The University of Texas Medical Branch Galveston
Research Protocol

Continuous Non-Invasive Measurement of Hemoglobin During Parturition

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1. **Introduction/Background/Purpose:** Obstetric hemorrhage remains the leading cause of maternal death worldwide (2). The most common culprits are uterine atony, placental disorders, and delivery trauma. Current detection and management of hemorrhage is heavily based on clinical judgment and laboratory results. Interventions such as fluid resuscitation and blood transfusion are often initiated after a significant hemorrhage has already taken place. Early detection and treatment of this potentially life threatening obstetric complication is of upmost importance in the field of obstetrics. Traditional methods for assessing hemoglobin levels involve collecting the patient's blood and sending it to the laboratory for analysis via complete blood count (CBC). This involves a delay and often patients are continuing to hemorrhage while the CBC is being processed. Novel technology has recently been approved by the FDA, which can continuously assess hemoglobin levels via a non-invasive monitor. This device works as a pulse oximeter, which is placed on the index finger and uses infrared technology to estimate hemoglobin levels (1). Despite its validation and use in many patient populations such as trauma, neurosurgery and orthopedic surgery, data is lacking in an obstetric population. Our hypothesis is that this device will enable clinicians detect hemorrhage early and initiate resuscitation such as fluid and/or blood transfusion before significant hemorrhage has taken place. This study will be a proof of concept prospective cohort study, in which we will attempt to detect the association between intra-operative and postoperative continuous non-invasive hemoglobin monitoring and postpartum decrease in hemoglobin.

2. **Concise summary of project:** This study will be a 'proof of concept' prospective cohort study. Patients who are in labor who meet criteria for inclusion in the study will be approached for participation. Written informed consent will be obtained from the patients by the primary investigator (PI), study coordinator, or collaborator. If patients agree to participate, a CBC (complete blood count) will be obtained via venous puncture. If the patient has a central line, blood may be drawn from it. If the patient does not have a central line, the blood draw will be via a new venous puncture. The amount of blood to be drawn will be one lavender top tube, which is about 6mL or 1.5 teaspoons. The non-invasive hemoglobin monitor will be placed on their finger during the delivery and will remain in place until discharge from the recovery room. Hemoglobin levels will be masked to the clinicians, but

recorded until the patient is discharged from the recovery room. Patients will be divided in quartiles based on drop in hemoglobin values between pre and post op. Cases will be those patients whose drop in hemoglobin falls in the upper quartile, while controls will be those patients whose drop in hemoglobin falls in other quartiles. Nadir hemoglobin levels and percent change in the continuous hemoglobin tracings will be compared between cases and controls in order to detect changes in the tracing.

Demographic information will be obtained from the electronic medical record. The data will be kept on a password secured UTMB computer. An encrypted USB flash drive will be used to transfer data. The data will be identified and linked to the patient using the medical record number (MRN). During data analysis all patient identifiers will be deleted.

3. **Study procedures:**
    - **3.1 Screening, Recruitment and Consenting:** when a patient meets inclusion criteria for participation in our study, the obstetrical team will contact one of the PIs. Written informed consent will be obtained from the patient by the PI, study coordinator, or collaborator. Study participation will be complete when the patient is discharged from the recovery room. The data collected will be kept on a password secured UTMB computer. An encrypted USB flash drive will be used to transfer data. The data will be linked via MRN, which is needed to access the demographic data and will be deleted when the data is analyzed. Our target sample size is 100 patients.

    - **3.2. Baseline Procedures**: there will be no baseline procedures aside from placing the monitor on the patient's finger and recording the hemoglobin value. A CBC will be obtained after consent is signed. Funding from the Ob/Gyn department will cover the cost of this test. Neither the subject's insurance nor the subject will be responsible for any charges. Please see attached budget and departmental letter of support.

    - **3.3. Study visits/Follow-up:** No study visits or follow up will be needed for this study. The subject participation will be considered complete when the subject is discharged from the recovery room.

