# Clinical trial results:
# Spinal or epidural fentanyl or sufentanil for labour pain in early phase of the labour

## Summary

| | |
|---|---|
| EudraCT number | 2016-000486-23 |
| Trial protocol | FI |
| Global end of trial date | 29 November 2017 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 24 January 2021 |
| First version publication date | 24 January 2021 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | #01/01.02.2016 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02885350 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Helsinki University central hopsital/Women's hospital |
| Sponsor organisation address | Haartmaninkatu 2, Helsinki, Finland, 00780 |
| Public contact | Women's hospital/Naistenklinikka/dept of anesthesia, Helsinki University Central Hospital, 358 504271850, antti.vaananen@hus.fi |
| Scientific contact | Women's hospital/Naistenklinikka/dept of anesthesia, Helsinki University Central Hospital, 358 504271850, antti.vaananen@hus.fi |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 26 April 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 29 November 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 November 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Alleviation of labour pain at 20 minutes after intervention

Protection of trial subjects:

Intervention performed by non-blinded anesthesiologist who did not participate in the collection of the data.

Background therapy:

Non medical alleviation of the labour pain
Nitrous oxide

Evidence for comparator:

All interventions and comparators have been used in previous studies to alleviate labour pain.

| | |
|---|---|
| Actual start date of recruitment | 16 September 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Finland: 80 |
| Worldwide total number of subjects | 80 |
| EEA total number of subjects | 80 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 80 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Parturients fulfilling the inclusion criteria were recruited from 16th Sep 2016 until completion of the trial 29th Nov 2017 from the Helsinki university central hospital.

### Pre-assignment

Screening details:

Parturients were informed about the trial beforehand in writing and by oral information. Upon final inclusion into the study they were to have maximum pain during contraction at 80 mm and not received other opioid medication within the prior 120 minutes.

### Period 1

| | |
|---|---|
| Period 1 title | Baseline (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Data analyst |

Blinding implementation details:

The study subject, data collector (present for the first 30 minutes in the delivery suite) and caretaking midwife were all blinded. Also the data analysis was carried out blinded for the fetal heart rate analysis.

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Spinal fentanyl |

Arm description:

Combined spinal epidural analgesia where a dose of 20 micrograms of fentanyl was given into intrathecal space

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Fentanyl citrate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

20 micrograms given in a total volume of 2 ml (dilution with saline)

| | |
|---|---|
| **Arm title** | Epidural fentanyl |

Arm description:

Normal epidural catheter placed and 100 micrograms of fentanyl citrate given epidurally

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Fentanyl citrate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Epidural use |

Dosage and administration details:

100 micrograms given in a total volume of 7 ml (dilution with saline)

| | |
|---|---|
| **Arm title** | Spinal sufentanil |

Arm description:

5 micrograms of sufentanil was given intrathecally by using combined spinal epidural technique

| | |
|---|---|
| Arm type | Active comparator |

| | |
|---|---|
| Investigational medicinal product name | sufentanil citrate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intrathecal use |

Dosage and administration details:

5 micrograms in a volume of 2 ml (diluted) with saline was given intrathecally

| **Arm title** | Epidural sufentanil |
|---|---|

Arm description:

20 micrograms of sufentanil given into epidural space

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | sufentanil citrate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Epidural use |

Dosage and administration details:

20 micrograms in a volume of 7 ml (diluted) with saline was given intrathecally

| **Number of subjects in period 1** | Spinal fentanyl | Epidural fentanyl | Spinal sufentanil |
|---|---|---|---|
| Started | 20 | 20 | 20 |
| Completed | 20 | 20 | 20 |

| **Number of subjects in period 1** | Epidural sufentanil |
|---|---|
| Started | 20 |
| Completed | 20 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Spinal fentanyl |
| Reporting group description: | |
| Combined spinal epidural analgesia where a dose of 20 micrograms of fentanyl was given into intrathecal space | |
| Reporting group title | Epidural fentanyl |
| Reporting group description: | |
| Normal epidural catheter placed and 100 micrograms of fentanyl citrate given epidurally | |
| Reporting group title | Spinal sufentanil |
| Reporting group description: | |
| 5 micrograms of sufentanil was given intrathecally by using combined spinal epidural technique | |
| Reporting group title | Epidural sufentanil |
| Reporting group description: | |
| 20 micrograms of sufentanil given into epidural space | |

