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 Units: Subjects			
Adults (18-64 years)	20	20	20
Gender categorical 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 Units: Subjects			
Adults (18-64 years)	20	80	
Gender categorical 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 Units: Subjects			
Adults (18-64 years)	20	20	20
Gender categorical 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 Units: Subjects			
Adults (18-64 years)	20		
Gender categorical 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: The duration of time in minutes until the parturient receives a new epidural dose	
End point type	Secondary
End point timeframe: 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