RESEARCH PROTOCOL

Date	December 27, 2022
Title	Evaluating the use of pre-epidural placement of SCDs to prevent hypotension
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Purpose of Study

Women given epidural analgesic during labor often experience hypotension. When this happens, it typically occurs in the first 30-60 minutes after epidural placement. This maternal low blood pressure can result in decrease perfusion of the placenta and ultimately impact blood flow to the infant which is seen through decreases in the infant's heart rate.

Hypothesis or Research Question

- Hypothesis 1: Laboring women who receive epidural analgesia and use sequential compression devices (SCDs) will experience a lower incidence of hypotension compared to laboring women who receive epidural analgesia and do not use SCDs.
  *hypotension is defined as SBP < 90 mmHg or an SBP decreases more than 20% from baseline
- Hypothesis 2: Infants of laboring women who receive epidural analgesia and use SCDs will experience a lower incidence of Category 2 tracings compared to laboring women who receive epidural analgesia and do not use SCDs.

Background

Women given epidural analgesic during labor can experience hypotension. Hypotension is defined as a systolic blood pressure of less than 90 mm Hg or diastolic blood pressure of less than 60 mm Hg. Maternal physiologic changes such as increased blood volume will have an impact on the circulation system; low maternal blood pressure can result in decreased perfusion of the placenta and ultimately impact blood flow to the fetus, which is seen via a category II or III fetal heart rate monitoring. While hypotension may not cause problems for some non-pregnant women, the fetus in utero is used to and dependent on a certain blood pressure threshold.

When hypotension related to epidural placement, this can occur within 15-60 minutes after placement. The purpose of this study is to build upon this preliminary work and to use a randomized controlled trial to examine the effectiveness of SCDs in preventing hypotension among a larger sample of laboring women who receive an epidural analgesia.

Lower limbs venous compression has been demonstrated to effectively decrease hypotension among women undergoing scheduled cesarean section (Cyna, Andrew, Emmett, Middleton, & Simmons, 2006; Goudie, Winter, & Ferguson,, 1988; Rout, Rocke, & Gouws, 1993; Sun et al., 2004; Van Bogaert, 1998). To date, only one study has examined the use of lower limbs venous compression to decrease hypotension in laboring women and found a significant reduction in maternal hypotension with the use of SCDs. This study compared women who used SCDs to a historical comparison group of women who received care before SCDs were provided and found a decrease in the incidence of maternal hypotension from 23.3% in the comparison group to 3.23% in the SCD group. and the researchers suggest a prospective randomized trial to investigate the phenomenon (Peyronnet et al., 2017). The purpose of this study is to build upon this preliminary work and to use a randomized controlled trial to examine the effectiveness of SCDs in preventing hypotension among a larger sample of laboring women who receive an epidural analgesia.

Research Plan

- **Study Design**
  This study will use a randomized, non-blinded, controlled design with two arms:
  - Arm 1: Patient will receive 1L of LR and have SCDs applied 15 minutes before epidural placement and will be removed 1 hour after epidural placement
  - Arm 2: Patient will receive 1L of LR during and after epidural placement with no use of SCDs

- **Setting for the study**
  The study will take place on Bethesda North Hospital's Labor and Delivery Unit. This unit houses 12 labor rooms and provides care to approximately 10-12 laboring women each day.

- **Participants**
  The study will enroll 120 women who meet the following inclusion/exclusion criteria:

  Inclusion Criteria:
  - Laboring at Bethesda North Hospital Labor & Delivery Unit
  - Will receive epidural analgesia
  - 37+ weeks gestation
  - Singleton pregnancy
  - Category 1 tracings only before epidural placement

  Exclusion Criteria:
  - Under 18 years old
  - Does not speak English
  - Unable to consent to involvement in the research study
  - Diagnosed with fetal demise
  - Diagnosis of pre-existing hypertension
  - Diagnosis of gestational hypertension

- Diagnosis of pre-eclampsia
- Diagnosis of diabetes
- Breech presentation
- Contraindications to lower leg compression (ex: fractured bones in leg, cellulitis, lower limb amputation, etc.)
- Contraindications to receiving 1L of LR
- Blood pressure on admission SBP>160 or DBP>110
- Fetal heart rate abnormalities before epidural

