Fall 2019

Developing a Local Anesthetic Systemic Toxicity Protocol in a Mississippi Hospital

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DEVELOPING A LOCAL ANESTHETIC SYSTEMIC TOXICITY PROTOCOL IN A MISSISSIPPI HOSPITAL

by

James Dearman and Terry Tieman

A Doctoral Project
Submitted to the Graduate School,
the College of Nursing and Health Professions
and the School of Leadership and Advanced Nursing Practice
at The University of Southern Mississippi
in Partial Fulfillment of the Requirements
for the Degree of Doctor of Nursing Practice

Approved by:

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ABSTRACT

Local anesthetic systemic toxicity (LAST) is a rare complication of administering local anesthetic medications. However, this complication is potentially deadly, especially without prompt and correct treatment. Due to the rarity of LAST and the fact that its treatment differs from the conventional treatment of cardiac arrest, the authors sought a best practice recommendation to guide its treatment. While the most effective treatment for LAST has been well established, a thorough review of literature and survey of clinical preceptors demonstrated that most providers have not encountered LAST in clinical practice. Additionally, lipid emulsion therapy is a somewhat controversial treatment amongst some providers, even though its effectiveness is well documented.

This doctoral project sought to develop a best practice recommendation to guide the treatment of LAST events and increase the confidence of providers in their ability to recognize and treat LAST. The recommendation was developed after a thorough review of the literature. The information was used to create a report of findings that were presented to a panel of experts. Feedback from the expert panel revealed that the respondents have not encountered a LAST event in their clinical practice. They all agreed that this practice recommendation would potentially help to guide the correct treatment of LAST. Their feedback, along with the report of findings was subsequently used to develop an executive review that was sent to a hospital affiliated with the Nurse Anesthesia Program at The University of Southern Mississippi in which the evaluation was performed. The executive summary also included an education module for the anesthesia staff.

ACKNOWLEDGMENTS

James Dearman and Terry Tieman would like to thank their committee chair, Dr. Mary Jane Collins, for all her assistance, encouragement, and patience. Without help from Dr. Collins, this project would have been exponentially more difficult.

DEDICATION

James would like to dedicate this project to his wife and son for all their love, support, patience and welcomed distractions. Terry would like to dedicate this project to his wife and kids who have been so loving and patient in this journey. They would both like to thank the Nurse Anesthesia Program 2019 Cohort at The University of Southern Mississippi for their support as classmates.

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LIST OF ABBREVIATIONS

AACN	American Association of Colleges of Nurses
AAGBI	Association of Anaesthetists of Great Britain and Ireland
ACL	Anterior Cruciate Ligament
ASRA	American Society of Regional Anesthesia and Pain Medicine
CI	Confidence Interval
CNS	Central Nervous System
COPD	Chronic Obstructive Pulmonary Disease
CRNA	Certified Registered Nurse Anesthetist
DNP	Doctor of Nursing Practice
IRB	Institutional Review Board
Kg	Kilogram
LAST	Local Anesthetic Systemic Toxicity
L	Liter
NCBI	National Center for Biotechnology Information
mL	Milliliter
RCT	Randomized Control Trials
UGRA	Ultrasound Guided Regional Anesthesia
USM	The University of Southern Mississippi

CHAPTER I - INTRODUCTION

Local anesthetic systemic toxicity (LAST) is a rare, but potentially fatal complication of administering local anesthetic medications. LAST can quickly lead to the central nervous system and cardiac compromise (Tetzlaff, 2000). LAST treatment differs in a few key areas from conventional treatment of cardiac arrest and, therefore, should be approached in a different, more precise manner (Dillane & Finucane, 2009). For example, calcium channel blockers and lidocaine are commonly used to treat arrhythmias that arise in a patient with cardiac compromise (Tetzlaff, 2000). However, these medications will lead to a further decline in the patient experiencing a LAST event. While the most effective treatment for LAST has been well established, both review of literature and survey of clinical preceptors have shown that its rarity makes it a condition that most providers have not encountered in clinical practice (Manavi, 2010; Nedialkov, Umadhav, Valdes, & Campbell, 2018). According to a 2012 study, "the incidence (per 1000 blocks) of adverse events across all peripheral regional anesthetics was 1.8 (95% confidence interval [CI]" (Sites, Taenzer, Herrick, & Gilloon, 2012, p. 478). Additionally, lipid emulsion has been shown to drastically improve resuscitation following local anesthetic systemic toxicity although its use remains controversial among anesthesia providers (Nedialkov et al., 2018).

Problem Description

The operating room is a dynamic healthcare practice setting. Due to this ever-changing environment, crises dictate a rapid response from healthcare professionals. The occurrence of LAST is rare (Sites et al., 2012). Failure to treat or incorrect treatment of LAST has the potential to result in patient injury or death (Barash et al., 2017). A review

of the literature and informal interviews with anesthesia providers revealed that a knowledge deficit exists surrounding the treatment of LAST (Corcoran et al., 2006, p. 1324-1325; Appendix A). Potential negative consequences of the failure to manage LAST include central nervous system (CNS) toxicity, cardiac toxicity, and death (Dillane & Finucane, 2009). To address this gap in knowledge, a best practice recommendation was compiled based on current evidence-based literature. The best practice recommendation was further used to create a treatment protocol that was presented to anesthesia administration at a University of Southern Mississippi (USM) clinical affiliate hospital, along with an educational tool that can be used for certified registered nurse anesthetist (CRNA) education of the proposed protocol.

Available Knowledge

Local Anesthetics

Local anesthetics are medications used to stop the transmission of pain sensation by blocking the conduction of nerve impulses along nerve fibers (Lin & Liu, 2017, p. 564). To understand the pharmacodynamics of local anesthetics, one must have a basic knowledge of nerve conduction. The transmission of a nerve impulse relies on the existence of an electrical gradient across the nerve cell membrane. This gradient is established by the influx and efflux of sodium and potassium ions. The propagation of a nerve impulse begins when a sufficient electrical stimulus causes a change in the membrane potential to the level of threshold potential. This phenomenon leads to depolarization, which is a rapid influx of sodium ions through a voltage-gated sodium channel from the extracellular to the intracellular space. This voltage-dependent gate is located on the intracellular portion of the cell membrane. Local anesthetics work by

reversibly inhibiting the influx of sodium through these voltage-gated sodium channels, preventing the transmission of pain signals (Lin & Liu, 2017).

Benefits of Local Anesthetics Use in Anesthesia Practice

Neuraxial Anesthesia

Many studies have focused on the differences in morbidity and mortality following surgical procedures using general vs neuraxial anesthesia. A meta-analysis including over 3,000 patients found that neuraxial anesthesia (subarachnoid and epidural anesthesia) was associated with a low risk of death in the 30 days immediately following surgery (Barash et al., 2017). Neuraxial anesthesia was also found to decrease the risk of post-operative pneumonia. Another meta-analysis involving over 18,000 patients who had undergone surgery to treat hip fracture found that the use of neuraxial anesthesia was associated with decreased intra-hospital death and pulmonary complications (Barash et al., 2017).

