, 2021

Aldwinckle R. Local Anesthesia-Induced Coma During Total Knee Arthroplasty. PSNet [internet]. 2021. <https://psnet.ahrq.gov/web-mm/local-anesthesia-induced-coma-during-total-knee-arthroplasty>

The Case

A 61-year-old male patient weighing 57 kg (126 lbs), with severe knee osteoarthritis and hypertension, was admitted for right total knee replacement under subarachnoid regional anesthesia.

The anesthesiologist performed a right femoral nerve block with 20 ml (100 mg) of 0.5% racemic bupivacaine for postoperative analgesia. Intraoperatively, the surgeon also infiltrated the arthroplasty wound with 200 mg of 0.5% ropivacaine, unaware that the anesthesiologist had already performed a femoral nerve block. The patient was sedated with an infusion of propofol throughout the procedure. To the surprise of the anesthesiologist, 100 mcg boluses of intravenous phenylephrine were required to maintain the patient's arterial blood pressure intraoperatively. At the end of the procedure, after stopping the propofol infusion, the patient remained unresponsive.

When the anesthesiologist inquired about the surgeon's use of local anesthesia, it was discovered that the surgeon had used a relatively large dose of ropivacaine. After diagnosing the patient with Local Anesthetic Systemic Toxicity (LAST), the anesthesiologist ordered an intravenous bolus and infusion of intralipid. The patient was observed in the surgical intensive care overnight. He recovered without further complications and was transferred to the surgical ward on the first postoperative day.

The Commentary

By Robin Aldwinckle, MD

Background

Local Anesthetic Systemic Toxicity (LAST) refers to complications affecting the cardiovascular (CVS) and central nervous (CNS) symptoms due to local anesthetic overdose. The underlying cause is believed to be rapidly rising blood concentration levels of local anesthetic due to direct injection into a blood vessel or, more commonly, due to rapid systemic uptake from soft tissue. The incidence of LAST has been estimated to be as low as 0.03%, but more recent empirical studies using administrative data suggest the incidence may be closer to 1 or 1.8 per 1000 after major joint replacement surgery.^{1,2} Milder cases of LAST probably go unreported, so the true incidence is likely higher.

The presentation of LAST varies but CNS symptoms are the most common and range from dizziness to seizures and unconsciousness. Cardiovascular complications range from arrhythmias to cardiac arrest. The underlying pathophysiology is related to the effect of local anesthetics on blocking fast sodium (Na) channels, leading to a decreased rate of depolarization. This increased refractory period leads to conduction blockade. In addition, there is a dose-dependent decrease in cardiac contractility, and in the case of bupivacaine, a pronounced vasoconstrictor effect, causing an increase in afterload, further impairing cardiac output. Cardiac toxicity can be compared across different local anesthetics using the CC/CNS ratio, which is the ratio of the dose causing cardiovascular collapse (CC) to the dose causing seizures. The lower the ratio, the more cardiotoxic the drug is. Bupivacaine has a CC/CNS ratio of approximately 2 indicating that it is particularly cardiotoxic compared to lidocaine, for example, which has a ratio of 7.³

Predisposing factors for LAST include both patient characteristics and drug factors. Patient characteristics include age, low weight, pregnancy, or renal, hepatic or cardiac disease. Drug factors include the drug administered, dose administered, use of vasoconstrictors (e.g., epinephrine), site of administration, use of ultrasound, and technique of injection (fractionated dose, frequent aspiration). In general, the speed of absorption is related to the vascularity of the tissue into which the local anesthetic was injected. Intercostal, caudal, epidural, and penile blocks tend to have relatively rapid absorption whereas peripheral nerve blocks and local infiltration have slower systemic absorption. The incidence of LAST is thought to be reduced by using ultrasound during regional anesthesia, likely due to the ability to limit anesthetic doses through better anatomic targeting and the reduced risk of vascular puncture.⁴

The maximum 'safe' doses for bupivacaine are 2 mg/kg (maximum dose 175mg) or 3 mg/kg if combined with epinephrine (maximum dose 225mg). The maximum 'safe' doses for ropivacaine are 3 mg/kg (maximum dose 200mg) or 3-4 mg/kg (maximum dose 250mg) if combined with epinephrine. In the case described, the patient received a nerve block with 20 milliliters of 0.5% bupivacaine (100 mg = 1.64 mg/kg), and subsequently also received 200 mg of ropivacaine infiltrated by the surgeon (3.3 mg/kg).⁵

A common mixture for local infiltration by surgeons is a long-acting local anesthetic (e.g., ropivacaine), combined with epinephrine (to limit systemic absorption), with or without adjunctive medications such as ketorolac, an injectable nonsteroidal anti-inflammatory agent. This combination was not used in this case; the absence of epinephrine may have accelerated local absorption. In this case, the femoral nerve block contributed 82% of the threshold dose for bupivacaine, and the surgeon's infiltration with ropivacaine contributed 110%. This combination was almost twice the recommended safe limit for local anesthetic

administration.