Sample Size Determination: A power analysis was conducted using the primary outcome variable, maternal hypotension, with an expected difference similar to that found in the Peyronnet and colleagues' (2017) study (3.23% vs. 23.3%) (0.3), power of 0.8, and level of significance 0.05. It was determined that 44 patients would be needed in each group, for a total sample size of 88 patients. To allow us to also examine the impact on occurrence of infant Category 2 tracings and to allow for the possibility of removing participants from the final analysis due to missing data, we plan to enroll 120 patients (60 in each group).

- **Data Collection**
  Before the study begins, information about the study will be provided to the providers. Providers who agree with involvement of their patients will be provided a hand-out about the study to give to their patients during prenatal visits and asked to mention to their patients that they may be approached about involvement of the study when they are admitted. The nurses on the L&D unit will be provided with education about the study purpose, exclusion criteria, and procedures. All nurses on the L&D unit have received training in the proper use of SCDs clinically. However, to validate and reinforce this knowledge, the nurses on the L&D unit will be provided education on proper measurement to determine boot size for SCDs and proper boot placement and SCD use. Nurses will be instructed to call a member of the study team immediately if any safety concerns occur related to the SCDs.

  When a patient who meets the inclusion/exclusion criteria is admitted, a nurse will describe the study, answer any questions the patient has, and if the patient wants to enroll in the study, the study team nurse will review the information consent form. After the patient provides written informed consent, the nurse will remove the next envelope out of a box of prefilled and sealed opaque envelopes. The envelope will provide the Subject ID number to be used on all study-related documentation and the study Arm that the patient has been randomized to, either:
  1. SCD Group + Fluid Bolus
  2. Fluid Bolus Group (no SCD)

  These envelopes will be filled using a computerized simple random number generator (1:1 randomization) prior to the start of the study.

In addition to the group assignment, the envelope will include a data collection form. Data will be recorded directly on this form during the patient's visit. The form will collect the following information:

- Whether patient was assigned to the SCD group or the standard care group
- Patient demographics including age, weight, and # pregnancies and # births
- Threshold systolic blood pressure (20% decrease from baseline) – The study team nurse will calculate threshold systolic blood pressure by calculating the admission systolic blood pressure multiplied by 0.8
- Biomed number of SCD machine (SCD group only)
- Leg measurement for SCD boot size determination (SCD group only)
- Size of boots placed (SCD group only)
- Biomed number of boots placed (SCD group only)
- Time SCDs placed on (SCD group only)
- Time of epidural placement
- Whether patient received 1L of LR
- Time SCDs removed (SCD group only)
- Did the RN have to perform any interventions to address decreased fetal heart rate during the 1 hour after epidural placement? Yes/No
- Did the anesthesia provider treat the maternal blood pressure during the 1 hour after epidural placement? Yes/No
- All BPs and times of maternal blood pressures with SBP<90 or >20% decrease from baseline within the 1 hour after epidural placement

After delivery, the RN will complete the data collection form and place the signed informed consent form and data collection form in a locked room designated for study materials.

On the data collection forms, RNs are instructed to call a member of the study team immediately if there are any safety concerns related to the SCDs. If the study team receives a call about a safety concern, recruitment and enrollment of new participants will stop until the study team meets and reviews the incident and determines it is safe to continue. Any adverse events and serious adverse events will be reported to the IRB in compliance with IRB safety policies.

Weekly, the research specialist will collect the data collection forms. The research specialist will review the data collection forms and compile the medical record numbers for any patient who the RN marked "yes" to "Did the RN have to perform any interventions to address decreased fetal heart rate?" The research specialist will send two study team nurses the compiled list for the week to conduct a review of the medical records of the patients requiring interventions to address decreased fetal heart rate. The same two study team nurses will review all charts throughout the study and they will separately determine category of the fetal heart tracings and send them to the research specialist. The two study team nurses assigned to determine tracing categories will be blinded to which group the patient was in. The

research specialist will conduct interrater reliability each week and any discrepancies will be sent back to the two raters to review together and come to a consensus on category assignment.