    - **3.6. Withdrawals:** subjects who withdraw from the study after randomization will be excluded from further follow-up. Data collected until the time of withdrawal will be analyzed.

    - **3.7 Outcomes**

i. **Primary outcome:** pattern differences in hemoglobin tracing between cases and controls
ii. **Secondary outcomes:** transfusion requirements, post partum hemorrhage or hemorrhagic shock

4. **Criteria for inclusion of subjects**:
   a. Pregnant women between the ages of 18-50
   b. Planned cesarean delivery after failed attempt of vaginal delivery (failure to progress or failed induction of labor)
   c. Planned cesarean delivery after failed TOLAC

5. **Criteria for exclusion of subjects:**
   a. Patients unwilling or unable to provide consent
   b. Patients under the age of 18
   c. Patients who are prisoners

6. **Sources of research material:** Electronic medical records

7. **Recruitment Methods and Consenting Process:** see 3.1 above

8. **Potential risks**
   - **8.1 Loss of confidentiality:** Any time information is collected, there is a potential risk for loss of confidentiality. Every effort will be made to keep the subject's information confidential; however, this cannot be guaranteed.

9. **Potential benefits**: with continuous non-invasive monitoring of hemoglobin during cesarean section, there are many potential benefits, including: decrease in the delay in diagnosis of hemorrhagic shock, decrease in delay of arrival of blood products. If the study shows that the non-invasive measurement is accurate, decrease in need for invasive monitoring of hemoglobin would result in less blood draws, higher patient satisfaction and lower health care costs. In addition, this data will be useful in designing a level 1 trial to measure outcomes such as transfusion rates, transfusion complications, hemorrhage and maternal death.

10. **Data Monitoring:** The PI, research coordinator, and collaborators will ensure that all aspects of data quality adhere to the study design. This will include monitoring for adherence to consent procedures, inclusion and exclusion criteria, valid abstraction, correct entry, timeliness and responsiveness to data queries. Data will be collected and stored with the participant ID code only. The master enrollment log linking patient identifiers with study ID numbers will be kept in a password protected database on the Ob/Gyn department's internal server. Several data collection forms will be used. Data on these forms will be devoid of personal identifiers and will be securely stored at the perinatal research division offices. The

research coordinator will be available to monitor the data and correct any discrepancies based on source documents if needed.

11. **Procedures to Maintain Confidentiality:** Each subject will be assigned a study number with personally identifiable information deleted or removed. If needed, charts will be reviewed in the medical records area. Subjects' information will be de-identified and tagged with a number. Data will be collected and stored on a UTMB password-protected computer.

12. **Statistical approach:** we are defining cases and controls based on a quartile system of pre and post operative hemoglobin levels, with cases having the highest quartile hemoglobin drop and controls the other quartiles. We will use univariable and multivariable analysis to check for associated between continuous hemoglobin tracings from the non-invasive monitor. Nadir hemoglobin levels and percent change in the continuous hemoglobin tracings will be compared between cases and controls.

References

1. Colquhoun, D.A., et al. "Ability of the Masimo pulse CO-Oximeter to detect changes in hemoglobin." Journal of Clinical Monitoring and Computing. 2012. 26: 69-73.

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2. Frasca, D., et al. "Continuous monitoring of haemoglobin concentration after in-vivo adjustment in patients undergoing surgery with blood loss." Anaethesia, 2015, 70, 803-809.

3. Ehrenfeld, J., et al. "Continuous Non-invasive Hemoglobin Monitoring during Orthopedic Surgery: A Randomized Trial." Journal of Blood Disorders and Transfusion, 2014, 5:9.

4. Awanda, W., et al. "Continuous and noninvasive hemoglobin monitoring reduces red blood cell transfusion during neurosurgery: a prospective cohort study." Journal of Clinical Monitoring and Computing. 2015, 29: 733-740.

5. Galvagno, S., et al. "Accuracy of continuous noninvasive hemoglobin monitoring for the prediction of blood transfusions in trauma patients." Journal of Clinical Monitoring and Computing. 2015, 29: 815-821.