Approximately 50% of LAST cases present with isolated CNS symptoms, about 1/3 present with both CNS and cardiovascular symptoms, and the remainder have isolated cardiovascular symptoms.⁶ In this case, the patient was receiving sedation with propofol, which may have raised the seizure threshold. As a result, seizure activity did not manifest before complete CNS depression occurred. Fortunately, no cardiovascular complications occurred.

The treatment of LAST is multifaceted, including circulatory and ventilatory support along with seizure suppression, but the primary treatment is the infusion of intralipid. Intralipid reverses LAST by increasing the removal of local anesthetic from affected tissues (e.g., heart and brain) by a partitioning effect, but it also has a direct inotropic effect on the heart. The rapid infusion of 100 milliliters of 20% intralipid (or 1.5 ml/kg if less than 70 kg) is required to establish a lipid sink in the plasma, as part of the initial treatment. Boluses can be repeated as necessary, and the total dose should not exceed 10-12 ml/kg. It is important to note that cardiopulmonary bypass should be considered as resuscitation can be prolonged. There are also notable differences to standard ACLS resuscitation protocols, which include reduced doses of epinephrine, and avoidance of drugs that may depress the myocardium or excessively increase afterload. Beta blockers, calcium channel antagonists and vasopressin should be avoided in resuscitating patients with LAST.

Following treatment of LAST, the patient should be observed for at least 2 hours after a CNS event and for 4-6 hours after a cardiovascular event, but clinical decision making should depend on the severity of the reaction.⁷

Approach to Improving Safety

This case highlights a lack of communication between the operating room (OR) team members concerning the safe dosing of local anesthetics, leading to the administration of nearly twice the recommended 'safe' dose of local anesthetic. It also highlights that the correct diagnosis and treatment of LAST in the operating room is critically important.

The anesthesiologist who plans to do a local anesthetic block in addition to surgeon-performed wound infiltration must advise the surgeon and other surgical team members of the safe total dose of local anesthetic that can be used for that patient, taking into consideration the weight of the patient and the type of local anesthetic used. Ropivacaine and levobupivacaine are safer, for this purpose, than racemic bupivacaine. The anesthesia provider must check constantly intraoperatively with the scrub nurses and the surgeon to ensure that they stay within the safe dose of the local anesthetic used.

This case highlights the importance of communication between team members to improve patient safety. In 2009, the World Health Organization (WHO) published [guidelines](#) for safe surgery,⁸ which recommended three phases of communication to improve patient safety in the operating room: (1) the period before induction of anesthesia, (2) the period after induction and before surgical incision, and (3) the period during

or immediately after wound closure but before moving the patient out of the operating room. In the second phase, each team member should introduce him or herself by name and role, confirm out loud that they are performing the correct operation on the correct patient and site and then verbally review with one another, in turn, the critical elements of their plans for the operation, using a checklist for guidance. Implementation of a 19-item surgical safety checklist based on these WHO guidelines was associated with significant reductions in death and complication rates across eight major hospitals.⁹

The Joint Commission's root cause analysis of 106 anesthesia-related sentinel events from 2004-2014 found that 57 were attributable to [communication failures](#) and 60 were attributable to human factors in general.¹⁰ In the United States, it is common for the entire surgical team to have a pre-induction "huddle", followed by a pre-incision "time out", and finally a "[debrief](#)" before the patient leaves the operating room. During the pre-induction huddle, information about any nerve blocks should be disclosed, along with guidance about how much additional local anesthetic can be safely administered. Similarly, before infiltration by the surgeon, there should always be a discussion about how much local anesthetic can be administered in adherence with published guidelines. It appears that these important discussions did not take place in this case, although the anesthesiologist's rapid diagnosis and intervention allowed the patient to recover without permanent sequelae.

Take-Home Points

- Widely published "safe" doses of local anesthetic should be adhered to.
- Communication between the OR team members must occur to minimize the risk of overdose.
- LAST can present with either CNS or CVS signs or symptoms, which are often non-specific.
- Effective treatment of LAST is multifactorial but the administration of intralipid is critical to a successful resuscitation.

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This project was funded under contract number 75Q80119C00004 from the Agency for Healthcare Research and Quality (AHRQ), U.S. Department of Health and Human Services. The authors are solely responsible for this report's contents, findings, and conclusions, which do not necessarily represent the views of AHRQ. Readers should not interpret any statement in this report as an official position of AHRQ or of the U.S. Department of Health and Human Services. None of the authors has any affiliation or financial involvement that conflicts with the material presented in this report. [View AHRQ Disclaimers](#)