Study Title: A Comparison of Two Methods of Lidocaine Injection on Propofol Injection Pain

Principal Investigator, Co-investigator: Timothy Harwood MD; Patrick Grace MD

Sponsor or funding source: WFUHS Department of Anesthesiology

Background, Rationale and Context

Intravenous lidocaine is routinely given through the IV prior to injection of propofol to reduce the amount of pain during propofol injection. We want to study if giving the lidocaine through the IV while the forearm with the IV has a tourniquet applied to it to prevent "washing out" of the lidocaine prior to propofol injection helps reduce propofol injection pain.

Objectives

We expect that tourniquet lidocaine will be superior to straight non-tourniquet lidocaine in reducing propofol injection pain. We also want to determine the association of tourniquet duration on reduction of pain with propofol administration. Small studies indicate that 60 seconds of tourniquet lidocaine is superior to 30 seconds or less of tourniquet duration or mixed lidocaine/propofol for injection. We suspect many clinicians do not use the 60-second tourniquet technique due to the extra time involved but hypothesize that a more practical application by applying the tourniquet as soon as the patient is positioned on the operating table will not only be more widely adopted by clinicians as it does not cause delay but also provide the necessary amount of time for benefit from the tourniquet. We plan to record the time from tourniquet application to start of propofol administration, which we predict will be at least 60 seconds, and see if there is a correlation between duration of venous stasis of IV lidocaine and pain benefit.

Methods and Measures

Design

This will be conducted as a randomized controlled trial of two methods of administering lidocaine prior to propofol injection.

Setting

The study setting is located within North Carolina Baptist Health, an academic medical center, in the Endoscopy Suite where 10-30 patients per day are scheduled to receive propofol as part of their sedation or anesthetic.

Subjects selection criteria

- **Inclusion Criteria**

  Any patient aged ≥18 years scheduled to receive propofol as part of their sedation or anesthetic.

- **Exclusion Criteria**

  Since children (age<18 years) frequently receive induction of anesthesia by mask, they will be excluded.

  Any patient receiving pre-medications prior to their sedation that could alter their recall or perception of the pain such as fentanyl or midazolam.

- **Sample Size**
  We estimate that 25 subjects in each of the two groups will be required to test the hypothesis based on prior studies.

Interventions and Interactions • There will be two groups: o Group 1: 50mg of 2% lidocaine given just prior to the propofol dose through the IV line.

o Group 2: 50mg of 2% lidocaine given IV with venous occlusion applied when the patient is positioned on the operating room table and timed until the onset of propofol administration. The tourniquet will either be a latex free tourniquet or McKesson Quick Release tourniquet applied to the forearm 10cm distal to the elbow joint in the tourniquet group. Venous stasis will be confirmed with cessation of flow from hanging IV fluid.

- For both groups, no premedication shall be given, which is the normal practice for these procedures. Study procedures will involve a 20 gauge intravenous (IV) catheter placed in a vein distal to the mid forearm. Venous occlusion will be achieved by either a latex free tourniquet or McKesson Quick Release tourniquet applied to the forearm 10cm distal to the elbow joint. Tourniquet pressure will be somewhat variable but sufficient to cause venous stasis as confirmed by no flow of hanging IV fluid. Injections will be delivered at roughly 1 ml/sec.
- For studies involving interactions the survey, questionnaire or method of observation should be described.
  - o Please see Data Collection Form Attached

- The time required should occur within their usual anesthetic parameters and should not delay their procedure nor increase the duration of anesthesia significantly.

- Table illustrating the schedule of events in the study:

Day prior to the procedure	Describe study to the patient by telephone
Day of procedure: holding area	Consent patient for
Day of procedure: holding area	Randomly assign patient to one of two groups
Day of procedure: procedure area	Accompany patient to the operating or procedure room, perform instructions from the group they are assigned to while noting outcome measures such as self-described discomfort and observer graded discomfort
Day of procedure: recovery area	Revisit patient in recovery to determine post-procedure recall of discomfort
Post-study period	Analyze data

Outcome Measures

1. Self-described discomfort level using 4-point verbal pain scale (None, mild, moderate, severe)

2. Observer-graded discomfort level (Nonverbal vocal complaints, verbal vocal complaints, facial grimace/winces, and restlessness/withdrawal)
3. Post-procedure recall of discomfort using 4-point verbal pain scale (same as #1)

Analytical Plan

We will analyze results initially using descriptive statistics. Comparison between groups will be done using chi square tests for proportions, and t-tests or ANOVA procedures for continuous variables. Regression analysis will be performed to identify independent outcome predictors. Other inferential statistical analysis will be conducted as appropriate.

