Intravenous Lidocaine: An Adjunct Treatment of Operative Pain

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Abstract

The purpose of this scholarly project was to assess the knowledge and understanding of intravenous lidocaine use as an adjunct to treatment of acute operative pain in the Student Registered Nurse Anesthetists (SRNA's) enrolled at Adventist University of Health Sciences. It is imperative for SRNA's to be cognizant of the side effects of opiate administration and establish proficiency in alternative pain treatment modalities. A literature review was conducted and demonstrated that lidocaine reduces patient's need for narcotics as treatment for post-operative pain and therefore reduces the amount of unwanted side effects resulting from narcotics by decreasing the quantity of narcotics used. The goal of this scholarly review was to increase the SRNA's awareness in the multimodal treatment of operative pain. Education was presented to SRNA's enrolled at Adventist University's Nurse Anesthesia program on October 5, 2017. A PowerPoint presentation was conducted as a formal educational presentation. Pre and post-tests underwent statistical analysis, a t-test for paired samples was conducted to analyze the data. The obtained t value (-11.275, $p < .001$) achieved statistical significance. Therefore, it can be concluded that the Power Point presentation was effective in increasing the SRNA's knowledge in the use of intravenous Lidocaine in the treatment of perioperative pain.

Keywords: Lidocaine, pain management, opiate, narcotic, analgesia, multimodal

Intravenous Lidocaine: An Adjunct Treatment of Operative Pain

Opioids are a well-accepted treatment of acute pain induced by surgical stimuli and included in most anesthesia plans. However, opiates regrettably are commonly associated with side effects such as lethargy, respiratory depression, nausea, vomiting, and constipation. Side effects may be difficult to manage and may extend the post-operative recovery time. Additionally, administration of opiates has also fallen under intense scrutiny as a growing epidemic of narcotic dependency plagues America. More than 2.5 million people begin abusing opioid painkillers each year, and prescription opioid abuse is now the second most common type of illegal drug use after marijuana (Whistler, 2012).

Anesthesia providers around the nation are making efforts to decrease opiate use in the peri-operative period. Development of Enhanced Recovery After Surgery (ERAS) protocols are directed toward multimodal pain management and limiting opioid administration. The protocol offers anesthesia providers an assortment of medications used to treat pain, including the use of lidocaine. This multimodal pain management technique aims to decrease the use of opiates and subsequently side effects caused by opiates. Therefore, it is important for SRNA's to be cognizant of not only the side effects caused by narcotic use, but also the potential for reducing both patient's need for narcotics and the amount of unwanted side effects from narcotics by decreasing narcotic use and adding lidocaine as an adjunctive treatment for pain.

The scholarly review focused on answering the following questions: In patients undergoing surgery, how does intravenous lidocaine, as an adjunct pain management use, compared to narcotics alone improve pain management throughout the perioperative period? In

Adventist University student registered nurse anesthetists, does an educational PowerPoint presentation regarding intravenous lidocaine use result in an increase in knowledge base?

Literature Review and Synthesis

Opioid use is prevalent in America for many types of surgeries. However, opioids come with a host of potential undesirable side effects, which in many cases can even delay patient's discharge from the hospital and subsequently burden the healthcare system with higher costs. The unwanted side effects from opioid use presents a clinical problem that warrants exploring, as some side effects are not only unpleasant but also delay discharge from the hospital. For example, slowed gastrointestinal motility is a common side effect which can delay discharge from the hospital, especially after abdominal surgery. McCarthy et al. (2010), found that intravenous lidocaine successfully reduced narcotic use and therefore avoided potential complications of opioids such as slowed bowels. Additionally, those patients who received lidocaine infusions had a 1.1-day reduction in the length of inpatient hospital time (McCarthy, 2010). Therefore, using opioid therapy alone instead of a combination of opioids with intravenous lidocaine resulted in a longer hospital stay due to the unwanted side effects from opioid therapy, which burdens the healthcare system with higher costs and puts patients at additional risks related to longer hospital stays.

Nausea associated with opioid use causes difficulty controlling post-operative pain with the use of oral pain medications; therefore, discharge from the hospital can be delayed until patient's pain can be controlled without the use of intravenous opioids. Most hospitals will not discharge patients if pain is not controlled by oral medications, as patients will not be able to receive intravenous opioids at home. Thus, the reduction of nausea is vitally important for patients to tolerate oral narcotics, facilitating discharge from the hospital. According to Kranke et

al. (2015), patients receiving lidocaine infusions peri-operatively had less nausea, which could be a result of less narcotic use (Kranke et al., 2015). Therefore, finding ways to reduce opioid use peri-operatively has many benefits for both the patient and the healthcare system, including reduction of nausea post-operatively, which can shorten hospital stays.

Unfortunately, surgeries by nature inflict pain and therefore some form of pain relief must be provided to patients for comfort post-operatively. Avoiding opioids completely is rarely feasible. According to McCarthy et al. (2010), lidocaine infusions reduce pain in patients undergoing several different types of surgeries. The design of this study involved reviewing data from three databases, then utilizing the Modified Oxford Scale as an instrument to measure the quality of the research collected. In order to account for variables, the study looked at 395 patients and used 369 controls. Results demonstrated that lidocaine drips caused "significant reductions in postoperative pain intensity and opioid consumption" (McCarthy et al., 2010). Furthermore, the study revealed an opioid consumption reduction of 85%. Therefore, this study demonstrates that opioid use can indeed be reduced by using intravenous lidocaine in the peri-operative period, and a combination of intravenous lidocaine with opioids for pain control is preferable to opioid use alone in pain control.

Intravenous lidocaine can be considered a method to reduce opioid use and negative side effects from opioids while still providing patients with pain relief. According to Kranke et al. (2015), lidocaine was found to be superior to placebo drugs in decreasing pain after various types of surgeries. The design of this study involved collecting data from four databases, then utilizing two separate pieces of research to apply exclusion criteria independently to measure results from 2802 patients. Results demonstrated that there is "low to moderate evidence" (Kranke et al.,

2015) of pain reduction after surgeries when lidocaine is used versus a placebo. Therefore, this study demonstrates that intravenous lidocaine is preferable to a placebo in controlling pain.

