Spinal or epidural fentanyl or sufentanil for labour pain in the early phase of the labour

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Abbreviated name: "Early phase labour analgesia by spinal or epidural analgesic".

Background

Approximately one third of the parturients experience unbearable pain during labour (1). Epidural or spinal opioids and local anesthetics given epidurally or spinally are one of the most effective methods to alleviate labour pain. This type of analgesia is widely used in our hospital; in 2015 at HUS/Katiloopisto hospital 6066 (88 %) of the 7471 parturients received either spinal or epidural analgesia for labour.

Neuraxial analgesia carries some side-effects although severe side-effects are very rare (2). One of the most common side effects is post-dural puncture headache (PDPH) caused by perforation of the membrane separating the spinal and epidural spaces. This risk is estimated to be approximately 1.7 % with the pencil point needles used in our hospital (3). With spinal drug administration this membrane is always perforated.

With epidural drug administration this intentional perforation of the dural membrane and its associated headache syndrome could be avoided. In addition spinal analgesia can be administered only at a rather low (lumbal) level of the spine in order to avoid spinal cord injury. In some parturients obesity or strong lordosis of the lumbal spine can result in technical difficulties in the safe placement of the spinal analgesia and it may be easier to use epidural analgesia.

Administration of intrathecal lipophilic opioid alone (fentanyl or sufentanil) has been shown to result in sufficient analgesia in the early phase of the labour without causing motor block of the lower limbs or drop of blood pressure due to blockade of the symphatetic neural system (4,5). This method is used routinely in our hospital with a spinal fentanyl dose of 25 micrograms. Until May 2013 our hospital routinely used sufentanil at a dose of 5 micrograms. Alternative option for the spinal opioid would be normal epidural analgesia where the local anesthetic dose is ropivacain 20 mg and fentanyl 100 micrograms. The fentanyl dose of 100 micrograms could be replaced by sufentanil at a dose of 20 micrograms (6).

Purpose of the study

In this prospective randomized study the efficacy of spinal or epidural opioid (fentanyl or sufentanil) to alleviate the pain during contraction is studied. The opioid is given as a single treatment without any local anesthetics. The primary outcome for the study is the level of analgesia achieved in 20 minutes after the administration of the analgesia. The secondary outcomes are the rate of on-set of the analgesia measured by visual analog scale bar (VAS 0-100 mm; 100 mm worst possible pain; 0 mm no pain) from above 80 mm value (peak during contraction) to under 30 mm value and the duration of the analgesia provided by the neuraxial opioid alone.

Methods

Parturients

A total of 80 primiparous parturients will be recruited (20 parturients in each of the four treatment arms). According to the power calculation we expect to detect a potential difference

of 15 mm in the VAS scores at standard deviation of 15 mm with an 80 % certainty. Potential differences of less than 15 mm are not considered clinically relevant.

The parturients are ensured not to have any contraindications for spinal/epidural analgesia and they have not received any opioid analgesics by any route within 120 minutes prior to analgesia administration. The randomization is performed when the parturient asks for regional pain relief (i.e. spinal fentanyl according to the institutional practice). The delivery must be in the early phase marked by cervical dilatation of 5 cm or less at the time of the investigational analgesia and the pain VAS during contraction on the 0-100 mm VAS scale shall be at 80 mm or more. The BMI of the parturient at the date of delivery must be 20-35, the pregnancy singleton and the parturient may not have allergy for fentanyl, sufentanil or lidocaine. Furthermore, the parturient's ability to read and speak Finnish must be adequate so that she can understand the study and she can be interviewed according to the protocol after the analgesia.

The parturient will be given the study brochure prior to painful contractions reach the randomization level (VAS 80 mm). If the parturient agrees to participate in the study and fulfills the inclusion criteria, she will be randomized in to one of the four treatment arms.

Interventions

According to the randomization (20 parturients per group) the parturient is randomized to receive either fentanyl 20 micrograms intrathecally, fentanyl 100 micrograms epidurally, sufentanil 5 micrograms intrathecally or sufentanil 20 micrograms epidurally. The intrathecal medications are diluted according to the institutional protocol into the total volume of 2 ml and epidural medication is diluted into 5 ml volume by sterile saline.

Epidural analgesia is given through the epidural catheter and in all cases epidural catheter is flushed with 2 ml of saline at the end of procedure. The neuraxial analgesia procedure is performed according to the institutional protocol using Portex combined spinal epidural (CSE) set but for epidural drug administration the spinal needle is not used. In both intrathecal (spinal) and epidural medication groups, an epidural G18 catheter is left in the lumbal epidural space.

Blinding

For safety reasons the study will be blinded in such a manner that the parturient or the data collector do not know which analgesia is administered. The anesthesiologist providing the analgesia will prepare the sterile table and draw the medications outside the delivery room. The anesthesia chart will show the randomization code of the parturient. The key to the randomization codes is always available in the anesthesia office. Otherwise, the anesthesia report will be filled in a normal manner and the subsequent epidural analgesia boluses will be marked normally in the chart. The parturient is informed about the procedure using standardized phrases, which do not reveal the (spinal or epidural) nature of the analgesia provided for the midwife or the parturient. In both treatment groups an identical Portex epidural catheter remains in the back of the parturient.