Human Subjects Protection

Subject Recruitment Methods

Informed Consent

Signed informed consent will be obtained from each subject. One of the two investigators will obtain informed consent. Patients will be contacted by telephone the day before their procedure is scheduled to discuss the general description of the study and the possibility of study inclusion. Full written consent, after answering questions, will have to be performed in the holding room prior to the procedure since most patients will have their pre-procedure examination performed in the holding room and will not be seen prior to the day of surgery.

Confidentiality and Privacy

Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected patient identifying information corresponding to the unique study identifier will be maintained on a linkage file, store separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. Following conclusion of data collection, subject-identifying information will be destroyed *three years after closure of the study by secure shredding,* consistent with data validation and study design, producing an anonymous analytical data set. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

Data and Safety Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB.

References

1. Jalota L, Kalira V, George E, Shi YY, Hornuss C, Radke O, Pace NL, Apfel CC; Perioperative Clinical Research Core. Prevention of pain on injection of propofol: systematic review and meta-analysis. BMJ. 2011 Mar 15;342:d1110. doi: 10.1136/bmj.d1110.
2. Shabana A. Prevention of propofol injection pain, using lidocaine in a large volume does it make a difference? A prospective randomized controlled double blinded study. Egyptian Journal of Anaesthesia 29(4):291–294 · October 2013
3. Walker BJ, Neal JM, Mulroy MF, Humsi JA, Bittner RC, McDonald SB. Lidocaine pretreatment with tourniquet versus lidocaine-propofol admixture for attenuating propofol injection pain: a randomized controlled trial. Reg Anesth Pain Med. 2011 Jan-Feb;36(1):41-5. doi: 10.1097/AAP.0b013e31820306da.

Appendix

Intravenous Lidocaine to Reduce Propofol Injection Pain:
A Comparison of Two Methods

MRN: _____

Date: _____

Observer: _____

PMH: Chronic Pain Syndrome: Y/N

Daily use of Opioids: Y/N

Group (check one): ☐A (no tourniquet) ☐ B (tourniquet)

Self-described discomfort level during injection using 4-point verbal pain scale:

☐None
☐Mild
☐Moderate
☐Severe

Investigator Assessments:

1) Induction Discomfort Scale (during injection and within 5 seconds after injection)

☐Grimace

☐IV forearm withdrawal

☐Moaning

☐Verbal statement of discomfort (“it hurts”, etc.)

2) Post-Procedure Discomfort Scale (in Recovery Area just prior to discharge). I recall _____ discomfort in my IV arm while I went to sleep:

☐No

☐Mild

☐Moderate

☐Severe

A COMPARISON OF TWO METHODS OF LIDOCAINE INJECTION ON PROPOFOL INJECTION PAIN

Informed Consent Form to Participate in Research
Timothy N. Harwood MD, Principal Investigator

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you have *going to receive propofol as part of your anesthetic*. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to *compare two different methods of giving lidocaine in reducing the pain of administration of intravenous propofol, which you will be receiving as part of your anesthetic. Giving lidocaine though the IV is known to reduce the discomfort of the injection of intravenous propofol, but the best method has yet to be determined.*

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

50 people at *Wake Forest Baptist Health* sites will take part in this study. In order to identify the 50 subjects needed, we may need to screen as many as 75 because some people will not qualify to be included in the study.

WHAT IS INVOLVED IN THE STUDY?

In this study, 2 ways of administering lidocaine in your IV will be studied. Both of these techniques are commonly used by anesthesia caregivers, but studies comparing the two techniques have not given us enough evidence to choose one over the other scientifically.