According to Grady et al. (2012), pain levels in fifty patients with lidocaine infusions during laparoscopic surgeries on female reproductive organs were reduced. The design of this study involved placebos and the double-blind method of research, which then utilized a verbal pain scale as an instrument to measure pain levels in both the placebo group and the lidocaine drip group of patients. In order to account for variables, the researchers "analyzed using descriptive and inferential statistics" (Grady et al., 2012). Results demonstrated that the group of patients receiving lidocaine infusion reported less pain on the third day after surgery compared to patients who received a placebo infusion. Implications of this study are that lidocaine can reduce pain post-operatively. Patients who experience less pain during the post-operative period will require a reduced quantity of narcotics compared to patients who report high levels of pain, therefore negative side effects from opioids can be abridged secondary to reduced narcotic requirement. Evidence quality was noted to be high, with $P = 0.02$ and no biases, methodological flaws, inconsistency, indirectness, imprecision, or publication bias noted.

According to Farag et al (2013), administration of intravenous lidocaine in the perioperative period during surgical interventions on the spine reduces pain and therefore decreasing opioid requirements the first two days after surgery (Farag et al., 2013). The study used lidocaine and a placebo in the setting of spinal surgery and immediately postoperatively on 116 adult patients and evaluating their pain using a verbal pain scoring system. In order to account for variables, the researchers "evaluated multivariable bidirectional noninferiority on both outcomes; superiority on either outcome was then evaluated only if noninferiority was established" (Farag et al., 2013). Results reveled lidocaine outperformed the placebo when

measured by the verbal response scale of pain ratings than the placebo group of patients. Therefore, the use of intravenous lidocaine peri-operatively outperforms any positive effects from the use of a placebo medication in patients recovering from surgery. Implications of this study are that lidocaine should be considered in the perioperative period for patients undergoing spinal surgery, and one could deduce the possibility of benefits during other surgery types based on this study. Evidence quality was noted to be high, with $P < 0.001$ on the verbal response scale and no biases, methodological flaws, inconsistency, indirectness, imprecision, or publication bias noted.

Khan et al. (2016) attempted to pinpoint the optimum lidocaine infusion time to decrease pain during the post-operative period. The design of this study involved a review of data from surgeries where lidocaine was discontinued sixty minutes or less after surgery stop time and surgeries where lidocaine was discontinued later than sixty minutes after surgery stop time in the setting of bowel operations. Researchers utilized data from six databases as instruments to measure a quantitative analysis. In order to account for variables, the researchers used the "random-effects model" (Khan et al., 2016), and results demonstrated that that running a lidocaine drip for longer than sixty minutes after surgery stop time does not add to the benefits of pain control and reducing post-operative complications such as gastrointestinal slowing. Implications of this study are that lidocaine infusions are useful only up to an hour after surgery, and more studies are needed to determine exactly how much time the infusion should be run. The study does, however, confirm the useful effect of lidocaine in patients during the post-operative period, which can result in less opioid use and therefore less negative side effects resulting from narcotic administration. Evidence quality was noted to be high, with $P <0.001$ and no biases, methodological flaws, inconsistency, indirectness, imprecision, or publication bias noted.

Reducing opioid use by supplementing with intravenous lidocaine can still be beneficial and can reduce negative side effects from opioids since less opioids are required. According to McCarthy et al. (2010), lidocaine drips resulted in a 1.1-day reduction in the length of inpatient hospital time, a 23-hour reduction in post-operative delay of flatus, and a 28-hour reduction of post-operative delay of bowel movements (McCarthy et al., 2010). Implications of this study are that lidocaine may successfully be used to reduce narcotic use and therefore avoid potential complications of opioids such as slowed bowel function. Reduction of opioid use is important in our own clinical setting, as many hospital systems are investigating ways to reduce the undesirable side effects from opioids and discover ways to reduce the amounts of opioids that patients require post-operatively. A reduced length of hospital stay saves the healthcare system money, which is a positive outcome to using intravenous lidocaine. Return of bowel motility is important post-operatively due to complications that can occur from bowel stasis, and therefore intravenous lidocaine use can reduce the risk of complications from delayed flatus and bowel movements.

In conclusion, this literature review demonstrates that intravenous lidocaine combined with opioid use, outperforms the use of opioids alone in controlling post-operative pain (Grady et al., 2012), reduces the negative side effects caused by opioids (McCarthy et al., 2010), and outperforms placebo drugs used to control pain (Farag et al., 2013 and Kranke et al., 2015). Therefore, SRNA's should be educated about the benefits of intravenous lidocaine use and implement intravenous lidocaine use into their own clinical practice and provide a reasonable rationale for the peri-operative use of intravenous lidocaine. More studies are needed to determine optimal duration of peri-operative lidocaine infusions (Khan et al., 2016), however the

benefits of intravenous lidocaine in reducing side effects from opioids has clearly been demonstrated.

Contribution, Dissemination, and Justification

This scholarly review contributed to the awareness of alternative medication for treatment of operative pain, specifically intravenous lidocaine. Additionally, the benefits of intravenous lidocaine over opiate use was discussed. We strived to increase the knowledge base of our target population, which was SRNAs enrolled at Adventist University. We disseminated per our project timeline, which included gathering research, compiling a presentation, and presenting to the SRNAs in the fall of 2017. We aimed to increase the SRNAs knowledge of intravenous lidocaine for treatment of operative pain.

Project Aims

Anesthesia providers should be familiar with alternative methods of pain treatment. The purpose of this scholarly project was to increase Student Registered Nurse Anesthetists (SRNA's) enrolled at Adventist University of Health Sciences (ADU) knowledge of intravenous lidocaine in the treatment of operative pain. A lecture was presented to the SRNA's at ADU on October 5, 2017. Pre- and post-test evaluations were conducted to establish the effectiveness of the lecture presentation. The aim was that the post-test evaluation scores would reflect higher scores, demonstrating an increase in knowledge.