| Reporting group values | Spinal fentanyl | Epidural fentanyl | Spinal sufentanil |
|---|---|---|---|
| Number of subjects | 20 | 20 | 20 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 20 | 20 | 20 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 20 | 20 | 20 |
| Male | 0 | 0 | 0 |
| Maximum pain during contraction | | | |
| Pain on 0-100 mm VAS scale during contraction at baseline | | | |
| Units: mm | | | |
| geometric mean | 84.3 | 87.2 | 86.2 |
| standard deviation | ± 11.7 | ± 8.9 | ± 8.3 |

| Reporting group values | Epidural sufentanil | Total | |
|---|---|---|---|
| Number of subjects | 20 | 80 | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 20 | 80 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 20 | 80 | |
| Male | 0 | 0 | |
| Maximum pain during contraction | | | |
| Pain on 0-100 mm VAS scale during contraction at baseline | | | |
| Units: mm | | | |
| geometric mean | 87.5 | | |
| standard deviation | ± 11.3 | - | |

| Subject analysis sets | |
|---|---|
| Subject analysis set title | Spinal fentanyl |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The twenty parturients who received the 20 microgram spinal fentanyl dose | |
| Subject analysis set title | Epidural fentanyl |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The 20 parturients who received the epidural 100 microgram fentanyl dose | |
| Subject analysis set title | Spinal sufentanil |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The 20 parturients who received the 5 microgram intrathecal sufentanil dose | |
| Subject analysis set title | Epidural sufentanil |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The 20 parturients who received the 20 microgram epidural sufentanil dose | |

| Reporting group values | Spinal fentanyl | Epidural fentanyl | Spinal sufentanil |
|---|---|---|---|
| Number of subjects | 20 | 20 | 20 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 20 | 20 | 20 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 20 | 20 | 20 |
| Male | 0 | 0 | 0 |
| Maximum pain during contraction | | | |
| Pain on 0-100 mm VAS scale during contraction at baseline | | | |
| Units: mm | | | |
| geometric mean | 24.7 | 51.5 | 19.1 |
| standard deviation | ± 30.9 | ± 25.2 | ± 25.7 |

| Reporting group values | Epidural sufentanil | | |
|---|---|---|---|
| Number of subjects | 20 | | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 20 | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 20 | | |
| Male | 0 | | |
| Maximum pain during contraction | | | |
| Pain on 0-100 mm VAS scale during contraction at baseline | | | |
| Units: mm | | | |
| geometric mean | 45.4 | | |
| standard deviation | ± 29.0 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Spinal fentanyl |
| Reporting group description: | |
| Combined spinal epidural analgesia where a dose of 20 micrograms of fentanyl was given into intrathecal space | |
| Reporting group title | Epidural fentanyl |
| Reporting group description: | |
| Normal epidural catheter placed and 100 micrograms of fentanyl citrate given epidurally | |
| Reporting group title | Spinal sufentanil |
| Reporting group description: | |
| 5 micrograms of sufentanil was given intrathecally by using combined spinal epidural technique | |
| Reporting group title | Epidural sufentanil |
| Reporting group description: | |
| 20 micrograms of sufentanil given into epidural space | |
| Subject analysis set title | Spinal fentanyl |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The twenty parturients who received the 20 microgram spinal fentanyl dose | |
| Subject analysis set title | Epidural fentanyl |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The 20 parturients who received the epidural 100 microgram fentanyl dose | |
| Subject analysis set title | Spinal sufentanil |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The 20 parturients who received the 5 microgram intrathecal sufentanil dose | |
| Subject analysis set title | Epidural sufentanil |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| The 20 parturients who received the 20 microgram epidural sufentanil dose | |

