Clinical trial results:
Etude clinique prospective randomisée en double aveugle de phase 4 comparant la durée d'analgésie postopératoire du fentanyl et du sufentanil administrés comme adjuvant en rachianesthésie dans le cadre de césariennes électives.

Summary

EudraCT number	2010-023528-25
Trial protocol	BE
Global end of trial date	05 August 2011

Results information

Result version number	v1 (current)
This version publication date	18 August 2021
First version publication date	18 August 2021

Trial information

Trial identification

Sponsor protocol code	SUFRACES

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	CHU Brugmann
Sponsor organisation address	4 Place A. Van Gehuchten, Brussels, Belgium, 1020
Public contact	Dr P. Van der Linden, CHU Brugmann, Philippe.VANDERLINDEN@chu-brugmann.be
Scientific contact	Dr P. Van der Linden, CHU Brugmann, Philippe.VANDERLINDEN@chu-brugmann.be

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	05 August 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 August 2011
Global end of trial reached?	Yes
Global end of trial date	05 August 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To delay the first use of morphine after intrathecal anesthesia.

Protection of trial subjects:

According to standard of care

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 March 2009
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	Belgium: 180
Worldwide total number of subjects	180
EEA total number of subjects	180

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)	180
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was achieved by the anaesthesiologist in charge of the patient, who explained the day before surgery the possibility of using one of the three different doses of opiates in addition to intrathecal bupivacaine.

Pre-assignment

Screening details:

409 patients were assessed for eligibility. 180 patients were enrolled in the study (204 had exclusion criteria, 25 refused to participate) and were allocated in the three groups (Fentanyl n=60, Sufentanil 2.5µg n=60, Sufentanil 5µg n=60). Two patients were excluded from the analysis because of spinal anesthesia failure.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Sufentanil 2,5µg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Sufentanil
Investigational medicinal product code	
Other name	Sufenta
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Sufentanil 2.5ug, intrathecal use. The pharmacist prepared the opioid solutions which were supplied to the Caesarean section theatre in numbered blinded sterile bags. To standardise the injected volumes, sufentanil 2,5 µg (Sufentanil® 5 µg/ml; Janssen-Cilag SA, Beerse, Belgium) and fentanyl 25 µg (Fentanyl® 50 µg/ml; Janssen-Cilag SA) were diluted by the pharmacist with 0,5 ml isotonic saline to obtain 1 ml of study drug, as for sufentanil 5 µg. The anaesthesiologist added 10 mg of hyperbaric bupivacaine (Hyperbaric Marcaine 0,5%®; Astra-Zeneca Inc) for a total volume of 3 ml, to be injected in each enrolled and randomized patient.

Arm title	Sufentanil 5µg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Sufentanil
Investigational medicinal product code	
Other name	Sufenta
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Sufentanil 5ug, intrathecal use. The pharmacist prepared the opioid solutions which were supplied to the Caesarean section theatre in numbered blinded sterile bags. To standardise the injected volumes, sufentanil 2,5 µg (Sufentanil® 5 µg/ml; Janssen-Cilag SA, Beerse, Belgium) and fentanyl 25 µg (Fentanyl® 50 µg/ml; Janssen-Cilag SA) were diluted by the pharmacist with 0,5 ml isotonic saline to obtain 1 ml of study drug, as for sufentanil 5 µg. The anaesthesiologist added 10 mg of hyperbaric bupivacaine (Hyperbaric Marcaine 0,5%®; Astra-Zeneca Inc) for a total volume of 3 ml, to be injected in each enrolled and randomized patient.

Arm title	Fentanyl 25µg
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Fentanyl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Fentanyl 25µg, intrathecal use. The pharmacist prepared the opioid solutions which were supplied to the Caesarean section theatre in numbered blinded sterile bags. To standardise the injected volumes, sufentanil 2,5 µg (Sufentanil® 5 µg/ml; Janssen-Cilag SA, Beerse, Belgium) and fentanyl 25 µg (Fentanyl® 50 µg/ml; Janssen-Cilag SA) were diluted by the pharmacist with 0,5 ml isotonic saline to obtain 1 ml of study drug, as for sufentanil 5 µg. The anaesthesiologist added 10 mg of hyperbaric bupivacaine (Hyperbaric Marcaine 0,5%®; Astra-Zeneca Inc) for a total volume of 3 ml, to be injected in each enrolled and randomized patient.