Project Methods

The design of this study included preparing an educational presentation for SRNA's, assessing their baseline knowledge, and comparing it to their post-presentation test scores to assess the level of knowledge increase. The setting was the SRNA classroom per ADU faculty, the targets of this intervention were the SRNA's, and recruitment methods was not necessary due

to the required attendance of SRNA's. Inclusion criteria encompassed the 54 SRNA's in the 2017 and 2018 cohorts present in class that day. Any SRNA's not present in class that day were excluded from data collection and evaluation. After administering an informed consent (Appendix A), the implementation strategy was to first assess the SRNA's baseline knowledge with the use of a pre-test (Appendix B), then to present a PowerPoint (Appendix C) with information regarding the benefits of lidocaine use. Finally, a post-test was administered to determine if the presentation was effective in increasing the SRNA's knowledge on the use of intravenous lidocaine.

The participants' privacy was protected using a number system so that all students remain anonymous, scores are compared based only on the number assigned to each envelope containing both the pre and post tests. Data storage was via paper and stored in a folder until the comparison analysis was complete, at which point all tests were destroyed via shredder. The only people to have access to the pre and post tests were the two persons conducting the study.

Timeline

Application for Scientific Review Committee (SRC) and Institutional Review Board (IRB) was submitted through the research office at Adventist University Web-based Research Project Submission Process. Data collection was initiated May 2017 with the completion of this paper. On June 27,2017, we submitted our completed SRC/IRB application with all required attachments in a Word Document. On July 16, 2017, we completed the Web-Based Scholarly Project Application and submitted applications for SRC, IRB, and GMC review to the research office through the ADU Web-based Research Project Submission Process. On August 28, 2017, the research office notified us about the summary of the SRC review and submitted the study proposal to the IRB. On September 28, 2017, we submitted a copy of the research office's

notification regarding the results of the SRC review. Final approval was received on October 4, 2017, and we presented our project to the SRNA cohorts enrolled in MSNA 501 and MSNA 504 on October 5, 2017. Post implementation data was collected from SRNA's immediately following the presentation on October 5, 2017, via post-tests.

Data Collection Plan

Each SRNA was required to sign and submit an informed consent (see Appendix A) prior to participation. Data for the scholarly project was collected using tests given to SRNAs. Prior to the presentation, participants were provided with a pre-test to assess baseline knowledge. We also provided a post-test in an envelope which was completed at the end of the presentation. Participants were instructed not to open the envelope containing the post-test until after the presentation was complete. Pre-tests were collected prior to the start of the presentation. Each set of tests was correlated with a numerical value placed at the top right-hand corner of the pre and posttest. The numerical system ensured that the pre-test and post-tests were completed by the same student. The test consisted of fifteen questions pertaining to the use of intravenous lidocaine as a treatment of post-operative pain in surgical patients.

Paper tests were kept in a folder located at the home of Cindy Baggelaar-Reyes and shredded once tests were evaluated for scores. Electronic data in the form of test scores were kept on the personal computer of Cindy Baggelaar-Reyes until completion of the Nurse Anesthesia program at Adventist University. After graduation all electronic data will be deleted from personal computers. The laptop will be secured with password protection.

Evaluation Plan

The scholarly project was submitted to ADU Scientific Review Committee (SRC) and the Institutional Review Board (IRB). Test questions contained content including dosing,

indications, side effects, adverse effects, contraindications, and potential benefits of intravenous lidocaine. All questions were configured in the form of multiple choice questions, allowing for analysis without interpretation of qualitative data analysis. Data collection underwent quantitative analysis, the pre and post-tests were evaluated to determine the total percentage correct on each individual test. Statistical analysis utilizing SPSS was performed, including a t-test, to determine the percentage increase of the post test. Data analysis was presented in the form of a chart including the mean, sample size, standard deviation, and standard error mean for both the pre-test and post-test. Success was defined as a knowledge increase on post test scores.

Limitations

Limitations to this study include a small homogenous sample of participants located in one specific setting. The sample size was 50 students, which is a small number with which to base conclusions. The SRNAs, while possibly from diverse backgrounds both personally and professionally, are homogenous in that they are all students enrolled in the same school and taking the same classes. Only one single site was used for this assessment since it took place in a one hour period of time in one classroom. Post-test evaluation was conducted immediately following the educational presentation, this reflects only short-term knowledge. It would be beneficial to conduct further evaluation at a longer time-point after the educational presentation to determine the long-term knowledge retention. Additionally, a questionnaire would be beneficial at that time to evaluate the SRNA's use of intravenous lidocaine in the clinical setting.

Findings

Prior to the presentation, participants were provided with a pre-test to assess baseline knowledge. Pre-tests were collected prior to the start of the presentation. A presentation titled, "Intravenous Lidocaine: An Adjunct Treatment of Operative Pain" was provided to Student

Nurse Anesthetists enrolled at Adventist University College of Health Sciences on October 5, 2017. After completion of the educational presentation, students completed a post-test. Each set of tests was correlated with a numerical value placed at the top right-hand corner of the pre and posttest. The numerical system ensured that the pre-test and post-tests being evaluated were completed by the same student. The tests consisted of fifteen questions pertaining to the use of intravenous lidocaine as a treatment of post-operative pain in surgical patients.

The sample size population was 50 SRNA's however, only 48 reposes were used for statistical analysis. One student completed a pre test however, failed to complete a post test and the other student completed a post test however did not complete a pre test. Both responses were omitted because pre and post test scores could not be compared. Statistical analysis was conducted, a t-test for paired samples was conducted to analyze the data. The pre test mean value was 3.8750 with a standard deviation of 1.85226. The post test mean value was 7.8542 with a standard deviation of 1.83337. A 95% confidence interval was achieved at a lower limit of -4.68914 and an upper limit of -3.26920. Additionally a paired sample test was performed and a t-value of -11.275 was achieved with a *P*-value of <.001 (Appendix D).