Data will be collected after the drug delivery by another anesthesiologist who is blinded regarding the analgesia provided.

Follow up and data acquisition

The on-set of analgesia is monitored during each contraction on a 0-100 mm VAS scale for up to 30 minutes after the analgesia. The maximum achievable analgesia is expected to be achieved within 30 minutes. The fetal heartrate and the parturient's blood pressure is monitored for

30 minutes according to institutional protocol for neuraxial analgesia. Pruritus is the most common side-effect of the neuraxial opioids and it will be monitored by interview at 0, 10, 20 and 30 minutes. The used measurement scale is: 0 = no pruritus; 1 = mild pruritus; 2 = moderate pruritus; 3 =severe pruritus; 4 = unbearable pruritus. Potential nausea and vomiting will be documented at 0, 10, 20 and 30 minutes (for the past 10 minute interval). Also potential changes in the fetal heart rate, potential ob/gyn consultations and actions due to these consultations will be recorded.

Rescue analgesia and subsequent labour analgesia

The parturient can receive additional analgesia through the epidural catheter at the earliest 30 minutes after the spinal or epidural opioid administration. At 30-45 minutes after the intervention the parturient may get 20 mg ropivacain in 20 ml saline, whereas after 45 minutes a dose of 20 mg of ropivacain and 50 micrograms of fentanyl in 20 ml can be given.

Data to be collected in the trial

Background information (height, weight, duration of pregnancy)

from primary health care maternity chart

Gestational data (duration of pregnancy)

from the hospital Obstetrics software

Prior analgesia during delivery

from the hospital Obstetrics software

Pain VAS (0-100 mm) immediately prior to investigational analgesia and for each contraction thereafter for 30 minutes

Interviewed from the parturient

Pruritus and nausea at 0; 10; 20; 30 minutes after the analgesia

Interviewed from the parturient

Timing of the next epidural analgesic dose, cervical dilatation prior to the next epidural dose. Information on the analgesia provided by the epidural dose.

from the hospital Obstetrics software

Time of delivery, mode of delivery (cesarean delivery, vacuum assisted delivery), potential postpartum operations in the operating theatre.

from the hospital Obstetrics software

Fetal heart rate (FHR)

automatically registered into the hospital Milou system

Archival of the collected data, processing of personal information regarding parturients

The collected data will be archived at the Department of Anaesthesiology in a locked cabinet to which only the investigators have access. When the information is transferred into the electronic data file all directly identifying information will be removed (name and date of birth). The

study participants can be subsequently identified by matching case number with the signed consent form. No directly identifying information is saved in the electronic form.

Analysis of the collected data

For statistical analysis the information is transferred into SPSS software, which is used for comparison of the continuous data (background information, pain VAS scores) and categorical data (adverse events such as nausea, pruritus).

The primary outcome is measured in millimeters on a 100 millimeter line and processed as a continuous variable with 0 mm indicating no detectable pain and 100 mm indicating the worst possible pain. Similarly secondary outcome marker, the duration of analgesia, will be recorded in minutes and processed as a continuous variable. The incidence of adverse events will be recorded as presence or absence of certain adverse events (pruritus, nausea) and analyzed as a categorical variable.

Chi-squared test will be used for categorical variables while Kruskal-Wallis test for independent samples is used for comparisons of continuous variables between the treatment arms.

The fetal heartrate (CTG) recordings will be retroactively analyzed by an obstetrician for potential pathology prior to analgesia and for 30 minutes thereafter. The obstetrician is blinded regarding the intervention.

All data and events are analyzed according to original allocation into respective intervention groups.

Completion of the study

Recruiting of the parturients will begin once the required permits have been received. The parturients will be recruited during 2016 and the results of the study will be published in a peer reviewed journal thereafter. The study will be completed at Helsinki University Central Hospital /Katilopisto delivery hospital without external sponsors or funding as part of normal quality improvement work.

Ethical considerations

The parturients will be recruited for the study at the very early phase of the labour. The institutional normal protocol is to give 25 micrograms of fentanyl intrathecally. The fentanyl dose used in this study (20 micrograms) does not differ in terms of efficacy from the 25 microgram dose and the efficacy of the other interventions is expected to be in the similar range. Epidural delivery of fentanyl or sufentanil alone without local anesthetic has not been previously studied in the early phase of the labour.

This study will provide information regarding possible replacement of spinal opioid administration with epidural opioid thus avoiding risks and limitations associated with spinal opioid delivery.

No placebo control is used in this study and the parturients will not be exposed to additional injections or painful maneuvers. It is possible that epidural analgesia does not have as fast on-set as spinal analgesia. The only viable option for spinal drug administration currently would be

epidural analgesia which is not routinely preferred at such early phase of the delivery. Therefore, the participating parturients are expected to receive at least as good labour analgesia as those parturients who do not participate in the trial.

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