Neuraxial anesthesia has also shown improved outcomes in specific patient populations. A small single-institution study found decreased postoperative pulmonary complications, arrhythmias, and shorter stays in intensive care for patients following lower extremity amputations when regional anesthesia was used instead of general anesthesia (Barash et al., 2017). Regional anesthesia has also been associated with decreased respiratory events in patients with chronic obstructive pulmonary disease (COPD), a condition that is known to cause complications in general anesthetics. A study of more than 14,000 patients undergoing knee arthroplasty found fewer wound infections, pneumonia, infections, and blood transfusions following regional anesthesia in comparison to general anesthesia (Barash et al., 2017). This same study also found a

shorter period of hospital stay for those patients who received neuraxial anesthesia. Interestingly, epidural anesthesia may be associated with an increased survival rate following cancer surgeries. The improved summary is attributed to the avoidance of immunosuppression that can occur with the use of general anesthesia and postoperative opioids (Barash et al., 2017). Epidural and spinal anesthesia are the techniques of choice for analgesia for labor and cesarean section, due to the prevention of unwanted drug delivery to the fetus.

Peripheral Nerve Blockade

Regional anesthesia allows the provider to administer long-acting anesthesia and analgesia to a specific site of the body. Regional anesthetic techniques can be implemented in a wide variety of surgical procedures. According to Barash et al. (2017), peripheral nerve blockade can reduce mortality and morbidity, and the need for additional surgical intervention following major surgical procedures. Peripheral nerve blockade is also associated with greater analgesia and improved patient satisfaction. Another study of randomized control trials demonstrated that single-shot peripheral nerve blocks were associated with decreased pain, decreased the need for a "rescue" pain medication, decreased nausea and vomiting, and increased patient satisfaction scores (Cousins, Carr, Horlocker, & Bridenbaugh, 2009). Additionally, an observational study of ambulatory patients demonstrated a 76% decrease in unplanned hospitalizations following anterior cruciate ligament (ACL) repair surgery (Cousins et al., 2009). Continuous indwelling peripheral nerve blocks offer the additional benefit of extending the analgesia farther into the postoperative period (Barash et al., 2017).

Local Anesthetic Systemic Toxicity

LAST is a life-threatening event that results from local anesthetic reaching significant systemic circulating levels. The symptoms of LAST most frequently appear within the first few minutes of injection of a local anesthetic. The toxicity most likely occurs because of inadvertent intravascular injection of local anesthetic or injection of higher than the therapeutic dose (Barash et al., 2017). LAST symptoms occur in the central nervous system and/or the cardiovascular system. "The effects on the CNS are determined by the plasma concentration of the local anesthetic. At low plasma concentration, mild disturbances to the sensory systems appear. As the plasma concentration increases, CNS excitation and seizure activities predominate." (Barash et al., 2017, p. 575). Untreated, these CNS symptoms can lead to respiratory depression, coma, and eventually death. Cardiovascular symptoms are seen at a higher plasma concentration than that which leads to CNS symptoms (Barash et al., 2017). While all local anesthetics can cause hypotension, dysrhythmias and myocardial depression, more potent agents, such as bupivacaine, ropivacaine, and levobupivacaine, are predisposed to devastating outcomes such as cardiovascular collapse and complete heart block (Barash et al., 2017). "Surveys from France and the United States of over 280,000 cases involving regional anesthesia show an incidence of seizures of approximately 1/10,000 with an epidural injection, and 7/10,000 with peripheral nerve blocks" (Barash et al, 2017, p. 453). This study magnifies the benefit versus risk ratio associated with regional anesthesia.

The exact mechanism that induces LAST is not clearly understood. To quote Clinical Anesthesia (Barash, 2017), "The underlying pathophysiology responsible for

local anesthetic-induced cardiovascular collapse has not been fully established" (Barash et al., 2017, p. 576). "Local anesthetics readily cross the blood-brain barrier and, as a result, central nervous system toxicity can occur with systemic absorption or inadvertent intravascular injections" (Barash et al., 2017, p. 575). The ease of local anesthetic diffusion across the blood-brain barrier explains why in some cases, confusion and seizure activity precedes cardiovascular symptoms. An especially dangerous drug that can present with cardiac symptoms is bupivacaine. "Bupivacaine has an inherently greater affinity for binding resting and inactivated cardiac sodium channels than lidocaine" (Barash et al., 2017 p. 577).

Measures to Prevent LAST

The optimal approach to treating LAST is to prevent it. Some issues with the information on LAST treatment and prevention are associated with its infrequency and the ethical issues of studying it. According to a 2011 National Association of Biotechnology Information article by Sandhya Yaddanapudi (para. 2),

> … providers should be aware of and adhere to maximum dose recommendations of various local anesthetics. The current recommendations are not entirely based on scientific evidence. They have been extrapolated from animal experiments, case reports of LAST, and some pharmacokinetic studies because human randomized control trials (RCT) are difficult to conduct for ethical reasons.

With the morbidity and mortality associated with LAST, every effort should be made to prevent intravascular injection. According to the same study,

> No single intervention can reliably eliminate the risk of LAST. Several steps must be taken to avoid intravascular injection and elevated blood concentration of

> the LA during the performance of the regional technique. Aspiration before injection of LA and the use of an intravascular marker such as epinephrine reduces the likelihood of accidental intravascular injection to a large extent. (Yaddnapudi, 2011, para. 2)

The use of ultrasound-guided regional anesthesia (UGRA) is a topic that is being explored as a best practice guideline to prevent LAST. In theory, visualization of anatomic structures and medication spread should reduce adverse outcomes associated with regional anesthesia, including LAST. Due to the extreme rarity of this complication, a statistically significant difference between nerve localization techniques, if indeed any difference exists, will likely never be realized. Evidence is conflicting regarding whether UGRA results in true reduction of LAST (Neal & Richard, 2010).

Evidence-Based Practice for Treatment of LAST

The American Society of Regional Anesthesia and Pain Medicine (ASRA) updated the checklist for the management of LAST as recently as 2017. The recommendations are described as "fundamentally different from conventional cardiopulmonary resuscitation. Insofar as toxic cardiomyopathy differs from other causes of CV collapse" (Neal & Barrington, 2017, para. 5). These guidelines recommend early airway support over immediate cardiac support. This approach prioritizes the prevention of hypercarbia and subsequent acidosis that can potentiate LAST. This article states succinctly, "Successful treatment of LAST seeks to effectively moderate or reverse the mechanisms underlying the local anesthetic toxicity" (Neal & Barrington, 2017, para. 6). Data retrieved from rat studies reinforce the practice of administering small doses of epinephrine when patient condition indicates (1mcg/kg or less) (Barrington, 2017).

"Lipid therapy is recommended at the first sign of arrhythmia, prolonged seizures, or rapid clinical deterioration of the patient" (Neal & Barrington, 2017, para. 8). Multiple case reports demonstrate successful resuscitation following LAST when intralipid is used as early treatment (Valera & Burns, 2010). However, the use of intralipid therapy remains controversial among anesthesia providers (Nedialkov et al., 2018).