Conclusion

It can be concluded that the post-test mean score is significantly higher than the pre-test mean score, implying that the educational presentation improved the SRNA's knowledge of intravenous Lidocaine. Limitations to this study include a small homogenous sample of participants located in one specific setting. The small sample size of 50 students, is a small number with which to base conclusions. The SRNA's, while possibly from diverse backgrounds both personally and professionally, are homogenous as far as all being students enrolled in the same school and taking the same classes. Only one single site was used for the assessment since

it took place in a one hour period of time in one classroom. Post-test evaluation was conducted immediately following the educational presentation, this reflects only short-term knowledge. It would be beneficial to conduct further evaluation at a longer time-point after the educational presentation to determine the long-term knowledge retention. Additionally, a questionnaire would be beneficial at that time to evaluate the SRNA's use of intravenous Lidocaine in the clinical setting.

References

Farag, E., Ghobrial M, .Sessler, D., Dalton J., Liu, J., Lee, J., Zaky, S. Benzel, E., Bingaman,W., Kurz, A. (2013). Effect of perioperative intravenous lidocaine administration on pain, opioid consumption, and quality of life after complex spine surgery. *Anesthesthesiology , 119*(4), 932-940. doi:10.1097/ALN.0b013e318297d4a5.

Grady, P., Clark, N., Lenahan, J., Oudekerk, C., Hawkins, R., Nezat, G., & Pellegrini, J. E. (2012). Effect of intraoperative intravenous lidocaine on postoperative pain and return of bowel function after laparoscopic abdominal gynecologic procedures. *AANA Journal, 80*(4), 282-288. Retrieved from http://www.aana.com/newsandjournal/Pages/aanajournalonline.aspx

Khan, J., Yousuf, M., Victor, C., Sharma, A., Siddiqui, N., (2016). An estimation for an appropriate end time for an intraoperative intravenous lidocaine infusion in bowel surgery: A comparative meta-analysis. *Journal of Clinical Anesthesia*. *28* 95,-104. Retrieved from https://www.journals.elsevier.com/journal-of-clinical-anesthesia/

Kranke P, Jokinen J, Pace NL, Schnabel A, Hollmann MW, Hahnenkamp K, Eberhart LHJ, Poepping DM, Weibel S (2015). Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery. *Cochrane Database of Systematic Reviews*. doi: 10.1002/14651858.CD009642.pub2.

McCarthy, G., Megalla, S., & Habib, A. (2010). Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery: A systematic review of randomized controlled trials. *Drugs, 70*(9), 1149-1163. doi:10.2165/10898560-000000000-00000

Menendez, M. E., Ring, D., & Bateman, B. T. (2015). Preoperative opioid misuse is associated

with increased morbidity and mortality after elective orthopaedic surgery. *Clinical Orthopaedics and Related Research, 473*(7), 2402-2412. doi:10.1007/s11999-015-4173-5

Whistler, J. (2012). Examining the role of mu opioid receptor endocytosis in the beneficial and side-effects of prolonged opioid use: From a symposium on new concepts in mu-opioid pharmacology. *Drug and Alcohol Dependence, 121*(3), 189-204. Retrieved from https://www.journals.elsevier.com/drug-and-alcohol-dependence/

Appendix A

ADU NAP SCHOLARLY PROJECT – INFORMED CONSENT

Our names are Cindy Baggelar-Reyes and Rebecca Maupin, and we are MSNA students in the Nurse Anesthesia Program (NAP) at Adventist University of Health Sciences (ADU). We are doing a Scholarly Project called *Intravenous Lidocaine: An Adjunct Treatment of Operative Pain*. This project is being supervised by Manuel Tolosa, DNAP. We would like to invite you to participate in this project. The main purpose of this form is to provide information about the project so you can make a decision about whether you want to participate.

WHAT IS THE PROJECT ABOUT?

The purpose of this project is to assess the knowledge and understanding of intravenous lidocaine use as an adjunct to treatment of acute operative pain in the Student Registered Nurse Anesthetists (SRNA's) enrolled at Adventist University of Health Sciences

WHAT DOES PARTICIPATION IN THIS PROJECT INVOLVE?

If you decide to participate in this project, you will be asked to complete an anonymous pre-assessment, attend a classroom presentation, and then complete an anonymous post-assessment. The assessment will address intravenous lidocaine. Your participation by attendance at the presentation and completion of the survey is anticipated to take approximately 15 minutes.

WHY ARE YOU BEING ASKED TO PARTICIPATE?

You have been invited to participate as part of a convenience sample of students currently enrolled in the ADU NAP. Participation in this project is voluntary. If you choose not to participate or to withdraw from the project, you may do so at any time.

WHAT ARE THE RISKS INVOLVED IN THIS PROJECT?

Although no project is completely risk-free, we don't anticipate that you will be harmed or distressed by participating in this project.

ARE THERE ANY BENEFITS TO PARTICIPATION?

We don't expect any direct benefits to you from participation in this project. The possible indirect benefit of participation in the project is the opportunity to gain additional knowledge intravenous lidocaine.

HOW WILL THE INVESTIGATORS PROTECT PARTICIPANTS' CONFIDENTIALITY?

The results of the project will be published, but your name or identity will not be revealed. To maintain confidentiality of assessments, the investigators will conduct this project in such a way to ensure that information is submitted without participants' identification. Participants' privacy will be protected using a number system so that all students remain anonymous, scores are compared based only on the number assigned to each envelope containing both the pre and post test assessments.. Thus, the investigators will not have access to any participants' identities.

WILL IT COST ANYTHING OR WILL I GET PAID TO PARTICIPATE IN THE PROJECT?

Your participation will cost approximately 15 minutes of your time, but will require no monetary cost on your part. You will not be paid to participate.

