Evaluation of Objective Pain Measurement Device

NCT03975660

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1. PURPOSE OF THE STUDY

a. Brief Summary

The aim of the study is to develop a device that can objectively measure pain. The study will attempt to objectively measure labor pain with an experimental device (CereVu ROPA). We will apply the device to determine if it is objectively able to measure patients reported pain due to uterine contractions before and after labor epidural analgesia. A brain oxygenation device, Edwards Foresight, will be used to concurrently to monitor brain oxygenation and hemodynamics, so the relationship between the CereVu ROPA device objective measure of pain and brain oxygenation/hemodynamic changes and patient-reported pain can be determined.

b. Objectives

The investigators hope to learn: If the pain measurement device (CereVu ROPA) is capable of reflecting different levels of pain ratings in patients in labor having uterine contractions and then changes in pain after receiving different neuraxial techniques for labor pain. Additionally determine the relationship between the CereVu ROPA device, brain oxygenation/hemodynamic changes and patient-reported pain scores.

c. Rationale for Research in Humans

The pain measurement device is intended to be used in humans. The study is using dynamic psychophysical testing, which necessitates the use of specific pain-related questions in order to get patients' feedback.

2. STUDY PROCEDURES

a. Procedures

This study contains two phases. In phase 1 (device algorithm development) and phase 2 (validating the device compared to your reported pain scores). Both phase will follow identical methods, only the data analysis is different. Qualified subjects will be identified and contacted by the anesthesia team prior to their clinical evaluation for labor neuraxial analgesia. Potential patients will be informed of the study, and if they choose to participate, all to investigate be answered and an informed consent form will be signed prior to any study related activities. When they request labor analgesia, the area where the sensors of the pain measurement devices (CereVu ROPA and Edwards Foresight) will be applied to will be prepped with an alcohol swab. After allowing to dry, the sensors will be applied to the forehead on each side of the head and connected to the devices. Data recording is then started. CereVu ROPA: Patients brain activity "objective pain" data

will be obtained by the sensor and will be stored on a custom-built, radio shielded device that stores the data for further offline analysis along with patient-reported pain measures. Edwards Foresight device: Will be used to concurrently to monitor brain oxygenation and hemodynamics, so the relationship between the CereVu ROPA device objective measure of pain and brain oxygenation/hemodynamic changes and patient-reported pain can be determined. After collection of baseline data for device algorithm development of up to 70 patients, we will be moving to clinical validation study in which patients will receive our institution's standard labor epidural based on clinician preference (either epidural, dural puncture epidural or combined spinal epidural) to provide labor analgesia. Patients will undergo their standard medical and obstetric treatment at the discretion of the obstetrical and anesthesia team. There will be no delay in their treatment due to this study, and the device data will not be available of influence care. During the time of preparation of block, we will be obtaining baseline data. The research staff will be recording pain scores with contractions at regular intervals until approximately 45 minutes after the epidural is placed and the patient is comfortable.

b. Procedure Risks

The above procedures pose minimal risk to the patients because the questionnaires should not cause any psychological or physical harm. There will be no change compared to standard treatment if the patient decides to participate in this study. The pain measurement will only be recording during standard clinical care. There will be no online display for "pain" on the device so potentially no change in medical treatment.

c. Use of Deception in the Study

No

d. Use of Audio and Video Recordings

No

e. Alternative Procedures or Courses of Treatment

The medical treatment will be the same for those patients involved in the study as for those in the general patient population. The alternative to participating in the study is not to participate. No standard treatments will be withheld in either case.

f. Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?

NA

g. Study Endpoint(s)

Study end-point will be the completion of sample size. We will complete the enrollment and then do the data analysis.