A) In your procedure room, we will give you a small dose of lidocaine through your IV mixed with the injection of propofol that will have you go to sleep.

Or:

B) In your procedure room, we will place a light tourniquet on the forearm above your IV site. We will then give the same amount of lidocaine through the IV line and let the lidocaine stay in your vein while we prepare you for the start of your anesthetic. This will usually take 1-2 minutes. We will then take the tourniquet off and give you the usual dose of propofol to have you go to sleep.

The only difference between the two techniques is when we inject the lidocaine and how long we let it stay in the vein in relation to when we give you propofol.

You will be randomized into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an ***equal*** chance of being placed in either group.

- If you take part in this study, you will have the following tests and procedures:
    - A 20 Gauge IV catheter will be placed for your procedure and anesthetic.
    - You will receive standard medications as normally planned for the procedure.
    - If you are in Group A:
        - You will have standard monitors placed on you.
        - When everything is ready, you will then be given 50 mg of intravenous lidocaine immediately followed by propofol in an amount judged appropriate by your anesthesia team.
    - If you are in Group B:
        - Once in the procedure room, you will then have a light tourniquet placed on your mid-forearm in your IV arm. We will then inject 50 mg of intravenous lidocaine.
        - You will then have standard monitors placed on you.
        - When everything is ready, you will have the tourniquet removed
        - You will then be given intravenous propofol in an amount judged appropriate by your anesthesia team.
    - We will observe you for signs of IV discomfort
    - After your procedure, before you are discharged, we will give you a short survey about any discomfort you recall while going to sleep.
    - In both groups, all other care will be as usual and you will be discharged per usual routine.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for about *until you have a survey of your recall of discomfort prior to your discharge from the procedure unit.*

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences, however, we expect no differences in your care.

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the *procedures or drugs* we are studying include:

- *Frequent (10-90%)*
    - *Discomfort in your IV during medication injection*
    - *Some mild to moderate sleepiness for 30-60 minutes after your procedure*
    - *Throat dryness from medication or the procedure*
    - You may experience discomfort, bruising and/or bleeding where the IV is inserted. Occasionally some people become dizzy lightheaded or feel faint.
- *Infrequent (2-10%)*
    - *Nausea*
- *Rare (<1%)*
    - *Infection in your IV area*
- *Extremely rare (<1/50,000)*

- *Hospitalization*
- *Death*

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

Reproductive Risks and other Issues to Participating in Research

Pregnant women are excluded from participation in this study. If you are a sexually active woman of childbearing potential and have not been using a reliable method of birth control, two negative pregnancy tests performed 15 days apart are required to check for possible early pregnancy prior to starting treatment.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be: *less pain in arm where your IV is inserted during medication administration*

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you have these options:

- You will be treated with *the same medications* even if you do not take part in the study.

WHAT ARE THE COSTS?

All study-related costs, including any study procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study and would be used regardless of the study, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

The purpose of this research study is to obtain data or information on the effectiveness of IV tourniquet lidocaine in relieving propofol injection pain; the results will be provided to the Food and Drug Administration and other federal and regulatory agencies as required.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a research study. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

WILL YOU BE PAID FOR PARTICIPATING?

You will receive no payment or other compensation for taking part in this study.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by *Wake Forest University Health Sciences Department of Anesthesiology*. The sponsor is providing support in terms of time to the investigators to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at (336) 716-3467.

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call *Dr. Timothy Harwood* at *336.716.4498 or 336.716.2011 after hours.*

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any *new information we collect from you* about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:**

- Medical Record Number
- Date of Birth
- Type of procedure performed
- Home medications
- Anesthesia medications given

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites

who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records *will be kept for three years after the study is finished. At that time any research information not already in your medical record will either be destroyed. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center.* You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Timothy Harwood that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Timothy Harwood
Department of Anesthesiology
Medical Center Blvd.
Winston-Salem, NC 27157

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because *it is in your best medical interest, you had an unexpected reaction, or you failed to follow instructions*.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, *Dr. Timothy Harwood* at *336.716.4498 or 336.716.2011 after hours.*

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at (336) 716-4542.

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm