Official Title:

Effect of different labor analgesics on maternal UtA, fetal UA and MCA blood flow index observed by Doppler ultrasonography: A prospective randomized double-blinded controlled trial

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Study protocol

1. Study design

Pregnant women of ASA grade I to II, aged 20 to 35 years, weighing 50 to 100 kg, 150-175 cm in height, and 37 to 41 weeks of gestation were included in the study. Women with contraindications of spinal anesthesia, maternal complications (such as pregnancy-induced hypertension, preeclampsia, cardiovascular and cerebrovascular diseases, etc.), abnormal uterine contractions, abnormal placental function or position, signs of fetal distress, and known fetal malformations were excluded. The patients who were failed to administer combined spinal and epidural block analgesia, those who were transferred from vaginal trial labor to cesarean section, those who could not cooperate with ultrasound detection, and those who needed to use oxytocin were excluded. The study was planned and implemented in accordance with the Declaration of Helsinki.

2. Randomization and blinding

90 parturients in the study were randomly assigned to Sufentanil group (S, n=30), Ropivacaine group (R, n=30) and Sufentanil added to Ropivacaine group (SR, n=30) by non-blind personnel according to the computer random number table, and the allocation was hidden. The solution was prepared by an unblinded anesthesiologist and packaged in a blind way and administered by another anesthesiologist. The patients, anesthesia providers, data recorders, ultrasound examiners, obstetrical staff, and nursing staff remained blinded to group assignment throughout the study.

3. Study intervention

At the time of request for labor analgesia, patients were randomized to receive either sufentanil 5 μg (Group S), ropivacaine 3mg (Group R), or sufentanil 2.5 μg added to ropivacaine 2.5 mg (Group SR) into the subarachnoid space. All groups received the standard epidural solution that contained 0.1% ropivacaine with 0.25 μg/ml sufentanil. Routine obstetric and anaesthetic monitoring was given after maternal entered the delivery room.

An experienced the anesthesiologist select L3-4 lumbar vertebra clearance to puncture with standard sterile technique using loss of resistance when the puerpera palace has expanded to about 3 cm. After the puncture reached the epidural space, a 25-gauge lumbar anesthesia needle was used to puncture into the subarachnoid space. 2 mL of anesthetic drug as determined by her group randomization were administered into the cavity through the lumbar anesthesia needle after cerebrospinal fluid flow out. A 19-gauge spring-wound catheter was threaded 4-6 cm into the epidural space. All patients received a test dose of 3 ml of 1.5% lidocaine followed by an initial loading dose of 5 ml of the standard epidural solution. Epidural catheters into vessels or subarachnoid space were excluded. An analgesic pump (PCEA pump, 100ml) containing standard epidural solution was then connected to the epidural catheter at a background continuous infusion rate of 5 mL/h. The visual analogue score for pain (VAS) was performed 15 minutes after the injection dose, and if the VAS score fell below 3, the case was included in the study.

An anesthesia provider assessed the adequacy of analgesia for the patients throughout the duration of labor. Any breakthrough pain was managed with a physician-administered epidural bolus. All obstetric analgesia procedures were performed by the same anesthesiologist to reduce errors due to technical reasons.

4. Ultrasonic examination method

The patients were placed in a supine position with calm breathing to perform doppler ultrasonography during the interval of contractions. Ultrasound probe was

placed on fetal head area. Middle cerebral arteries (MCA) run anteriorly on both sides of the ring of cerebral arteries at the position of the double head diameter (see Figure 1A). We can get waveforms of MCA examined by pulsed wave doppler (see Figure 1B). The probe was placed at the placenta area, and we can see the fetal umbilical cord connecting to the center of the placenta. Umbilical artery (UA) could be identified by color flow, and its waveforms were examined by pulsed wave doppler (see Figure 1C and 1D). The probe was placed at the midpoint of the groin. The right and left uterine arteries (UtA) could be identified by color flow at the apparent crossover with the external iliac arteries, and pulsed wave doppler was used to obtain waveforms (see Figure 1E and 1F). 3 to 10 arterial spectrograms with clear edges and no background noise at baseline were selected. The above arterial blood flow indexes were measured three times and the average value was taken. The S/D、PI、 RI value of MCA、UA、UtA can be measured automatically by ultrasound instrument. All doppler examinations were performed by the same sonographer.

5. Primary outcomes

The main indexes were doppler blood flow indexes (S/D, PI, RI value) of UtA, UA, MCA before analgesia (T_0) and 30 min (T_1), 60min (T_2), 90 min (T_3) after analgesia in the three groups.

6. Secondary outcomes

Fetal heart rate (FHR) and mean artery pressure (MAP) at T_0, T_1, T_2 and T_3, neonatal weight, time of each stage of labor, rate of midwifery, neonatal umbilical artery blood gas index and Apgar score at 1 min, 5 min, 10 min after birth of the three groups were included in the secondary indicators.

7. Statistical Analysis Plan

In this study, SPSS 13.0 was used for statistical analysis, and GraphPad Prism 8 was used for mapping. Measurement data were expressed as mean ± standard deviation (x±s), and categorical data were expressed as frequency, percentage, or rate. Paired t

test was used for intra-group comparison and independent sample t test was used for inter-group comparison of measurement data conforming to normal distribution. The measurement data with non-normal distribution were analyzed by rank sum test. Chi-square test was used for statistical analysis of categorical data. $P<0.05$ indicates statistical significance.