VOLUNTARY CONSENT

By signing this form, you are saying that you have read this form, you understand the risks and benefits of this project, and you know what you are being asked to do. The investigators will be happy to answer any questions you have about the project. If you have any questions, please feel free to contact Cindy at

Cindy.Baggelaar-reyes@my.adu.edu .If you have concerns about the project process or the investigators, please contact the Nurse Anesthesia Program at (407) 303-9331.

_____ **Date** _____

Participant Signature/ Participant Name (PRINTED LEGIBLY)

_____ **Participant Name (PRINTED LEGIBLY)**

Appendix B

Intravenous Lidocaine: An Adjunct Treatment of Operative Pain

1. Which of the following is responsible for the metabolism of Lidocaine?
   A. Lungs
   B. CYP450 3A4
   C. Kidneys
   D. Hoffman
2. Which of the following is false about Lidocaine?
   A. Possesses anti-inflammatory properties
   B. Inhibits release of pro-inflammatory cytokines
   C. Is a local anesthetic
   D. Causes leukocyte adhesion
3. What level of Lidocaine plasma level results in systemic analgesia?
   A. <5 µg/mL
   B. 10 µg/mL
   C. 15 µg/mL
   D. 20 µg/mL
4. Which of the following is true regarding the analgesic effects of Lidocaine?
   A. Causes an action in the CNS
   B. Affects peripheral nerves and cutaneous nerve endings
   C. Can treat chronic neuropathic pain
   D. Can predict efficacy for oral Na+ channel blocking drugs such as mexiletine
   E. All of the above
5. What percentage can epinephrine prolong the duration of lidocaine by?
   A. 20%
   B. 30%
   C. 40%
   D. 50%
6. Lidocaine works on sodium channels in the ____ state.
   A. Open/Inactivated
   B. Closed/Deactivated
   C. Closed/Resting
   D. All of the above
7. Lidocaine is an anti-arrhythmic drug class _____.
   A. Ib
   B. IIa
   C. IIb
   D. IIIa
8. Which of the following drugs is similar to Lidocaine?
   A. Phenytoin
   B. Tocainide
   C. Amiodarone
   D. Mexiletine
9. Lidocaine is contraindicated in which of the following cardiac conditions?
   A. Ventricular tachycardia
   B. Ventricular fibrillation
   C. Premature ventricular contractions
   D. Sinus bradycardia
10. Lidocaine causes which of the following effects of vasculature?
    A. Massive vasoconstriction
    B. Peripheral vasoconstriction
    C. Vasodilation
    D. Arterial vasospasms

Appendix C

INTRAVENOUS LIDOCAINE: AN ADJUNCT TREATMENT OF OPERATIVE PAIN

Presenters: Cindy Baggelaar-Reyes, RN, BSN, SRNA , Rebecca Maupin, RN, BSN, SRNA
Project Mentor: Adam Billen, BSN, MSNA, CRNA
Committee chair: Manuel Tolosa, DNAP, CRNA
Adventist University of Health Sciences

Objectives

By the end of the presentation, the audience members should be able to:

- Identify the risks opioid use
- Describe the benefits of using Intravenous Lidocaine
- Integrate Intravenous Lidocaine as an adjunct treatment of operative pain

Introduction

Opioids

- Universal treatment for acute surgical pain
- Side effects extend post-operative recovery time
- Abused by >2.5 million new people annually
- Second most abused drug after marijuana

Lidocaine

- Decreases opiate use after surgery
- Blunts pain pathways at receptor level
- Decreases post-operative pain scores
- Decreases length of stay after surgery

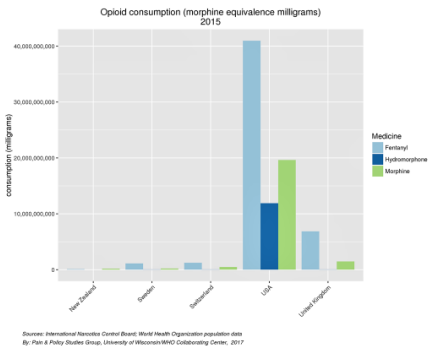
(ASAM, 2016)
(Whistler, 2012)

Opiates as Universal Treatment

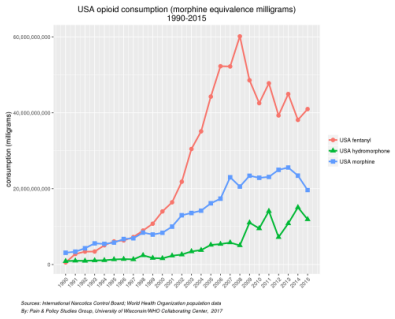
- In 1805 morphine isolated from opium
- Opioids are now a mainstay treatment for painful surgical stimuli
- Approximately 80% of the global opioid supply is consumed by US
- Hydrocodone, oxycodone, morphine, and hydromorphone significantly increased
- 200% increase opioid overdose deaths since 2000

(CDC, 2016)
(ASAM, 2016)

Global Picture



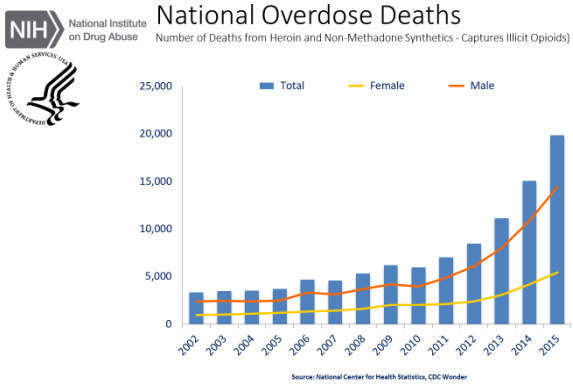
Annual US Consumption



Rising Opioid Use

- Over 249 million opioid prescriptions in 2013
- 300% increase in opioid prescription sales since 1999
- As many as 1 in 4 receiving long term opioid therapy struggle with opioid addiction

