CSE vs. Epidural for Postpartum Depression

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STUDY PROTOCOL:

The clinical procedure that will be used for research purposes is labor epidural analgesia initiation by combined spinal-epidural (CSE) or epidural (E).

Study participants, prior to enrollment, will have already made a decision for themselves to use labor epidural analgesia to manage pain during labor (decision made is one eligibility criteria). The study intervention, CSE or E, are both commonly used techniques in the initiation of epidural analgesia, but currently the utilization of one or the other of these strategies is left to the discretion of the anesthesia clinician and is dictated primarily by clinician preference. Thus an RCT will address this level of bias. Both CSE and E can be considered the standard of care for any laboring woman requesting labor epidural analgesia.

BASELINE: At the first encounter, an assessment will include measurements of depression (EPDS), anxiety (STAI inventory), resiliency (ER 89), pain catastrophizing (PCS), perceived social support (MSPSS) and pain (BPI-long form). For women recruited at the 3rd trimester visit, Quantitative sensory testing (QST) will be performed. The pain sensitivity test will involve the use of a small pad attached to the participant's arm. The thermal device will gradually heat up from the moment the participant feels the heat until the pain sensation becomes uncomfortable; the participant is instructed to tell investigators when to discontinue the test at the first moment of discomfort, at which time the test is stopped. The pain sensitivity test also includes pressure devices to assess pressure pain. These devices are widely and commonly used in clinical pain research. From these test, we will determine the participant's sensitivity profile which we will use in our study analysis.

To enhance recruitment, we will also approach women in early labor who have not yet received an epidural after consultation with their bedside nurse and once it has been established that they meet eligibility criteria. These women will answer the aforementioned baseline surveys but will not participate in QST.

Upon hospital admission for labor and delivery: confirmation of term (>/= 37 weeks) planned vaginal delivery will occur. The participant will be randomized to one of two groups: combined spinal-epidural (CSE) or epidural (E). Randomization will occur by block allocation. At the moment of patient request for labor epidural analgesia, one sealed and opaque envelope containing the next assignment group will be opened. The envelopes will be located in a designated location in the anesthesia workroom of the birth center, and thus no delays in the laboring person's ability to receive the requested epidural is anticipated. Should any delay occur for any reason, no randomization will occur and the patient will receive the epidural per routine request and clinical flow. Initiation of each labor analgesic strategy will be standardized to minimize variability of analgesia, and is outlined on the study figure attached. Management of breakthrough pain will be standardized and will occur by the strategy outlined on the study figure attached ("supporting documentation").

Throughout labor, pain will be assessed hourly using 100mm visual analog scales for both pain intensity and pain unpleasantness. Regardless of onset of labor (spontaneous or induction), hourly assessments are required to measure with accuracy and density the change in pain that is

experienced over time for women in labor, in response to both the progress of labor and any changes in response to medications via the epidural infusion. For the entire labor, labor variables will be recorded, including sterile vaginal exam (SVE) at the time of epidural request, duration of labor (time from admission to unit until time of delivery), number of manual epidural supplemental doses, total dose of local anesthetic and epidural opioid required, and the outcome of labor -- both maternal (normal spontaneous vaginal delivery, instrumental delivery, cesarean delivery, perineal lacerations, total oxytocin dose requirements) and neonatal (sex, Apgar scores, need for resuscitation, need for neonatal ICU). Study procedures will continue should the need arise for a cesarean delivery or if there are any other complications to the pregnancy/fetus.

Postpartum measurements will be made as follows:

Postpartum day 0-2: Within 2 days we will measure co-variates of pain (BPI short), breastfeeding (yes/no) and perceived stress (PSS).

At 6 weeks, we will measure the primary outcome of EPDS score as well as co-variates including pain (BPI short), maternal infant attachment (MPAS), parenting self-efficacy (PMP-SE), child development (ASQ-3), and breastfeeding (yes/no) (i.e. "Are you currently breasfteeding? Yes or no.") A margin of 7 days around the 6 week postpartum mark will be allowed for the patient to respond.

At 3 months, we will assess breastfeeding (Y/N), Depression (EPDS), Pain (BPI – Short Form), Mother-infant attachment (MPAS), Parenting self-efficacy (PMP-SE), Child development (ASQ-3). A margin of 7 days around the 3 month postpartum mark will be allowed for the patient to respond.

Should a participant not respond to follow-up surveys at the specified time, we will exclude their data from analysis; depending upon the volume and nature of such missing data, we reserve the ability to impute missing data if MAR or MNAR.

Interactions with participants will occur in person, electronically (email), or by phone. Investigators will consent participants to retain the ability to re-contact participants at a future date for follow-up questions.

STATISTICAL ANALYSIS PLAN:

The estimated incidence of PPD in U.S. American women is 20%, commensurate with estimates of institutional rates of PPD at Magee-Womens Hospital.36 As a pilot, we will target 10% of the sample required for a full study. The primary outcome is risk for PPD, measured by EPDS score at the 6-week postpartum visit. A sample of 394 participants, 197 in each group, will have 80% power to detect a 10% reduction in PPD symptoms at a significance level of 5% (two-tailed). With an optimistic estimated attrition of 15%, a full trial would aim to enroll 454 participants, 227 in each group. For this pilot we will target a sample of 23 patients in each group (total 46), to yield 10% of the full study sample. Given a yet unknown attrition rate, we estimate that study procedures in a maximum of 60 participants in each group will be the maximum number of participants necessary to establish a clear protocol. We will review and refine the protocol every 5 patients until no further changes to the protocol are made over 5 consecutive participants. We will prospectively gather data on screening eligibility, consent and decline rates, crossover rates, and provider and subject feedback.

Linear regression will be used to examine the relationship between EPDS scores and treatment group, both over time in participants and by group. The relationship between pain and EPDS will also be examined using linear regression. T-tests, linear regression, and chi-squared tests will be used, where appropriate, to examine the relationships between treatment group and pain, infant attachment, infant development, and breastfeeding.