Existing Protocols

As stated before, in 2017 the ASRA updated the checklist for the treatment of local anesthetic system toxicity treatment. Recommendations by The Association of Anaesthetists of Great Britain and Ireland (2010) and Medscape (2019) echo the treatment described by the ASRA. The initial treatment suggested is to stop or limit the insulating substance and get assistance. If serious signs of LAST occur, consider lipid emulsion therapy immediately (ASRA 2017). Due to the gravity of a cardiovascular event from LAST, notifying the nearest cardiopulmonary bypass team is also recommended. Providers are encouraged to ventilate with 100% oxygen, avoid hyperventilation, and insert advanced airway if needed to control seizures. Benzodiazepines are the preferred method of seizure management. Propofol is to be avoided due to its cardiac depressive properties. If the patient weighs greater than 70 kilograms, a bolus of 100 milliliters 20% lipid emulsion over a 2-3-minute period is recommended, followed by an infusion of 200-250 milliliters over 15-20 minutes. For a patient less than 70 kilograms a bolus of 1.5 milligram/kilogram (ideal body weight) lipid emulsion over 2-3 minutes, followed with an infusion of 0.25 milligram/kilogram is recommended. With a dosing limit of 12 milligram/kilogram, the total volume of lipid emulsion can approach 1 liter in a prolonged resuscitation (ASRA, 2017).

Protocol Creation

Having standardized protocols in place for crises is imperative. The airline industry has gained a record of safety that has become an example of success in other professions. This success is largely attributed to protocols. Despite success in other industries, process standardization in healthcare has been slow to gain traction or to demonstrate a positive impact on the safety of care (Leotsakos, Zheng, & Croteau, 2014). The human variables of practitioners and sick patients are complex and often not easily predicted. A study in the International Journal for Quality in Health Care states, "In health care, evidence shows that divergent patterns of care result in worse clinical outcomes and that removal of variance can reduce risk, and costs" (Leotsakos et al., 2014, para. 8).

Rationale

Evidence shows many benefits of local anesthetic use, including decreased length of hospital stay, increased pain control, decreased pulmonary complications, decreased opioid use, and even increased survival rates in some cases (Baresh et al., 2017). For these reasons, the practice of regional anesthesia is on the rise. As with any anesthetic procedure, risks must be acknowledged and properly managed. True local anesthetic systemic toxicity is a rare event; thus, most anesthesia providers have not encountered it in training or clinical practice. This inconsistency leads to a possible gap in provider understanding of the proper treatment for LAST. Evidence shows that the use of checklists or protocols can improve the selection of the appropriate treatment modality in uncommonly encountered clinical events (Harrison, Manser, Howard, & Gaba, 2006; Ziewacz, Ariaga, Bader et al., 2011). Therefore, a LAST treatment checklist was

presented to ensure an effective treatment in the event of LAST. The evidence-based research indicates that this protocol is readily available in all operative environments where local anesthetics are to be administered (ASRA, 2017).

Specific Aims

From a review of the evidence and informal interviews with anesthesia providers, the authors have found that a knowledge deficit exists surrounding the treatment of LAST (Corcoran et al., 2006) (Appendix-C). This project aimed to develop a best practice guideline to direct the appropriate treatment of LAST. The rarity at which LAST is encountered in clinical practice predisposes providers to a gap in experience with its treatment. This project aimed to bridge that gap by providing an easily accessible and concise aid that can be readily used to guide providers in the treatment of local anesthetic systemic toxicity. The intent is that this checklist will increase providers' confidence in their ability to treat LAST, encouraging local anesthetics to use in their clinical practice.

DNP Essentials

This DNP project fulfilled all eight DNP Essentials set forth by the American Colleges of Nursing (AACN) (2006), as referenced in Appendix E. These essentials describe the fundamental competencies that are required for advanced practice nurses. The essentials also set forth the required elements of the curriculums of DNP programs.

Summary

Through informal interviews with anesthesia administration and CRNAs at a USM clinical affiliate hospital, it was determined that the hospital lacked a best practice clinical policy regarding the treatment for LAST, a rare yet potentially deadly complication of local anesthetic administration. Therefore, available knowledge was

examined to determine the best practice for the treatment of LAST. The research was consistent on the appropriate treatment for LAST (Association of Anesthetists of Great Britain and Ireland [AAGBI], 2010; ASRA, 2017), and the American Society of Regional Anesthesia and Pain Medicine has developed a checklist that includes the major points of LAST treatment (ASRA, 2017).

CHAPTER II – METHODS

Context

A current best practice investigation regarding local anesthetic systemic toxicity was conducted at a USM affiliate hospital in Mississippi. Through informal interviews with anesthesia administration and CRNAs and a review of literature, it was determined that some hospitals lacked a best practice clinical policy regarding the treatment for LAST. The 260-bed facility reported in 2016 an average total daily census of 134.6 patients. The hospital reported, 215 babies delivered in 2016 (Mississippi State Department of Health, 2018). According to Jason Coleman, CRNA, "this hospital provides surgical services, utilizing regional anesthesia with the administration of local anesthetics" (J. Coleman, personal communication).

Intervention, Study of Intervention, and Measures

Upon completion of clinical rotations at various surgical facilities in Mississippi, it was recognized that no distinct policy existed at a clinical affiliate hospital for the treatment of local anesthetic systemic toxicity. In addition, an informal survey of anesthesia providers demonstrated little experience with the treatment of LAST. Therefore, available knowledge was examined and synthesized to determine the best practice for the treatment of LAST. A literature search was performed to analyze best practice guidelines for LAST prevention and treatment. A secondary search was done to explore the benefits of using checklists, protocols, and/or cognitive aids in the treatment of anesthetic emergencies. Several databases including CINAHL, Cochrane, Google Scholar, and PubMed were used to find relevant articles. The following search terms were used: local anesthetic systemic toxicity, LAST treatment, LAST prevention,

anesthesia emergency protocol, and anesthesia cognitive aids. The initial search had limitations of publication dates between 2008 and 2018. This search resulted in 752 articles. The articles that were included in this project were chosen based on their relevance to the topic studied. Also, leading textbooks in the field of anesthesia were reviewed and the applicable sections selected for use in this project.

The literature review included the ASRA Checklist for Treatment of Local Anesthetic Systemic Toxicity and evidence that supports the steps on the list. Additional protocols by Medscape (2019) and The Association of Anaesthetists of Great Britain and Ireland (2010) concur on the appropriate LAST treatment. These protocols, along with the supporting peer-reviewed literature was used as a guide for the development of a policy recommendation regarding the treatment of LAST. Once the project was approved by the committee, it was submitted to the Institutional Review Board (IRB) with the intention to seek exemption for this project (IRB Protocol # 19-327, Appendix A).

The available knowledge was synthesized to compile a report of findings, as shown in Appendix C. This report of findings, along with the ASRA checklist for treatment of local anesthetic systemic toxicity was presented to a panel of experts (Appendix A). This panel of experts was assembled by way of face-to-face invitation. This group of the chosen facility personnel included the Chief CRNA, a pharmacist, a supervising registered nurse, and a health policy expert. The Chief CRNA was asked to join the panel of experts due to his expertise in anesthesia, as well as, his familiarity with the facility and its available resources. A pharmacist was included on the panel because of their pharmacological expertise and their knowledge of the availability, price, and storage requirements of medications. The panel also included a registered nurse who

supervises the block/preparation area, due to their knowledge of the block procedures and the resources available in this area where local anesthetics are frequently administered. Finally, the healthcare policy expert was included, because of her expertise and experience with health policy creation.