National Overdose Deaths



Public Health Threat

- Bridge from prescription opiate to heroin
- illicitly manufactured fentanyl is a significant threat to public health
- Heroin laced with fentanyl and carfentanil
- Sept 22, 2016 US DEA released warning about carfentanil

(CDC, 2016)
(DEA, 2016)

Opioid Side Effects

Common Side Effects

- Nausea
- Slowed Gastrointestinal Motility
- Constipation
- CNS Depression
- Pruritus

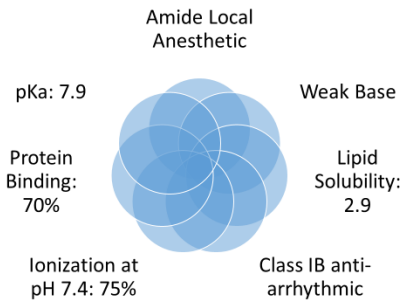
Less Common Side Effects

- Urinary Retention
- Myoclonus
- Hyperalgesia
- Seizure
- Respiratory Depression

(Stoelting, 2015)

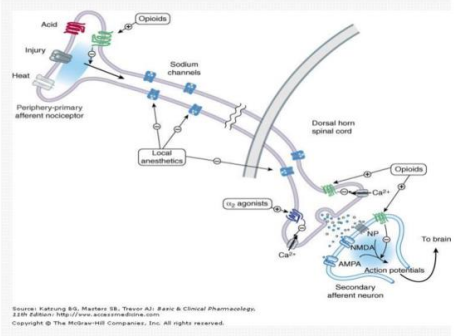
Intravenous Lidocaine

Lidocaine Overview



(Stoelting, 2015)

Voltage Gated Sodium Channels



Benefits of Perioperative Lidocaine

1

Decreased Post-Operative Pain

- Grady et al. (2012) found that pain levels in fifty patients with lidocaine drips running during laparoscopic surgeries on female reproductive organs were less on post-operative day 3 compared to patients who received a placebo drip
- Kranke et al. (2015) found that lidocaine was superior to placebo drugs in decreasing pain after various types of surgeries

Benefits of Perioperative Lidocaine

2

Decreased Narcotic Use

- Farag et al (2013) found IV lidocaine in the peri-operative period during spinal surgical interventions reduces pain and therefore patient's need for narcotics for 2 days post-operatively
- McCarthy et al. (2010) found that lidocaine drips resulted in "significant reductions in postoperative pain intensity and opioid consumption" with opioid use reduced by 85%

Benefits of Perioperative Lidocaine

3

Decreased Opioid Side Effects

- McCarthy et al. (2010) found that lidocaine drips resulted in a 23-hour reduction in post-operative delay of flatus, and a 28-hour reduction of post-operative delay of bowel movements
- Kranke et al. (2015) found that patients receiving lidocaine peri-operatively had less nausea

Benefits of Perioperative Lidocaine

4

Shorter Inpatient Stay

- McCarthy et al. (2010) found that lidocaine drips resulted in a 1.1-day reduction in the length of inpatient hospital time

Benefits of Perioperative Lidocaine

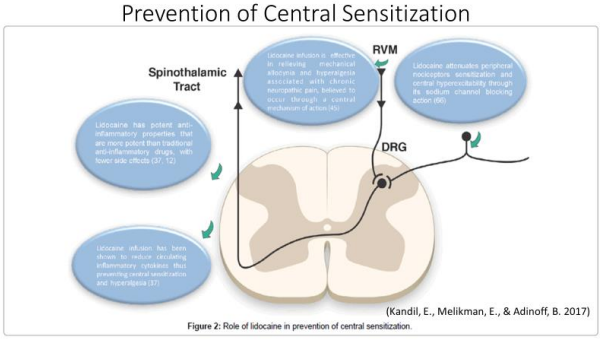
5

Other Benefits

- Predicts efficacy for oral Na+ channel blocking drugs such as mexiletine, an oral analogue of lidocaine
- Used for regional anesthesia
- Addition of epinephrine can significantly reduce absorption of lidocaine by nearby vessels, allowing more lidocaine to enter neural compartment and prolonging duration of action by up to 50%

(Stoelting, 2015)

Prevention of Central Sensitization



(Kandil, E., Melikman, E., & Adinoff, B. 2017)

Figure 2: Role of lidocaine in prevention of central sensitization.

Lidocaine: Analgesic Effect

Acute Pain

- Used to treat post-operative, burn, and cancer pain
- Used as continuous infusion to **maintain a plasma concentration of 1-2 µg/mL**
- Decreases severity of postoperative pain and requirements for opioids
- Does not produce systemic toxicity
- Effective in temporarily treating stump pain (neuromas) after amputation
- Not effective in treating phantom pain (cortical reorganization) after amputation

(Stoelting, 2015)
(Hemmings & Egan, 2013)

Lidocaine: Analgesic Effect

Chronic Pain

- Has been administered as an infusion to treat chronic neuropathic pain
- Meta-analysis performed on use of lidocaine and mexiletine in treating neuropathic pain
- Produced no major adverse events in controlled clinical trials
- Were superior to placebo to relieve neuropathic pain
- Were as effective as other analgesics used for this condition

(Stoelting, 2015)
(Hemmings & Egan, 2013)

Lidocaine: Analgesic Effect

Pain Treatment

- Profoundly suppresses increased peripheral neuronal firing from injury and inflammation
- Profoundly suppresses central sensitization of wide dynamic range neurons In dorsal horn

(Stoelting, 2015)
(Hemmings & Egan, 2013)

Lidocaine: Analgesic Effect

Mechanism of Action

- Suppresses **open/inactive voltage-gated sodium channels** in neurons responding to noxious stimuli
- Prevents nerve conduction and pain transmission
- Exact mechanism of action of IV lidocaine in pain control is unknown
- May involve selective blockade of pain fibers within spinal cord or dorsal root ganglia
- Systemic analgesia possibly also from affecting peripheral nerves or cutaneous nerve endings

(Stoelting, 2015)
(Hemmings & Egan, 2013)