### Primary: Reduction of maximum pain during contraction at 20 minutes on 0-100 mm VAS scale

| | |
|---|---|
| End point title | Reduction of maximum pain during contraction at 20 minutes on 0-100 mm VAS scale |
| End point description: | |
| at 20 minutes after the investigational drug or comparator administration | |
| End point type | Primary |
| End point timeframe: | |
| 20 minutes | |

| End point values | Spinal fentanyl | Epidural fentanyl | Spinal sufentanil | Epidural sufentanil |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 20 | 20 | 20 | 20 |
| Units: mm | | | | |
| geometric mean (confidence interval 95%) | 60 (46 to 74) | 36 (24 to 47) | 67 (54 to 81) | 42 (30 to 55) |

| Attachments (see zip file) | VAS during contraction/VAS kuvaaja.png |
|---|---|

**Statistical analyses**

| Statistical analysis title | Difference between spinal and epidural sufentanil |
|---|---|
| Comparison groups | Spinal sufentanil v Epidural sufentanil |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | < 0.05 |
| Method | ANOVA |

| Statistical analysis title | Difference between spinal and epidural fentanyl |
|---|---|
| Comparison groups | Spinal fentanyl v Epidural fentanyl |
| Number of subjects included in analysis | 40 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | < 0.05 |
| Method | ANOVA |

| Secondary: Duration of analgesia until the next epidural analgesia dose | |
|---|---|
| End point title | Duration of analgesia until the next epidural analgesia dose |
| End point description:<br>The duration of time in minutes until the parturient receives a new epidural dose | |
| End point type | Secondary |
| End point timeframe:<br>Within 5 hours | |

| End point values | Spinal fentanyl | Epidural fentanyl | Spinal sufentanil | Epidural sufentanil |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 20 | 20 | 20 | 20 |
| Units: minutes | | | | |
| geometric mean (confidence interval 95%) | 177 (121 to 234) | 112 (80 to 143) | 151 (111 to 192) | 130 (93 to 168) |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| 30 minutes after the intervention | |
| Adverse event reporting additional description: | |
| PRuritus and nausea interviewed for 30 minutes, fetal heart rate monitored continuously until delivery as per institutional protocol | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 27 |

| Reporting groups | |
|---|---|
| Reporting group title | Spinal fentanyl |
| Reporting group description: | |
| Combined spinal epidural analgesia where a dose of 20 micrograms of fentanyl was given into intrathecal space | |
| Reporting group title | Epidural fentanyl |
| Reporting group description: | |
| Normal epidural catheter placed and 100 micrograms of fentanyl citrate given epidurally | |
| Reporting group title | Spinal sufentanil |
| Reporting group description: | |
| 5 micrograms of sufentanil was given intrathecally by using combined spinal epidural technique | |
| Reporting group title | Epidural sufentanil |
| Reporting group description: | |
| 20 micrograms of sufentanil given into epidural space | |

| Serious adverse events | Spinal fentanyl | Epidural fentanyl | Spinal sufentanil |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 20 (0.00%) | 0 / 20 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

| Serious adverse events | Epidural sufentanil | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| **Non-serious adverse events** | Spinal fentanyl | Epidural fentanyl | Spinal sufentanil |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 18 / 20 (90.00%) | 8 / 20 (40.00%) | 12 / 20 (60.00%) |
| Pregnancy, puerperium and perinatal conditions | | | |
| Foetal heart rate abnormal | Additional description: Changes in foetal heart rate | | |
| subjects affected / exposed | 3 / 20 (15.00%) | 3 / 20 (15.00%) | 6 / 20 (30.00%) |
| occurrences (all) | 3 | 3 | 6 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 18 / 20 (90.00%) | 8 / 20 (40.00%) | 12 / 20 (60.00%) |
| occurrences (all) | 18 | 8 | 12 |

| **Non-serious adverse events** | Epidural sufentanil | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 20 (40.00%) | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Foetal heart rate abnormal | Additional description: Changes in foetal heart rate | | |
| subjects affected / exposed | 4 / 20 (20.00%) | | |
| occurrences (all) | 4 | | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 8 / 20 (40.00%) | | |
| occurrences (all) | 8 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/31286476