Official Title: An Open-Label Application of the NSS-Bridge Device for Post-Cesarean Pain

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Project Title: Feasibility and Tolerability of the Use of NSS-Bridge Device for Post-Cesarean Pain Management

Introduction

The current opioid epidemic has led to a renewed interest in exploring non-pharmacological techniques to treat post-operative pain. An increasing number of patients are suffering from the adverse effects of opioid use following surgery, including post-operative nausea and vomiting, respiratory depression, immunosuppression, constipation, and most recently, addiction. In the United States, over $600 billion is spent every year on opioid addiction, including $79 billion related to opioid addiction following surgery. Despite many initiatives to decrease the use of opiates in the preoperative setting, opioids continue to be regularly prescribed before, during and after surgery. Although the risk of opioid addiction following surgery is recognized, the percentage of patients becoming addicted to opioids following surgery is not well understood. To date, there has been virtually no agreement regarding the duration and dosage that qualify for opioid dependence following surgery, nor that a clear estimation of the factors such as biological, psychosocial and socioeconomic that increase the risk of using opioids for extended periods of time after surgery. Therefore, in order to combat this growing health crisis at the ground level, it is incumbent upon the medical community to explore alternative methods of pain control to treat the surgical population in order to reduce the incidence of post-operative opioid addiction.

Project Aims/Goals

Percutaneous Nerve Field Stimulation (PNFS) is one of these recognized methods that ongoing research has shown to be effective as a complementary method of pain management. While PNFS is not a novel concept, clinical indications of auricular field stimulation have been limited in the past due to requirement of bulky, stationary and non-disposable stimulators and electrodes. These technological

limitations made it difficult to establish the real clinical potential of auricular stimulation for the perioperative management of pain in surgical patients, despite the demonstration that auriculotherapy has been shown to relieve pain in the postoperative setting.

The NSS-2 BRIDGE (Appendix 1) is a battery operated and disposable percutaneous auricular nerve field stimulator (Innovative Health Solutions, Versailles, IN, USA), that was recently cleared by the FDA and assigned a Class II Risk Designation; a class which includes surgical drapes, pumps and power wheelchairs. The indication for the NSS-2 BRIDGE is for the treatment of clinical symptoms related to opioid consumption and opioid withdrawal. These symptoms include abdominal pain, anxiety and post-operative nausea and vomiting; conditions which are also present following Cesarean-Section surgery. The use of the NSS-2 BRIDGE device has been demonstrated to provide significant analgesia in patients with abdominal pain syndrome, and clinical trials are ongoing to assess the benefit of this approach for post-operative pain management. As compared to the present use of opioids for perioperative pain management, the use of a complementary, non-pharmacologic approach offers the advantage of analgesia without the associated side effects. This is especially true in the post Cesarean Section population, in that many of these women want to breast feed and because of this are very motivated to not use opioids and other analgesics, allowing us to explore the additional benefits of non-pharmacological complementary pain management techniques.

Mechanism of action of the Auricular Percutaneous Electrical Nerve Field

The NSS-2 BRIDGE devise allows for stimulation to branches of Cranial Nerves V, VII, IX and X, and the occipital nerves, identified by transillumination. Such a stimulation is transmitted to the central nervous and especially the limbic system, which is known to be a key component of the central nervous system response to stress, anxiety and the pain pathway. The nucleus involved by the stimulation include the amygdala (structure involved in the response to fear and anxiety), the thalamus (structure

involved in the management of visceral and somatic pain, addiction), the nucleus of tractus solitarie (structure involved in the control blood pressure) etc…. The stimulation of these nucleus produces a decrease in the transmission of pain impulses from visceral and/or somatic structures to supraspinal areas, a reduction in anxiety and control of blood pressure and associated changes of the sympathetic and parasympathetic nervous system.

The primary end point will be the frequency of patients who experience an excellent tolerability along with a decrease of at least 20% in pain score. Also pain score and opioid consumption will be compared to data obtained 5 consecutive who underwent a C-section the month before.

Specific Aims

Specific Aims:

1. Tolerability and feasibility of applying the device following Cesarean Section

2. Look at the trend of opioid consumption and pain in five post- Cesarean section women wearing device, compared to five historical consecutive controls of women who underwent cesarean section in January 2019

Study Design

The proposed pilot study will be conducted as a single-center prospective open-label trial at the University of Pittsburgh Medical Center (UPMC) Magee-Womens Hospital. The data collected during this period will be compared to historical controls who have had elective C-Sections in the period of January, 2019. Institutional review board approval will be obtained before eligible patients are recruited and consented. Trial will be registered at www.clinicaltrial.gov before beginning recruitment.

Recruitment

Potential subjects will be recruited in the Magee Womens Hospital obstetrical unit when they arrive for elective Cesarean Section surgery. The Principal Investigator, Dr. Katherine Grace Lim, will already have access to these patients as their primary OB Anesthesiologist. Patients will be asked for their interest in pursuing a research study that involves wearing a percutaneous, auricular field stimulator for five days as a supplementary method of post-operative pain control after their Cesarean-Section. Patients who agree to participate in the trial will sign an IRB approved Informed Consent Form.