Lidocaine Pharmacodynamics

Cardiac

- **Vasodilation** inhibition of action potentials of sodium channel blocking vasoconstrictor sympathetic nerves
- Shortens action potential duration and refractory period in ventricles
- Delays rate of spontaneous phase 4 depolarization
- Does not alter phase 4 in atria, so ineffective against SVT
- May increase defibrillation threshold – important to note with implantable defibrillator

Respiratory

- Depresses ventilatory responses to arterial hypoxemia
- Caution in patients with carbon dioxide retention who depend on hypoxic drive

(Stoelting, 2015)
(Hemmings & Egan, 2013)

Lidocaine Pharmacodynamics

Central Nervous System

- **CNS depression**
- Decreased MAC
- Seizures

Immune

- **Anti-inflammatory**
- **Inhibits release of pro-inflammatory cytokines** and prevents leukocyte adhesion
- Appears to block priming of polymorphonuclear leukocytes (PMNs) and decrease tissue damage
- Reduces formation of leukotriene B4 and IL-1
  - -Leukotriene B4 is a potent stimulator of PMNs - leads to PMN margination, degranulation, diapedesis, and superoxide release and enhances vascular permeability

(Stoelting, 2015)
(Hemmings & Egan, 2013)

Lidocaine: Pharmacokinetics

First-Pass Pulmonary Uptake	Approximately 65% Infusion for 1 minute is followed by a rapid decrease in plasma concentration and an initial high uptake into the lungs and distribution to highly perfused tissues
Redistribution	High lipid solubility First distributed to highly perfused tissues (brain, heart, kidneys) Later redistributed to less well perfused tissues, including skeletal muscles and fat Cardiac output is important in overall tissue distribution and intercompartmental clearance Ultimately eliminated from plasma by metabolism and excretion

(Stoelting, 2015)
(Hemmings & Egan, 2013)

Lidocaine: Pharmacokinetics

Hepatic Metabolism	Extensive hepatic extraction and metabolism **Hepatic enzyme CYP450 3A4** Causes large differences in effects between PO and IV doses Prilocaine is most rapidly metabolized amide; lidocaine and mepivacaine are intermediate; and etidocaine, bupivacaine, and ropivacaine are least rapidly metabolized
Considerations	Resulting metabolites may possess cardiac antiarrhythmic activity CYP 3A4-5 has reduced activity in 6% of Caucasians, which can lead to higher plasma levels

(Stoelting, 2015)
(Hemmings & Egan, 2013)

Lidocaine: Pharmacokinetics

Metabolic Pathway

- Principal metabolic pathway is oxidative dealkylation in the liver to monoethylglycinexylidide (MEGX)
- Monoethylglycinexylidide (MEGX) has approximately 80% of the activity of lidocaine for protecting against cardiac dysrhythmias in an animal model
- Prolonged elimination half-time accounts for its efficacy in controlling cardiac dysrhythmias after the infusion of lidocaine is discontinued
- Monoethylglycinexylidide (MEGX) is then hydrolyzed to xylidide
- Xylidide has approximately 10% of the cardiac antidysrhythmic activity of lidocaine
- Approximately 75% of xylidide is excreted in the urine as 4-hydroxy-2,6-dimethylaniline

(Stoelting, 2015)

Lidocaine: Pharmacokinetics

Factors That Slow Metabolism
(May need 50% or more reduction of initial dose and infusion rate to maintain therapeutic levels)

- Hepatic disease
- Decreased hepatic blood flow
- Decreased cardiac output
- Volatile anesthetics (decreased hepatic metabolism)
- Pregnancy-induced hypertension (maternal clearance is prolonged)
- Advanced age
- Cimetidine
- Propranolol (can decrease hepatic blood flow and inhibition of hepatic metabolism)

(Stoelting, 2015)

Lidocaine: Safety Considerations

Drug Interactions	• Can increase pharmacologically active, unbound portion of highly protein-bound drugs such as verapamil and nifedipine • Mixing with propofol may cause coalescence of oil droplets - risk of pulmonary embolism
Methemo-globinemia	• Rare but potentially life-threatening complication with decreased oxygen carrying capacity • Lidocaine can cause oxidation of hemoglobin to methemoglobin faster than methemoglobin is reduced to hemoglobin • Neonates may be at greater risk because of more readily oxidized fetal hemoglobin
Lidocaine Toxicity	• Risk Factors: Hyperkalemia, mexiletine use, arterial hypoxemia, acidosis • Dose-Dependent Effects: May cause prolonged P-R interval, widened QRS, and **bradycardia** - CNS is more susceptible to toxicity than cardiovascular system • Treatment: Manage cardiac dysrhythmias and seizures, consider IV lipid therapy

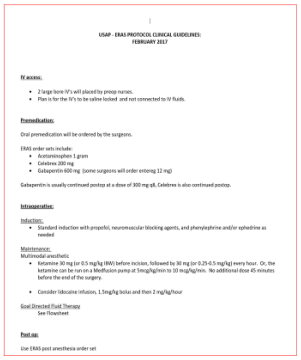
(Stoelting, 2015)

Lidocaine: Perioperative Dosing

Study	Surgical Procedure	Bolus Dose (mg/kg)	Infusion Dose (mg/kg/hr)
Choi 2012	Breast	1.5	1.5
De Oliveira 2012	Lap outpatient	1.5	2
De Oliveira 2014	Lap bariatric	1.5	2
Farag 2013	Spine	no bolus	2
Grady 2012	Hysterectomy	1.5	2
Grigoras 2012	Breast	1.5	1.5
Kim 2013	Lap gastrectomy	1.5	2
Omar 2013	Endoscopic sinus	1.5	1.5
Soltani 2013	Ophthalmologic	no bolus	2.5
Tikuisis 2014	Lap colon resection	1.5	2 in surgery, 1 for 24 hr
Yang 2014	Lap cholecystectomy	1.5	2

(Adapted from Kranke et al, 2015)

Lidocaine: Role in ERAS



USAP - ERAS PROTOCOL CLINICAL GUIDELINES:
FEBRUARY 2017

IV access:

- 2 large bore IV's will placed by preop nurses.
- Plan is for the IV's to be saline locked and not connected to IV fluids.