3. BACKGROUND

a. Past Experimental and/or Clinical Findings

Despite astonishing progress in our understanding of the basic mechanisms leading to the sensation of pain in the last few decades, the gold standard for measuring pain is still a subjective verbal numeric rating scale rating (0-10 or 0-100) obtained from the individual reporting pain. This is by no means objective, nor is it available whenever such a rating is warranted, for example from patients who are sedated or confused or anesthetized e.g. in intraoperative or intensive care settings. Pilot studies have shown promising correlations between subjective pain ratings and "pain" measured by similar pain measurement devices like the one we will use in this study. We, therefore, want to investigate the possible use of these objective pain devices in a clinical setting.

b. Findings from Past Animal Experiments

None

4. PARTICIPANT POPULATION

a. Planned Enrollment

This study will be done in two phases.
i) In the validation study, 70 patients in labor will be recruited to get the baseline data.
ii)Then in the clinical trial, we will be enrolling 60 patients to determine how the objective pain devices measurements correspond with the patient's reported pain score before and after labor epidural analgesia. The study population will be representative of the general laboring patient population receiving epidural analgesia (epidural, combined-spinal epidural and dural puncture epidural as per clinician preference).

b. Age, Gender, and Ethnic Background

All ethnicities will be included. All females from 18 to 50 years will be included in the study.

c. Vulnerable Populations

The study will involve 130 pregnant women. Patients will be connected to the pain measurement devices via a sensor that will be applied to their forehead on each side. This carries a minimal risk of skin irritation. Patients will be monitored closely in the hospital per routine labor pain management. Analgesia will be provided by the obstetric anesthesia team per hospital routine, using all of the guidelines required to minimize risk. Every effort will be made to make sure subjects are comfortable while they complete the questionnaires.

d. Rationale for Exclusion of Certain Populations

Minors will not be included in this study.

e. Stanford Populations

These groups will not be targeted. If anyone from these groups will participate, they will be subject to the same inclusion/exclusion criteria, and provide the same written informed consent.

f. Healthy Volunteers

NA

g. Recruitment Details

In the LPCH labor and delivery, research personnel will first identify the patients suitable for the study by chart review and then they will be given information leaflets for the study. Research personnel will conduct all discussions about the study and answer any questions in a private manner.

h. Eligibility Criteria

i. Inclusion Criteria

1. Age 18-50
2. ASA I-III +/-E
3. Patient requesting epidural labor analgesia
4. Good toco tracing (clearly showing contractions at least every 5 minutes)
5. Pain score greater than or equal to 3 out of 10 with contractions

ii. Exclusion Criteria

1. History of chronic pain
2. History of chronic opioid use
3. BMI > 45
4. Allergy to sensor adhesive material, local anesthetic or opioids
5. Contraindication to neuraxial block
6. Patient on magnesium infusion
7. Inability to give informed consent
8. Severe co-morbidities

i. Screening Procedures

Prospective subjects will be asked if they want to participate in this research study. If their answer is yes this will be documented on a Screening Questionnaire and they will be considered eligible to participate. Informed consent will then be obtained.

j. Participation in Multiple Protocols

Subjects will be asked if they are currently participating in other studies. If they are, each case will be evaluated separately to determine the potential for harm to subjects, or confounding study data. If it is determined that participating in more than one study at a time compromises either subject health or viability of the study data, subjects will not be enrolled.

k. Payments to Participants

There will be no payment for patients participating in this study.

l. Costs to Participants

There will be no charge to study subjects.

m. Planned Duration of the Study

The study is anticipated to take 1-1.5 years.
The total time per participant will likely be:
i) Patients requesting labor epidural will be screened. If interested, the study is described in more detail to them and written informed consent will be obtained. This screening process will take 10 minutes.
ii) The period of active participation will be approximately 1 hour to obtain baseline data while setting up for the epidural (15 minutes), and then measure pain for 45 min after epidural placement.
iii) Individual data analysis will take approximately 4 weeks.