- **Intervention or experimental aspect of the study**
  Patients randomized to Arm 1 will have SCDs placed on their lower limbs 15 minutes before the epidural placement and they will be removed one hour after epidural placement. SCD use is in the Epic order set for laboring patients but is rarely used in practice on the unit. The SCD in clinical use at Bethesda North Hospital is the Kendall SCD Express Sleeves, knee length 700 series, Ref: 29525. In this study, the study team is using the device according to the indicated description "as the sleeves/cuffs compress the legs/feet, veins collapse, forcing the blood to move upward towards the heart" but not for the indicated outcome of "prevention of DVTs"; instead the study is testing the use of this device for a new indication – for prevention of maternal hypotension.

  Patients randomized to Arm 2 will receive standard care.

- **Statistical Analysis**
  Data recorded on paper data collection forms will be entered into a password protected database. Only study team members will have access to the database. No personal information will be entered into the electronic database. Data will undergo range checks when entered into the database, and quality control procedures will be performed to ensure accuracy of the data in the electronic database.

  Statistical analyses will be performed using Intellectus Statistics statistical software. The following analyses will be performed to address each hypothesis:

  Hypothesis 1: Laboring women who receive epidural analgesia and use SCDs will experience a lower incidence of hypotension compared to laboring women who receive epidural analgesia and do not use SCDs.
  To compare the effects of the SCDs, a Chi Square test will be used to compare occurrence of maternal hypotension for patients who used SCDs to patients who did not use SCDs. A level of significance of $\alpha=0.05$ will be used.

  Hypothesis 2: Infants of laboring women who receive epidural analgesia and use SCDs will experience a lower incidence of Category 2 tracings compared to laboring women who receive epidural analgesia and do not use SCDs.
  To compare the effects of the SCDs, a Chi Square test will be used to compare occurrence of Category 2 tracings of infants of patients who used SCDs to infants of patients who did not use SCDs. A level of significance of $\alpha=0.05$ will be used.

Interim data analysis will occur (1) once approximately 1/3 of the participants have been enrolled in each group and (2) once approximately 2/3 of the participants have been

enrolled in each group. If interim calculations at time (1) or time (2) note a significant difference between groups in maternal hypotension or frequency of category 2 tracings, data collection will be completed at that time and final analysis will be completed.

Ethical Considerations

- **Informed consent**
  All study staff will complete CITI training. A study staff member will meet with potentially eligible patients and describe the study and answer any questions. If the patient is interested and meets all the inclusion/exclusion criteria, the study staff will review the *Informed Consent Form* and obtain written informed consent. Patients will receive a copy of their signed Informed Consent form.

  Informed Consent forms will be stored in a locked room that only staff will have access to. After the study closes, the signed Informed Consent forms will be boxed and sent to off-site storage and securely stored until the infant turns 21 years of age. At that time, the hard copy forms will be shredded.

- **Privacy information**
  Personal identifiers will not be entered into the electronic database. Hard copy data collection forms and Informed Consent forms will be stored in a locked room that only staff will have access to. Electronic data will be stored on a password-protected folder on the U drive. Only study staff will have access to the electronic study documents. After data analysis and dissemination is completed, hard copy forms will be boxed and sent to off-site storage and securely stored until the infant turns 21 years of age. At that time, the hard copy forms will be shredded.

Cost/Budget

There will be no costs to conduct this study and no additional charges to patients.

Estimated Period of Time to Complete Study	
When will study begin?	2.25.2021
Protocol Development Completed	1 week
Admin Review Time	2 weeks
IRB Approval	6 weeks
Data collection	3 months
Data analysis	1 month
Presentation development (if applicable)	2 weeks
Manuscript Development (if applicable)	1 month
Journal submission process	3 months

(if applicable)	
Study closure	1 week

- **When and how will results be disseminated?**
  Results will be disseminated internally to the TriHealth perinatal leadership team and system-wide through the TriHealth Research Council. Results will be disseminated nationally through presentation at a professional organization conference. Finally, results will be disseminated nationally and internationally by publication in a relevant peer-reviewed journal.

References

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