Comparing Effectiveness of CSE Versus DPE for Labor Analgesia

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After obtaining written informed consent, parturients are randomised in a 1:1 ratio by computer-generated random sequence to CSE or DPE arms, stratified by parity (nulliparous versus multiparous) and class of obesity (BMI <40 vs. 40-50 $kg.m^{-2}$). Allocation is concealed in sequentially numbered opaque envelopes. Patients, obstetricians, nurses, and anesthesia providers involved in follow-up of labour analgesia and data collection are blinded to group allocation. The anesthesia provider placing the neuraxial block and the supervising attending anesthesiologist are not involved in data collection or in follow up of labour analgesia.

Before neuraxial placement, all patients have an intravenous catheter placed with automated non-invasive blood pressure, pulse oximetry, and external tocodynamometry monitors applied. All women receive a 500 ml intravenous bolus of crystalloid solution immediately before the initiation of neuraxial analgesia. The epidural space is identified using a 17-gauge Tuohy needle with the patients in the seated position at the estimated L3-4 or L4-5 interspace, via a midline approach using a loss of resistance to saline technique. After identification of the epidural space, a needle-through-needle technique is performed using a 25-G Whitacre needle, placed into the shaft of the previously sited epidural needle to create a single dural puncture. After confirmation of free flow of CSF, initial dosing consists of intrathecal 0.25% bupivacaine 2 mg (0.8 ml) and 10 µg (0.2 ml) fentanyl in the CSE group. Subsequently, the spinal needle is removed and the epidural catheter (19-gauge Duraflex wire-reinforced multiport catheter (Smith Medical, USA)) is advanced 5 cm into the epidural space and secured with the patient in the sitting upright position, using Tegaderm clear occlusive dressing (3M, USA). In the DPE group, after confirmation of free flow of CSF, the spinal needle is withdrawn and the epidural catheter advanced 5 cm into the epidural space. After negative aspiration for blood and CSF, initial dosing consists of 20 ml of 0.1% ropivacaine plus fentanyl 2 $\mu g.ml^{-1}$ (premixed) administered in divided doses of 5 ml every 2 min. In both groups, analgesia is maintained using programmed intermittent epidural boluses of 8 ml of ropivacaine 0.1% with fentanyl 2 $\mu g.ml^{-1}$ every 45 min starting 30 min after the initial spinal or epidural loading dose, with patient-controlled epidural analgesia (PCEA) of 10 ml, a lockout of 10 min and maximum dose of 50 ml per hour.

If analgesia is inadequate (defined as a patient request for supplemental analgesia beyond self-administered PCEA boluses), an anesthesia provider blinded to group assignment assesses and, if warranted, administers top-up doses according to a predefined algorithm.

The end time of administration of the loading dose (end of spinal dose injection in the CSE group or epidural medication administration in the DPE group) is designated time 0 (t = 0). A blinded investigator collects data at 15 and 30 min and subsequently at 2-h intervals from time zero until delivery. Analgesia is evaluated at all time points using the verbal numeric pain rating scale (NPRS) for the last contraction (0=no pain, 10=worst possible pain). The upper and lower sensory levels are evaluated at 15 and 30 min using temperature discrimination to ice. Motor blockade is assessed at all time points using the modified Bromage score.

The following additional data are recorded every 2 h until delivery: presence of pruritus; nausea; hypotension (defined as systolic blood pressure ≤ 20% from the patient's admission blood pressure); need for physician top-up; catheter adjustment and catheter replacement. We also assess for the presence of asymmetric blockade, defined as a difference > 2 dermatomal sensory levels between the left and right side as assessed at 15 and 30 min or at any time that sensory levels are checked because of complaints of pain. An obstetrician blinded to group assignments accesses the electronic medical record to review tocometry and continuous fetal monitoring strips and extract uterine contraction and fetal heart rate monitoring patterns in 10-min epochs, for 1 h before and 1 h after the initial spinal (CSE group) or epidural (DPE group) dosing. On the first postpartum day, we assessed for postdural puncture headache and satisfaction with labour analgesia (0-10, 0= very dissatisfied, 10=very satisfied)

The primary outcome of the study is the quality of labour analgesia, which is defined by a composite of five components: asymmetric block after 30 min of initiation (difference in sensory level of more than two dermatomes); epidural top-up interventions; catheter adjustment; catheter replacement; failed conversion to neuraxial anesthesia for cesarean delivery, requiring general anesthesia or replacement of the neuraxial block.

Secondary outcomes include: pain scores; Bromage scores; sensory levels at 15 and 30 min; adverse events (hypotension, nausea, pruritus, postdural puncture headache, fetal heart rate changes); duration of second stage of labor; mode of delivery; total anesthetic dose; PCEA use; and overall satisfaction with analgesia.

Based on the study by Chau et al a sample size of 50 patients per group had an 80% power at alpha 0.05 to detect a reduction in the composite primary outcome from 50% in the CSE group to 22.5 % in the DPE group. To account for dropouts, we aim to enrol up to 60 patients per group to have complete data on 100 subjects.

Descriptive statistics for patient characteristics and outcomes are calculated and reported as median (IQR [range]) or number (proportion) as appropriate. The primary composite outcome is compared between exposure groups using a chi-squared test and an effect size is reported as a risk ratio. Secondary outcomes are assessed using chi-squared or Fisher exact tests as appropriate, with associated risk ratios for categorical measures and univariate log-linear regression with mean ratios for continuous measures. All p values for the secondary outcomes are adjusted for multiple comparisons using the Bonferroni-Holm method to control family-wise error rate and adjusted p values are reported. Only p values and adjusted p values < 0.05 are considered statistically significant. Analysis is performed using R version 4.3.1, with the power calculation performed using NQuery.