An evaluation tool, shown in Appendix D, was developed by the ASRA and was used to gather feedback on the presented data. The evaluation included the clarity of the presented information, the quality of the information, and relevance to practice. In addition, consideration was given to whether or not the best practice should be implemented, a space for additional comments was provided. The feedback was reviewed and no revisions to the policy recommendation were deemed necessary, nor to the executive summary (Appendix F). The executive summary containing the report of findings, the policy recommendation, and the associated educational module were then presented to the Chief CRNA for consideration of implementation. The participants were sent an anonymous survey link and asked not to include any identifying information on their surveys in order to keep their comments confidential. Data was kept on a personal password-protected laptop, and files were kept in a locked drawer. Data was retained until project completion, then all files were permanently deleted from the storage device and written documentation was shredded.

Analysis

Qualitative data was collected using an evaluation tool (Appendix D). The data was gathered in a face-to-face manner along with a presentation of the policy. The information was reviewed and entered into Table 1 where responses were given quantitative values. The data processing was accomplished before presenting the policy

recommendation along with the executive summary (Appendix F) along with an educational module for the CRNAs. Statistical analysis would have been of little value due to the small panel of experts and was therefore not done. A quantitative analysis from the provided feedback was performed to determine common feedback and concerns for the adoption of this evidence-based protocol.

Table 1

Survey Questions

Questions	Response 1	Response 2	Response 3
This best practice recommendation was presented clearly.	Strongly Agree	Strongly Agree	Strongly Agree
The presented information is of high quality.	Strongly Agree	Strongly Agree	Strongly Agree
The information is relevant to clinical practice.	Strongly Agree	Strongly Agree	Strongly Agree
Do you believe that this best practice recommendation should be implemented in your facility?	Yes	Yes	Yes
Please provide any additional comments and/or suggestions.	Add mock drills	Alternative to lipids if unavailable to facility	None

Ethical Considerations

The ethical considerations for this project were minimally related to all presented recommendations have been endorsed by leading anesthesia organizations and supported by evidence-based and peer-reviewed literature. Specific concerns center around the

facility's inability to provide access to intralipid or supplies as well as adherence to protocol. Limited access to the necessary supplies and knowledge deficit can lead to the potential of providing a level of care not based on the latest evidence-based research.

Summary

Informal interviews were done with anesthesia administration and anesthesia providers. After an analysis of the feedback, the data shows that many hospitals lack the best practice clinical policy regarding the treatment for local anesthetic systemic toxicity. A literature search was performed to analyze best practice guidelines for LAST prevention and treatment. The available knowledge was synthesized in order to compile a report of findings. This report of findings, along with the ASRA Checklist for Treatment of LAST, was be presented to a panel of experts. An evaluation tool was used to gather feedback on the presented data. The feedback guided revision of the policy recommendations and develop an executive summary. The executive summary and policy recommendation were then presented to the Chief CRNA for consideration of implementation.

CHAPTER III - RESULTS

This DNP project's goal was to develop the best practice recommendation for the treatment of local anesthetic systemic toxicity in a Mississippi hospital. A report of findings was presented to the panel of experts, along with the ASRA's checklist for Treatment of LAST, an evaluation tool (ASRA, 2017) was used to determine the quality of information presented, relevance to clinical practice, and potential for implementation of the protocol. Additionally, each responding member of the expert panel was provided the opportunity for further comments and suggestions in the form of the evaluation tool.

The panel of experts was comprised of the Chief CRNA, a pharmacist, a registered nurse frequently involved with regional anesthesia, and a health policy expert. Each member of this panel was chosen due to their familiarity with local anesthetic use, availability of resources, and familiarity with policy development. The responses and recommendations from this expert panel were reviewed and incorporated into an executive summary that was presented to the Chief of the Anesthesia Department for consideration, along with an accompanying educational module. The educational module featured a pre- and post-test based on the information in the executive summary. The project was intended that this module may be used in order to help with the implementation of this best practice recommendation.

One member of the panel of experts was not able to be reached at the time of the presentation. The responses are described in Table 1. All participants strongly agreed that the information was presented clearly. They also strongly agreed that the information was of high quality and relevant to clinical practice. Finally, all participants reported that this best practice recommendation should be implemented. None of the

panel members had ever experienced an event of LAST, echoing findings in the review of medical database literature that demonstrated the rarity of LAST occurrence. One participant had an additional comment, “this hospital practices mock drills to familiarize the staff with the location of needed supplies. The drill includes identifying the location of the intralipid medication.” The recommendation was added to the executive summary. Another recommendation was for an alternative to lipid infusion for hospitals that did not have access to it. While the literature does not support an alternative at this time, the best practice protocol that was recommended lists all the other steps that should be taken. Without the use of intralipid, cardiopulmonary bypass may be needed, as resuscitation may be prolonged (ASRA, 2018).

Summary

A best practice protocol was presented to a selected hospital-based panel of experts, along with a treatment checklist that was developed by the ASRA. The expert panel was then asked to complete an evaluation and provide any wanted comments or recommendations. All the respondents strongly agreed that the information was clearly presented, of high quality, and relevant to their practice. They also reported that the best practice recommendation should be followed in their facility. The recommended idea of mock drills to be prepared for a possible LAST event was an idea that is worthy of future research.

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CHAPTER IV – DISCUSSION

Summary

This project was undertaken with the intent of decreasing the potential negative consequences of LAST, while also increasing provider confidence in the ability to treat such events. The literature review led to the discovery of a Checklist for Treatment of LAST (ASRA, 2017). This checklist, along with supporting evidence, was used to develop a best practice recommendation that was presented to a panel of experts. The recommendation was presented to stakeholders at a USM affiliated hospital for input. The feedback was then used to reinforce an Executive Summary (Appendix F) that was sent to the panel upon completion.

Interpretation

The completed expert panel evaluations demonstrated the willingness to adopt this best practice recommendation into use. The panel also provided potential areas of improvement in the recommendation. These areas of recommended improvements included mock drills to reinforce the recommendations. Additionally, one panelist questioned the treatment options if lipids were not available, a concern that was addressed in the executive summary. The panel's responses and comments helped to solidify the information presented in the executive summary.

Limitations

This project's results were limited by the small sample size of the panel that was presented and offered the opportunity to evaluate this project. Presenting these findings to a larger audience would have provided the opportunity for more feedback and the potential for a wider range of responses. While the review of literature featured

information from a wide range of practices, the evaluation and expert panel were from one hospital.

Conclusion

In conclusion, this doctoral project intended to improve the recognition and treatment of LAST. From a review of the literature and informal interviews with anesthesia providers, the data showed that a knowledge deficit exists surrounding the treatment of LAST (Corcoran et al., 2006) (Appendix A). Potential negative consequences of the failure to manage LAST include CNS toxicity, cardiac toxicity, and death (Dillane & Finucane, 2009). A review of the literature was performed to identify the best practice for the treatment of LAST. This information was compiled into a Report of Findings that was then presented to a panel of experts. After presenting the information, the panel of experts was asked to fill out a brief evaluation and provide any comments they would like regarding the information provided. The panel unanimously agreed that this best practice recommendation should be adopted in their clinical practice. Their feedback was considered when developing the final executive summary, which was presented to the anesthesia department along with an education module (Appendix-F) to be used to improve knowledge of LAST in their department. Adoption of this best practice recommendation has the potential to prevent the CNS toxicity, cardiac toxicity, and deaths that may occur from improper recognition or treatment of LAST.

APPENDIX A – IRB Exemption

IRB-19-327 - Initial: Sacco Committee Letter – Exempt

irb@usm.edu
Tue 8/6/2019 12:40 PM

To: James Dearman <James.D.Dearman@usm.edu>; Mary Collins <Mary.J.Collins@usm.edu>; Terry Tieman <Terry.Tieman@usm.edu>; Michael Howell <Michael.Howell@usm.edu>; Michaela Donohue <Michaela.Donohue@usm.edu>

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NOTICE OF INSTITUTIONAL REVIEW BOARD ACTION

The project below has been reviewed by The University of Southern Mississippi Institutional Review Board in accordance with Federal Drug Administration regulations (21 CFR 26, 111), Department of Health and Human Services regulations (45 CFR Part 46), and University Policy to ensure:

- The risks to subjects are minimized and reasonable in relation to the anticipated benefits.
- The selection of subjects is equitable.
- Informed consent is adequate and appropriately documented.
- Where appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of the subjects.
- Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of all data.
- Appropriate additional safeguards have been included to protect vulnerable subjects.
- Any unanticipated, serious, or continuing problems encountered involving risks to subjects must be reported immediately. Problems should be reported to ORI via the Incident template on Cayuse IRB.
- The period of approval is twelve months. An application for renewal must be submitted for projects exceeding twelve months.

PROTOCOL NUMBER: IRB-19-327
PROJECT TITLE: Developing a Local Anesthesia Systemic Toxicity Protocol in a Mississippi Hospital
SCHOOL/PROGRAM: School of LANP
RESEARCHER(S): James Dearman, Terry Tieman, Mary Jane Collins

IRB COMMITTEE ACTION: Exempt
CATEGORY: Exempt
Category 2.(i). Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording). The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects.

APPROVED STARTING: August 6, 2019

Donald Sacco Jr.

Donald Sacco, Ph.D.
Institutional Review Board Chairperson

APPENDIX B – Literature Matrix

Table A1.

Literature Matrix

Date of Publication	Author/Editor's Name	Type of Evidence	Summary
February 2010	Manavi, M. V.	Literature Review	Evidence suggests that intralipid should be readily available in all areas where local anesthetics injections are performed and should be used as first-line treatment for local anesthetic toxicity. However, the slow adoption by providers may endanger patients.
October 2010	Varela, H., Burns, S. M.	Case Report	The increasing number of case reports involving the successful use of lipid emulsion for the treatment of local anesthetic toxicity demonstrates the viability of intralipid rescue as a treatment modality.

Table A1 (continued).

2017	American Society of Regional Anesthesia and Pain Medicine	Practice Advisory	This practice advisory provides recommendations pertaining to prevention, recognition, and treatment of local anesthetic systemic toxicity.
2017	Barash, P. G., Cullen, B. F., Stoelting, R. K., Cahalan, M. K., Stock, C. M., Ortega, R., Holt, N. F.	Book Chapter	The use of local anesthetics in the form of neuraxial and peripheral anesthesia has the potential to improve patient outcomes.
August 2018	Nedialkov, A. M., Umadhay, T., Valdes, J. A., Campbell, Y.	Best Practice and Review of Literature	Lipid rescue should be readily available and used as a first-line treatment for local anesthetic toxicity.

APPENDIX C – Report of Findings

LAST is a rare, but potentially fatal complication of administering local anesthetic medications. LAST can quickly lead to the central nervous system and cardiac compromise (Tetzlaff, 2000). This treatment differs in a few key areas from conventional treatment of cardiac arrest, and therefore should be approached in a different, more precise manner (Dillane & Finucane, 2009). For example, calcium channel blockers and lidocaine are commonly used to treat the arrhythmias that arise in a patient with cardiac compromise (Tetzlaff, 2000). However, these medications will lead to a further decline in the patient with LAST. While the most effective treatment for LAST has been well established, it was found through both reviews of literature and survey of clinical preceptors that its rarity makes it a condition that most providers have not encountered in clinical practice (Manavi, 2010; Nedialko et al., 2018). Additionally, lipid emulsion use remains controversial among anesthesia providers although it has been shown to drastically improve resuscitation following LAST (Nedialkov et al., 2018).

While the occurrence of LAST is rare, failure to treat or incorrect treatment of LAST has the potential to result in patient injury or death (Barash et al., 2017; Sites et al., 2012). From the review of the literature and informal interviews with anesthesia providers, evidence was found that a knowledge deficit exists surrounding the treatment of LAST (Corcoran et al., 2006). Potential negative consequences of the failure to manage LAST include CNS toxicity, cardiac toxicity, and death (Dillane & Finucane, 2009). To address this gap in knowledge, a best practice recommendation was compiled based on current evidence-based literature. The best practice recommendation was used to create a treatment protocol that will be presented to anesthesia administration at a

USM clinical affiliate hospital, along with an educational tool to facilitate dissemination of the information.

The symptoms of LAST most frequently appear within the first few minutes of injection of a local anesthetic. LAST most often occurs because of inadvertent intravascular injection of local anesthetic or a higher than the therapeutic dose (Barash, Cullen, & Stoelting, 2017). LAST symptoms occur in the central nervous system (CNS), and/or the cardiovascular system. CNS symptoms can lead to respiratory depression, coma, and eventually death. Cardiovascular symptoms are seen at a higher plasma concentration than that which leads to CNS symptoms (Barash et al., 2017). While all LA's can cause hypotension, dysrhythmias and myocardial depression, more potent agents, such as bupivacaine, ropivacaine, and levobupivacaine, are predisposed to devastating outcomes such as cardiovascular collapse and complete heart block (Barash et al., 2017). The exact mechanism that induces LAST is not clearly understood. To quote Clinical Anesthesia (Barash, 2017), "The underlying pathophysiology responsible for local anesthetic-induced cardiovascular collapse has not been fully established" (Barash et al., 2017, p. 576). "Local anesthetics readily cross the blood-brain barrier and, as a result, CNS toxicity can occur with systemic absorption or inadvertent intravascular injections" (Barash et al., p. 575). The ease of diffusion across the blood-brain barrier explains why in some cases, confusion and seizure activity precedes cardiovascular symptoms. An especially dangerous drug that can present with cardiac symptoms is bupivacaine. "Bupivacaine has an inherently greater affinity for binding resting and inactivated cardiac sodium channels than lidocaine" (Barash et al., 2017 p. 577).

Prevention of LAST

With the morbidity and mortality associated with LAST, every effort should be made to prevent intravascular injection. No single intervention has been proven to definitively eliminate the risk of LAST. Steps must be taken to avoid intravascular injection and elevated blood concentration of the LA during the performance of the regional technique. "Aspiration prior to injection of LA and the use of an intravascular marker such as epinephrine reduces the likelihood of accidental intravascular injection to a large extent" (Yaddnapudi, 2011, para. 2). The use of ultrasound-guided regional anesthesia (UGRA) is a topic that is being explored. In theory, visualization of anatomic structures and medication spread should reduce adverse outcomes associated with regional anesthesia, including LAST. Due to the extreme rarity of this complication, a statistically significant difference between nerve localization techniques, if indeed any difference exists, will likely never be realized. However, there exists conflicting evidence of whether UGRA results in a true reduction of LAST (Neal & Richard, 2010).

Evidence-Based Practice for Treatment of LAST

The American Society of Regional Anesthesia and Pain Medicine (ASRA) updated the checklist for the management of LAST as recently as 2017. The recommendations are described as "fundamentally different from conventional cardiopulmonary resuscitation. Insofar as toxic cardiomyopathy differs from other causes of CV collapse" (Neal & Barrington, 2017, para. 5). These guidelines recommend early airway support over immediate cardiac support. This approach prioritizes the prevention of hypercarbia and subsequent acidosis that can potentiate LAST. This article states succinctly, "Successful treatment of LAST seeks to effectively moderate or reverse

the mechanisms underlying the local anesthetic toxicity" (Neal & Barrington, 2017, para. 6). Data retrieved from rat studies reinforce the practice of administering small doses of epinephrine when patient condition indicates (1mcg/kg or less) (Neal & Barrington, 2017). "Lipid therapy is recommended at the first sign of arrhythmia, prolonged seizures, or rapid clinical deterioration of the patient" (Neal & Barrington, 2017, para. 8). The exact mechanism of action for lipid therapy is unknown, but several theories exist. The "lipid sink" theory states that the intravenous infusion of lipids creates a lipid compartment in which the local anesthetic will be drawn, lowering the effective dose in the aqueous plasma (Manavi, 2010). Other theories are related to the lipids increasing available energy for cardiac muscle contraction (Nedialkov et al., 2018). Multiple case reports demonstrate successful resuscitation following local anesthetic toxicity when intralipid are used as early treatment (Valera & Burns, 2010). However, the use of intralipid therapy remains controversial among anesthesia providers (Nedialkov et al., 2018).

Existing Protocols

As stated before, in 2017 the American Society of Regional Anesthesia and Pain Medicine (ASRA) updated the checklist for the treatment of local anesthetic system toxicity treatment. Recommendations by The Association of Anaesthetists of Great Britain and Ireland (2010) and Medscape (2019) echo the treatment described by the ASRA. The initial treatment suggested is to stop or limit the insulating substance and get help. If serious signs of LAST occur, consider limpid emulsion therapy immediately (ASRA, 2017). Because of the gravity of a cardiovascular event from LAST, notifying the nearest cardiopulmonary bypass team is also recommended. Providers are

encouraged to ventilate with 100% oxygen, avoid hypoventilation, and insert advanced airway if needed to control seizures. Benzodiazepines are the preferred method of seizure management. Propofol is to be avoided due to its cardiac depressive properties. If the patient weighs greater than 70 kilograms, a bolus of 100ml 20% lipid emulsion over a 2-3-minute period is recommended, followed by an infusion of 200-250 milliliters over 15-20 minutes. For a patient, less than 70 kilograms a bolus of 1.5 milligrams-per-kilogram (ideal body weight) lipid emulsion over 2-3 minutes, followed with an infusion of 0.25 milligram-per-kilogram is recommended. With a dosing limit of 12 milligrams-per-kilogram, the total volume of lipid emulsion can approach 1 liter in a prolonged resuscitation (ASRA, 2017). The Checklist for Treatment of Local Anesthetic Systemic Toxicity is included at the end of this document.

Summary

There are many benefits of local anesthetic use, including decreased length of hospital stay, increased pain control, decreased pulmonary complications, decreased opioid use, and even increased survival rates in some cases (Baresh et. al., 2017). For these reasons, the practice of regional anesthesia is on the rise. As with any anesthetic procedure, there are always risks that must be acknowledged and properly managed. True LAST is a rare event; thus, most anesthesia providers have not encountered it in training or clinical practice. The rarity leads to a possible gap in provider understanding of the proper treatment for LAST. Evidence shows that the use of checklists or protocols can improve the selection of the appropriate treatment modality in uncommonly encountered clinical events (Harrison et al., 2006; Ziewacz et al., 2011). Therefore, a LAST treatment protocol is presented in order to ensure an effective treatment in the

event of LAST. The protocol will be recommended to be readily available in all operative environments where local anesthetics are to be administered.

AMERICAN SOCIETY OF REGIONAL ANESTHESIA AND PAIN MEDICINE

CHECKLIST FOR TREATMENT OF LOCAL ANESTHETIC SYSTEMIC TOXICITY (LAST)

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 not crucial)	
Greater than 70 kg patient	Less than 70 kg patient
Bolus 100 mL Lipid Emulsion 20% rapidly over 2-3 minutes • Lipid emulsion infusion 200-250 mL over 15-20 minutes	**Bolus 1.5 mL/kg Lipid Emulsion 20%** rapidly over 2-3 minutes • 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 (12mL/kg) • Total volume of lipid emulsion can approach 1 L in a prolonged resuscitation (e.g., > 30 minutes)	

- Continue monitoring
  - At least 4-6 hours after a cardiovascular event
  - Or, at least 2 hours 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
- See reverse side of this checklist for further details

Risk Reduction (Be sensible)

- Use the least dose of local anesthetic necessary to achieve the desired extent and duration of block.
- Local anesthetic blood levels are influenced by site of injection and dose. It is important to identify patients at increased risk of LAST prior to using local anesthetics, e.g., infants <6 months old, small patient size, advanced age and frailty, heart failure, ischemic heart disease, conduction abnormalities, or rhythm disorders, metabolic (e.g., mitochondrial) disease, liver disease, low plasma protein concentration, acidosis, and medications that inhibit sodium channels. Patients with very low ejection fraction are more sensitive to LAST and may be especially prone to elevated local anesthetic levels associated with 'stacked' injections.
- Consider using a pharmacologic marker and/or test dose, e.g. epinephrine 2.5 to 5 mcg/mL (total 10-15 mcg). Know the expected response, onset, duration, and limitations of a "test dose" in identifying intravascular injection.
- Aspirate the syringe prior to each injection while observing for blood in the syringe or tubing
- Inject incrementally, while observing for signs and inquiring for symptoms of toxicity between each injection.
- Consider discussing local anesthetic dose as part of the pre-procedural or pre-surgical pause ("time out").

Detection (Be vigilant)

- Monitor the patient during and after completing injection. Clinical toxicity can be delayed 30 minutes or longer.
- Use standard American Society of Anesthesiologists (ASA) monitors.
- Communicate frequently with the patient to query for symptoms of toxicity.
- Consider LAST in any patient with altered mental status, neurological symptoms or signs of cardiovascular instability after a regional anesthetic (e.g., change in HR, BP, ECG). Consider LAST even when the local anesthetic doses is 1) small (susceptible patient), 2) atypically administered (subcutaneous, mucosal, topical), 3) administered by the surgeon, or 4) after recent tourniquet deflation.
- Central nervous system signs (may be subtle, atypical, or absent)
  - Excitation (agitation, confusion, vocalization, muscle twitching, seizure)
  - Depression (drowsiness, obtundation, coma, or apnea)
  - Non-specific (metallic taste, circumoral numbness, diplopia, tinnitus, dizziness)
- Cardiovascular signs (occasionally the only manifestation of severe LAST)
  - Initially may be hyperdynamic (hypertension, tachycardia, ventricular arrhythmias), then
    - Progressive hypotension
    - Conduction block, bradycardia or asystole
    - Ventricular arrhythmia (ventricular tachycardia, Torsades de Pointes, ventricular fibrillation or asystole)
- Sedation may abolish the patient's ability to recognize or report LAST-related symptoms.

Treatment

Suggested components of a "LAST Rescue Kit"

- 1 L (total) lipid emulsion 20%
- Several large syringes and needles for administration
- Standard IV tubing
- ASRA LAST Checklist

- Administer lipid emulsion at the first sign of a serious LAST event.
- Lipid emulsion can be used to treat LAST caused by any local anesthetic.
- Standard dose epinephrine (1 mg) can impair resuscitation from LAST and reduce the efficacy of lipid rescue. Use smaller doses than typical for ACLS, e.g., ≤ 1mcg/kg boluses, or for treating hypotension.
- Propofol should not be used when there are signs of cardiovascular instability.
- Prolonged monitoring (2-6 hours) is recommended after any signs of LAST, since cardiovascular depression due to local anesthetics can persist or recur after treatment.
  - If LAST event is short-lived and without signs of cardiovascular instability, one may consider proceeding with surgery after an uneventful ~30 minute interval of monitoring.

Please report LAST events to www.lipidrescue.org

The Third American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Local Anesthetic Systemic Toxicity. Executive Summary 2017. Reg Anesth Pain Med 2018;43:113-123

The ASRA LAST™ smart phone app can be purchased from The Apple App Store or Google Play

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APPENDIX D – Evaluation Tool

Please circle your answers to the following questions.

1. This best practice recommendation was presented clearly.

Strongly Disagree Disagree Neutral Agree Strongly Agree

2. The presented information is of high quality.

Strongly Disagree Disagree Neutral Agree Strongly Agree

3. The information is relevant to clinical practice.

Strongly Disagree Disagree Neutral Agree Strongly Agree

4. Do you believe that this best practice recommendation should be implemented in your facility? Yes No

5. If you answered "No" to question 4, please briefly explain your answer.

_____

_____

_____

_____

_____

6. Please provide any additional comments and/or suggestions below.

_____

_____

_____

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APPENDIX E – DNP Essentials

Table A2.

DNP Essentials

DNP Essentials	Clinical Implications
Essential One: Scientific Underpinnings for practice	Research of evidence-based protocols to manage an anesthesia-crisis.
Essential Two: Organizational and Systems Leadership for Quality Improvement and Systems Thinking	Involving department leaders in the development of a cognitive aid to improve patient care.
Essential Three: Clinical Scholarship and Analytical Methods for Evidence-Based Practice	Synthesis and analysis of available knowledge for the treatment of local anesthetic systemic toxicity.
Essential Four: Information Systems/Technology and Patient Care Technology for the Improvement and Transformation of Health Care	Introduction of a cognitive aid to guide to improve patient outcomes from a potential anesthetic crisis.
Essential Five: Health Care Policy for Advocacy in Health Care.	This project advocates for the implementation of a cognitive aid for use in identifying and treating local anesthetic systemic toxicity.
Essential Six: Interprofessional Collaboration for Improving Patient and Population Health Outcomes	Communication with an interdisciplinary panel of experts on proposed protocol and seeking feedback on how to implement in a real-world situation.
Essential Seven: Clinical Prevention and Population Health for Improving the Nation's health	Potential prevention of negative sequelae by guiding the correct treatment of a LAST event.
Essential Eight: Advanced Nursing Practice	Interpreting available knowledge to determine best practice, identifying a relevant guideline, and assessing the potential implementation of said evidence into clinical practice.

APPENDIX F – Executive Summary

EXECUTIVE SUMMARY OF DEVELOPING A LOCAL ANESTHETIC SYSTEMIC TOXICITY PROTOCOL IN A MISSISSIPPI HOSPITAL

by

James Dearman and Terry Tieman

The University of Southern Mississippi

This document is an executive summary of full report Developing a LAST Protocol in a Mississippi Hospital. The student registered nurse anesthetists performed a literature review regarding the best practice recommendations for the treatment of LAST. These findings, along with a potential protocol for using best practice recommendations, were presented to a panel of experts to determine suitability for these recommendations in clinical practice.

Report of Findings

Local anesthetic systemic toxicity (LAST) is a rare, but potentially fatal complication of administering local anesthetic medications. LAST can quickly lead to the central nervous system and cardiac compromise (Tetzlaff, 2000). Its treatment differs in a few key areas from conventional treatment of cardiac arrest, and therefore should be approached in a different, more precise manner (Dillane & Finucane, 2009). For example, calcium channel blockers and lidocaine are commonly used to treat the arrhythmias that arise in a patient with cardiac compromise (Tetzlaff, 2000). However, these medications will lead to a further decline in the patient with LAST. While the most effective treatment for LAST has been well established, it was found through both reviews of literature and survey of clinical preceptors that its rarity makes it a condition that most providers have not encountered in clinical practice (Manavi, 2010; Nedialkov et al., 2018). Additionally, although lipid emulsion has been shown to drastically improve resuscitation following local anesthetic systemic toxicity, its use remains controversial among anesthesia providers (Nedialkov et al., 2018).

While the occurrence of LAST is rare, failure to treat or incorrect treatment of LAST has the potential to result in patient injury or death (Barash et al., 2017; Sites et al., 2012). With the recent movement towards reducing opioid use, as well as, the increasing use of ultrasound for peripheral nerve blocks, local anesthetics use is on the rise. From the review of the literature and informal interviews with anesthesia providers, the authors found that a knowledge deficit exists surrounding the treatment of LAST (Corcoran et al., 2006). Potential negative consequences of the failure to manage LAST include CNS toxicity, cardiac toxicity, and death (Dillane & Finucane, 2009). To address this gap in knowledge, a best practice recommendation was compiled based on current evidence-based literature. The best practice recommendation was used to create a treatment protocol that will be presented to anesthesia administration at a USM clinical affiliate hospital, along with an educational tool to facilitate dissemination of the information.

The symptoms of LAST almost always appear within the first few minutes of injection of a local anesthetic. LAST most often occurs because of inadvertent intravascular injection of local anesthetic or a higher than the therapeutic dose (Barash et al., 2017). LAST symptoms occur in the central nervous system (CNS), and/or the cardiovascular system. CNS symptoms can lead to respiratory depression, coma, and eventually death. Cardiovascular symptoms are seen at a higher plasma concentration than that which leads to CNS symptoms (Barash et al., 2017). While all LA's can cause hypotension, dysrhythmias and myocardial depression, more potent agents, such as bupivacaine, ropivacaine, and levobupivacaine, are predisposed to devastating outcomes such as cardiovascular collapse and complete heart block (Barash et al., 2017). The exact mechanism that induces LAST is not clearly understood. To quote Clinical Anesthesia

(Barash et al., 2017). “The underlying pathophysiology responsible for local anesthetic-induced cardiovascular collapse has not been fully established” (Barash et al., 2017, p. 576). “Local anesthetics readily cross the blood-brain barrier and, as a result, CNS toxicity can occur with systemic absorption or inadvertent intravascular injections (Barash et al., 2017). This action explains why in some cases, confusion and seizure activity precedes cardiovascular symptoms. An especially dangerous drug that can present with cardiac symptoms is bupivacaine. “Bupivacaine has an inherently greater affinity for binding resting and inactivated cardiac sodium channels than lidocaine” (Barash et al., 2017, p. 577).