5. RISKS

a. Potential Risks

i. Investigational devices

Patients will be connected to two objective pain measurement devices (CereVu ROPA and Edwards Foresight) via a sensor that will be applied to their forehead (one sensor on each side of their forehead).

ii. Investigational drugs

NA

iii. Commercially available drugs, biologics, reagents or chemicals

NA

iv. Procedures

Non-investigational procedures include:
1) Neuraxial blocks, risks of which may include (but are not limited to) injection pain, perivascular or inadvertent arterial injection with the risk of necrosis, postoperative nausea, and vomiting, nerve injury, post dural headache, rarely meningitis, compression of the spinal cord secondary to clot formation or abscess, paresthesia, and weakness. Patients will receive neuraxial analgesia as part of standard care and unrelated to this study.

Study-related procedures include:
1) Answering questions. This carries no risk.
2) Applying a sensor with adhesive on the forehead of the patient. This carries a minimal risk of skin irritation.

v. Radioisotopes/radiation-producing machines

NA

vi. Physical well-being

Very mild risk of skin irritation due to sensor placement.

vii. Psychological well-being

No risks from study procedures.

viii. Economic well-being

No risks from study procedures.

ix. Social well-being

No risks from study procedures.

x. Overall evaluation of risk

Low

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b. International Research Risk Procedures

NA

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c. Procedures to Minimize Risk

Patients will be monitored closely in the hospital per routine labor pain management. Analgesia will be provided by the ob anesthesia team per hospital routine, using all of the guidelines required to minimize risk. Every effort will be made to make sure subjects are comfortable while they complete the questionnaires.

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d. Study Conclusion

The experiment terminates after all data has been collected from the patients.
Patients will be free to opt out of this study at any time. Patients will be able to contact any member of the research team in order to inform them about opting out. Patients can also opt out of the study by informing a member of the nursing staff. We will liaise with the nursing staff to ensure that the research team is informed if patients opt out by informing a member of the nursing staff. Once this is confirmed, no further patient or study data will be included in this study. A study investigator will confirm in writing that the patient has opted out of the study with relevant documentation in the patient's chart. We will ensure that our study does not detract from or interfere with any aspect of clinical management for each enrolled patient. If this occurs, study investigators will terminate the participation of individual participants in this study, and all data will be destroyed.

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e. Data Safety Monitoring Plan (DSMC)

i. Data and/or events subject to review

Initial data collection will occur at labor and delivery in LPCH. Patients will be asked to fill out the questionnaires.
The sensors will then be applied to the forehead and the pain measurement device recording will be started. From this point on, the patient will receive the standard medical treatment as chosen by the anesthesia team. Any adverse event will be reviewed by research team.

ii. Person(s) responsible for Data and Safety Monitoring

The PD will monitor data and communicate if any concerns arise. This study is observing the usual standard of care with no interventions that could affect safety.

iii. Frequency of DSMB meetings

Data will be captured monthly. In case of any serious adverse event, the meeting can be called earlier too.

iv. Specific triggers or stopping rules

Patient discomfort will dictate if action is required.

v. DSMB Reporting

Outcome of the reviews by the ME will be communicated via secured e-mail.

vi. Will the Protocol Director be the only monitoring entity? (Y/N)

Y

vii. Will a board, committee, or safety monitor be responsible for study monitoring? (Y/N)

N

f. Risks to Special Populations

NA

6. BENEFITS

There are no potential direct medical benefits for subjects participating in this research. Indirect benefits subjects may gain are a feeling of helping contribute to society, contributing to increased scientific knowledge, increased information about one's own health or knowledge of resources, improvement in psychological well-being due to interacting with research staff or content of interviews/questionnaires. Potential benefits this research has to society is the ability to quantify pain objectively in subjects undergoing labor pains. It will also help to improve our knowledge of pain processing in patients undergoing different types of neuraxial blocks.

7. PRIVACY AND CONFIDENTIALITY

All participant information and specimens are handled in compliance with the Health Insurance Portability and Accountability Act (HIPAA) and privacy policies of Stanford University, Stanford Health Care, and Stanford Children's Health.