Premedication:

Oral premedication will be ordered by the surgeons.

ERAS order sets include:

- Acetaminophen 1 gram
- Celebrex 200 mg
- Gabapentin 600 mg (some surgeons will order entengi 12 mg)

Gabapentin is usually continued postop at a dose of 300 mg q8. Celebrex is also continued postop.

Intraoperative:

Induction:

- Standard induction with propofol, neuromuscular blocking agents, and phenylephrine and/or ephedrine as needed

Maintenance:
Multimodal anesthetic

- Ketamine 30 mg (or 0.5 mg/kg IBW) before incision, followed by 30 mg (or 0.25-0.5 mg/kg) every hour. Or, the ketamine can be run on a Medfusion pump at 5mcg/kg/min to 10 mcg/kg/min. No additional dose 45 minutes before the end of the surgery.
- Consider lidocaine infusion, 1.5mg/kg bolus and then 2 mg/kg/hour

Goal Directed Fluid Therapy
See Flowsheet

Post op:
Use ERAS post anesthesia order set

(USAP website)

Lidocaine: Role in ERAS

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Questions

References

DEA.gov / Headquarters News Releases, 09/22/16. (n.d.). Retrieved from https://www.dea.gov/divisions/hq/2016/hq092216.shtml

Farag, E., Ghobrial M., Sessler, D., Dalton J., Liu, J., Lee, J., Zaky, S. Bansel, E., Bingaman,W., Kurz, A. (2013). Effect of perioperative intravenous lidocaine administration on pain, opioid consumption, and quality of life after complex spine surgery. *Anesthesiology , 119*(4), 932-940. doi:10.1097/ALN.0b013e318297d4a5.

Grady, P., Clark, N., Lenahan, J., Chadelwirk, C., Hawkins, R., Nezat, G., & Pellegrini, J. E. (2012). Effect of intraoperative intravenous lidocaine on postoperative pain and return of bowel function after laparoscopic abdominal gynecologic procedures. *AANA Journal, 80*(4), 282-288. Retrieved from http://www.aana.com/newsandjournal/Pages/aanajournalonline.aspx

Hemmings, Hugh C. and Egan, Talmadge D. (2013). Pharmacology and Physiology for Anesthesia. Philadelphia, PA: Saunders, an imprint of Elsevier Inc.

Increases in Drug and Opioid Overdose Deaths — United States, 2000–2014 (n.d.). Center for Diseases and Control. Retrieved from https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm

Kandil, E., Mellekman, S., & Adinoff, B. (2017). Lidocaine Infusion: A Promising Therapeutic Approach for Chronic Pain. *Journal of Anesthesia & Clinical Research, 8*(1), 697. doi.org/10.4172/2155-6148.1000697

Katzung, B. G., Masters, S. B., & Trevor, A. J. (2009). *Basic & clinical pharmacology*. New York: McGraw-Hill Medical

Khan, J., Yousuf, M., Victor, C., Sharma, A., Siddiqui, N., (2016). An estimation for an appropriate end time for an intraoperative intravenous lidocaine infusion in bowel surgery: A comparative meta-analysis. *Journal of Clinical Anesthesia, 28* 95, 104. Retrieved from https://www.journals.elsevier.com/journal-of-clinical-anesthesia/

Kranke P, Jokinen J, Pace NL, Schnabel A, Hollmann MW, Hahnenkamp K, Eberhart LH, Poeppling DM, Weibel S (2015). Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery. *Cochrane Database of Systematic Reviews*. doi: 10.1002/14651858.CD009642.pub2.

McCarthy, G., Megalla, S., & Habib, A. (2010). Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery: A systematic review of randomized controlled trials. *Drugs, 70*(9), 1149-1163. doi:10.2165/10898560-000000000-00000

Opioid Addiction 2015 Facts & Figures. (n.d.). American Society of Addiction Medicine. Retrieved September 7, 2017, from https://www.asam.org

Opioid Consumption. (n.d.). Retrieved from http://www.painpolicy.wisc.edu/opioid-consumption-data

Overdose Death Rates. (2017, January). Retrieved from ttps://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates

Overdose Deaths Related to Fentanyl and Its Analogs — Ohio, January-February 2017 | MMWR. (n.d.). Retrieved from https://www.cdc.gov/mmwr/volumes/66/wr/mm6634a3.htm

Prescription Opioid Overdose Data | Drug Overdose | CDC Injury Center. (n.d.). Retrieved from https://www.cdc.gov/drugoverdose/data/overdose.html

Stephan, Bradley C. & Parsa, Feroydoun D (2016). Avoiding Opioids and Their Harmful Side Effects in the Postoperative Patient: Exogenous Opioids, Endogenous Endorphins, Wellness, Mood, and Their Relation to Postoperative Pain. Hawaii J Med Public Health.v.75(3); 2016 MarPMC4795331. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4795331/

Stoelting, R. K. (2015). Pharmacology and physiology in anesthetic practice (7th ed). Philadelphia, PA: Wolters Kluwer Health

Understanding the Epidemic | Drug Overdose | CDC Injury Center. (n.d.). Retrieved from https://www.cdc.gov/drugoverdose/epidemic/index.html

Whistler, J. (2012). Examining the role of mu-opioid receptor endocytosis in the beneficial and side-effects of prolonged opioid use: From a symposium on new concepts in mu-opioid pharmacology. *Drug and Alcohol Dependence, 121*(3), 189-204. Retrieved from https://www.journals.elsevier.com/drug-and-alcohol-dependence/

Appendix D

Results

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Pre-Test - Post-Test	-3.97917	2.44505	.35291	-4.68914	-3.26920	-11.275	47	.000

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Pre-Test	3.8750	48	1.85226	.26735
	Post-Test	7.8542	48	1.83337	.26462