Prevention of LAST

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Summary

Literature shows many benefits of local anesthetic use, including decreased length of hospital stay, increased pain control, decreased pulmonary complications, decreased opioid use, and even increased survival rates in some cases (Baresh et al., 2017). For these reasons, its practice is on the rise. As with any anesthetic procedure, there are always risks that must be acknowledged and properly managed. True local anesthetic systemic toxicity is a rare event; thus, most anesthesia providers have not encountered it in training or clinical practice. This leads to a possible gap in provider understanding of the proper treatment for LAST. Evidence shows that the use of checklists or protocols can improve the selection of the appropriate treatment modality in uncommonly encountered clinical events (Harrison, Manser, Howard, & Gaba, 2006; Ziewacz, Arriaga, Bader et al., 2011). Therefore, a local anesthetic systemic toxicity treatment protocol is presented in order to ensure an effective treatment in the event of LAST. It was recommended that this protocol be readily available in all operative environments where local anesthetics are to be administered. The authors also recommend that the pre- and post-test be used, as well as, mock drills in order to train the anesthesia staff on the proper treatment of LAST. Worth noting is the fact that in the event that lipids are not available, cardiopulmonary bypass may be needed, as resuscitation may be prolonged (ASRA, 2018).

AMERICAN SOCIETY OF REGIONAL ANESTHESIA AND PAIN MEDICINE

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  - Consider lipid emulsion therapy at the first sign of a serious LAST event
  - Call for the LAST Rescue Kit
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- Local anesthetic blood levels are influenced by site of injection and dose. It is important to identify patients at increased risk of LAST prior to using local anesthetics, e.g., infants <6 months old, small patient size, advanced age and frailty, heart failure, ischemic heart disease, conduction abnormalities, or rhythm disorders, metabolic (e.g., mitochondrial) disease, liver disease, low plasma protein concentration, acidosis, and medications that inhibit sodium channels. Patients with very low ejection fraction are more sensitive to LAST and may be especially prone to elevated local anesthetic levels associated with 'stacked' injections.
- Consider using a pharmacologic marker and/or test dose, e.g. epinephrine 2.5 to 5 mcg/mL (total 10-15 mcg). Know the expected response, onset, duration, and limitations of a "test dose" in identifying intravascular injection.
- Aspirate the syringe prior to each injection while observing for blood in the syringe or tubing
- Inject incrementally, while observing for signs and inquiring for symptoms of toxicity between each injection.
- Consider discussing local anesthetic dose as part of the pre-procedural or pre-surgical pause ("time out").

Detection (Be vigilant)

- Monitor the patient during and after completing injection. Clinical toxicity can be delayed 30 minutes or longer.
- Use standard American Society of Anesthesiologists (ASA) monitors.
- Communicate frequently with the patient to query for symptoms of toxicity.
- Consider LAST in any patient with altered mental status, neurological symptoms or signs of cardiovascular instability after a regional anesthetic (e.g., change in HR, BP, ECG). Consider LAST even when the local anesthetic doses is 1) small (susceptible patient), 2) atypically administered (subcutaneous, mucosal, topical), 3) administered by the surgeon, or 4) after recent tourniquet deflation.
- Central nervous system signs (may be subtle, atypical, or absent)
  - Excitation (agitation, confusion, vocalization, muscle twitching, seizure)
  - Depression (drowsiness, obtundation, coma, or apnea)
  - Non-specific (metallic taste, circumoral numbness, diplopia, tinnitus, dizziness)
- Cardiovascular signs (occasionally the only manifestation of severe LAST)
  - Initially may be hyperdynamic (hypertension, tachycardia, ventricular arrhythmias), then
    - Progressive hypotension
    - Conduction block, bradycardia or asystole
    - Ventricular arrhythmia (ventricular tachycardia, Torsades de Pointes, ventricular fibrillation or asystole)
- Sedation may abolish the patient's ability to recognize or report LAST-related symptoms.

Treatment

Suggested components of a "LAST Rescue Kit"

- 1 L (total) lipid emulsion 20%
- Several large syringes and needles for administration
- Standard IV tubing
- ASRA LAST Checklist

- Administer lipid emulsion at the first sign of a serious LAST event.
- Lipid emulsion can be used to treat LAST caused by any local anesthetic.
- Standard dose epinephrine (1 mg) can impair resuscitation from LAST and reduce the efficacy of lipid rescue. Use smaller doses than typical for ACLS, e.g., ≤ 1mcg/kg boluses, or for treating hypotension.
- Propofol should not be used when there are signs of cardiovascular instability.
- Prolonged monitoring (2-6 hours) is recommended after any signs of LAST, since cardiovascular depression due to local anesthetics can persist or recur after treatment.
  - If LAST event is short-lived and without signs of cardiovascular instability, one may consider proceeding with surgery after an uneventful ~30 minute interval of monitoring.

Please report LAST events to www.lipidrescue.org

The Third American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Local Anesthetic Systemic Toxicity. Executive Summary 2017. Reg Anesth Pain Med 2018;43:113-123

The ASRA LAST™ smart phone app can be purchased from The Apple App Store or Google Play

(ASRA, 2017).

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APPENDIX G – Pre- and Post-Test Evaluations

Pre-Test Evaluation

1. Management of a LAST event can be managed with standard ACLS protocols for optimal outcomes? True or False
2. The first line mediation for treatment of LAST induced seizures is. A. Propofol B. Intralipid C. Phenytoin D. Benzodiazepines
3. Which medication is proven to be the most beneficial in the treatment of LAST at the first sign of cardiac arrhythmia, prolonged seizures, or rapid clinical deterioration of the patient? A. Amiodarone B. Epinephrine C. Lidocaine D. Intralipid
4. The Initial dose of intralipid for a patient greater than 70 kg is? A. 50 ml B. 200 ml C. 100 ml D. 25 ml

Post Test Evaluation

1. Management of a LAST event can be managed with standard ACLS protocols for optimal outcomes? True or False
2. The first line mediation for treatment of LAST induced seizures is. A. Propofol B. Intralipid C. Phenytoin D. Benzodiazepines
3. Which medication is proven to be the most beneficial in the treatment of LAST at the first sign of cardiac arrhythmia, prolonged seizures, or rapid clinical deterioration of the patient? A. Amiodarone B. Epinephrine C. Lidocaine D. Intralipid
4. The Initial dose of intralipid for a patient greater than 70 kg is? A. 50 ml B. 200 ml C. 100 ml D. 25 ml

Answer Key:

1. False

2. D. Benzodiazepines

3. D. Intralipid

4. C. 100 ml

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