Inclusion Criteria:

Over 18 years of age

Elective Cesarean-Section Surgery

Exclusion Criteria:

History of active depression, anxiety or catastrophizing

Active alcoholism or drug abuse

Severe chronic pain condition that requires daily preoperative opioid dependence

History of hemophilia

Patients with cardiac pacemakers

Patients with psoriasis vulgaris diagnosis

Data Collection and Outcome Measures

The primary purpose of this pilot study is to demonstrate feasibility/acceptability of the NSS-2 Bridge device applied after a C-section. Is the acceptability is confirmed, the C-section model will be included in an RFA NIH request (RFA-NS-19-018: HEAL Initiative: Clinical Devices to Treat Pain (UH3 Clinical Trial Optional) DEADLINE IS MARCH 8, 2019) for proposal related to the use of devises for reduction of opioid use. In this pilot, no changes will be made in the other analgesia/postpartum care. Potential subjects will

be recruited in the Magee-Womens Hospital obstetrical unit when they arrive for cesarean delivery. Patients will be asked if they are interested in using the NSS-2 Bridge system as a way to control pain after the C-section. They will offer to review a video explaining the mechanism of action of the NSS-2 Bridge system. Subject will be informed of the purpose of this pilot evaluation and if they agree to participate in the trial, they will sign an IRB approved Informed Consent Form.

Once patient has given and signed informed consent to participate in the study, demographic information and medical history will be collected from each participant on the day of the C-section. Data will be de-indemnified and kept in a lock cabinet. The NSS-2 BRIDGE device will be applied to one ear by trained research staff in the immediate post-operative setting. The patient will be informed at the time of consent and after the implantation of the device that they can have the device removed any time after its application.

As per standard of care, at 12, 24, 48, 72, 96 and 120 hours post-operatively will be collected pain score at rest and movement, total opioid consumption, as well as the devise tolerability. Additionally as per other pain pilot IRB approved projects, we shall also collect common medical information including time to bowel movement, PONV, time to oral intake (liquid and regular diet), time to hospital discharge, intensive care unit (ICU) admission, readmission to the hospital, readmission due to pain related issues, quality of recovery after cesarean delivery, overall patient satisfaction, and patient satisfaction related to pain management. When the patient is discharged from the hospital, they will be asked to complete a patient satisfaction survey. For patients discharged with the device attached, removal instructions will be given to patient to remove and dispose of the device at 120 hours.

Standard opioid conversion table will be used to convert the oral and IV narcotic utilized by the patients to IV morphine equivalent doses (MED) for analysis purposes.

Overall patient satisfaction and satisfaction of pain management during hospitalization will be measured by a numerical rating scale with 0- worst satisfaction and 10 being the best satisfaction. The patient satisfaction test will be administered by a member of the research team.

No statistical analysis will be performed. The primary end point will be the frequency of patients who experience an excellent tolerability along with a decrease of at least 20% in pain score. Also pain score and opioid consumption will be compared to data obtained 5 consecutive who underwent a C-section the month before

Pre-and-Post Metric Evaluation

The use of a non-pharmacological NSS-2 BRIDGE has the possibility of providing analgesia to post-surgical patients and reducing the number of opioids required following Cesarean-Section surgery. This will significantly impact patient outcomes, as patients will experience fewer opioid-related side effects (such as respiratory depression, post-operative nausea and vomiting, constipation and delirium, as well as transfer of opioids to the breast milk). This will also impact clinicians caring for post-operative patients, as there is the real potential they will have fewer conditions to monitor and treat as the patient recovers from surgery. The projected number of patients served by this project will initially be five (5) enrolled participants at Magee-Womens Hospital however, the data collected from this trial will serve countless patients and the community at large as physicians strive to move away from opioid use following surgery. Data collected from this pilot study will support a future proposal to the National Institute of Heath (NIH) to fund a full-scale, randomized, placebo-controlled trial using the NSS-2 BRIDGE device.

Perhaps most importantly, the investigative use of the non-invasive NSS-2 BRIDGE device has the ability to significantly increase patient satisfaction in individuals who are opioid naïve or adverse to taking opioids as a method of pain control. Being able to offer the post-partum patients at Magee

Womens Hospital of UPMC such an alternative represents a great opportunity to increase patient satisfaction, outcomes and compliance as many patients increasingly fear the use of opioids. The NSS-2 BRIDGE will remain effective on the participant for five days, and will have lasting effects even after discharge from the hospital, which is a time when many patients turn to opioids to control pain. The way the efficacy of this device will be measured will be by comparing total perioperative opioid consumption between study participants (n=5) historical controls who have had C-Sections at Magee Womens hospital in January 2019. Other outcome measures include the incidence of respiratory depression, PONV, constipation and length of stay between the study group and historical control group.

Appendix 1: NSS- 2 BRIDGE device