Number of subjects in period 1	Sufentanil 2,5µg	Sufentanil 5µg	Fentanyl 25µg
Started	60	60	60
Completed	59	60	59
Not completed	1	0	1
Spinal anaesthesia failure	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Sufentanil 2,5µg
Reporting group description: -	
Reporting group title	Sufentanil 5µg
Reporting group description: -	
Reporting group title	Fentanyl 25µg
Reporting group description: -	

Reporting group values	Sufentanil 2,5µg	Sufentanil 5µg	Fentanyl 25µg
Number of subjects	60	60	60
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	60	60	60
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	60	60	60
Male	0	0	0

Reporting group values	Total		
Number of subjects	180		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	180		
From 65-84 years	0		
85 years and over	0		
Gender categorical Units: Subjects			
Female	180		
Male	0		

End points

End points reporting groups

Reporting group title	Sufentanil 2,5µg
Reporting group description: -	
Reporting group title	Sufentanil 5µg
Reporting group description: -	
Reporting group title	Fentanyl 25µg
Reporting group description: -	

Primary: Effective analgesia duration (PCA)

End point title	Effective analgesia duration (PCA)

End point description:

End point type	Primary

End point timeframe:

Time from intrathecal injection to the first morphine request by the patient as recorded by the PCA delivery system.

End point values	Sufentanil 2,5µg	Sufentanil 5µg	Fentanyl 25µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	57	60	59	
Units: minutes				
median (inter-quartile range (Q1-Q3))	214 (189 to 251)	236 (190 to 372)	187 (151 to 230)	

Statistical analyses

Statistical analysis title	Statistical analysis

Statistical analysis description:

Continuous variables were tested for normality using the Shapiro–Wilk normality test: the population has a non-gaussian distribution. Continuous variables were compared using a Kruskall–Wallis test to investigate overall differences and then a Mann–Whitney U-test for specific differences between groups. No adjustment for multiple comparisons was made. Categorical variables were compared using chi-squared. Statistical significance was set at $p < 0,05$. Fentanyl is the control treatment.

Comparison groups	Sufentanil 2,5µg v Sufentanil 5µg v Fentanyl 25µg
Number of subjects included in analysis	176
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Primary: Effective analgesia duration (VAS)

End point title	Effective analgesia duration (VAS)

End point description:

End point type	Primary

End point timeframe:

Effective analgesia duration determined as the time from intrathecal injection to VAS score superior or equal to 4.

End point values	Sufentanil 2,5µg	Sufentanil 5µg	Fentanyl 25µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	60	59	
Units: minutes				
median (inter-quartile range (Q1-Q3))	420 (240 to 1200)	600 (300 to 1440)	300 (225 to 720)	

Statistical analyses

Statistical analysis title	Statistical analysis

Statistical analysis description:

Continuous variables were tested for normality using the Shapiro–Wilk normality test: the population has a non-gaussian distribution. Continuous variables were compared using a Kruskall–Wallis test to investigate overall differences and then a Mann–Whitney U-test for specific differences between groups. No adjustment for multiple comparisons was made. Categorical variables were compared using chi-squared. Statistical significance was set at $p < 0,05$. Fentanyl is the control treatment.

Comparison groups	Sufentanil 2,5µg v Sufentanil 5µg v Fentanyl 25µg
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: Mophine/4h

End point title	Mophine/4h

End point description:

End point type	Secondary

End point timeframe:

Number of morphine boluses administered during 4h after the first morphine requirement

End point values	Sufentanil 2,5µg	Sufentanil 5µg	Fentanyl 25µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	60	59	
Units: mg				
median (inter-quartile range (Q1-Q3))	6 (4 to 9)	6 (2 to 10)	9 (5 to 13)	

Statistical analyses

No statistical analyses for this end point

Secondary: Morphine/24h

End point title	Morphine/24h

End point description:

End point type	Secondary

End point timeframe:

Total morphine consumption during 24h after the spinal injection

End point values	Sufentanil 2,5µg	Sufentanil 5µg	Fentanyl 25µg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	59	60	59	
Units: mg				
median (inter-quartile range (Q1-Q3))	18 (9 to 28)	15 (5 to 30)	22 (14 to 31)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall trial	
Assessment type	Systematic
Dictionary used	
Dictionary name	Clinical practice
Dictionary version	N/A
Reporting groups	
Reporting group title	Sufentanil 2,5µg
Reporting group description: -	
Reporting group title	Sufentanil 5µg
Reporting group description: -	
Reporting group title	Fentanyl 25µg
Reporting group description: -	

Serious adverse events	Sufentanil 2,5µg	Sufentanil 5µg	Fentanyl 25µg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 59 (0.00%)	0 / 60 (0.00%)	0 / 59 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

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

Non-serious adverse events	Sufentanil 2,5µg	Sufentanil 5µg	Fentanyl 25µg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 59 (37.29%)	22 / 60 (36.67%)	20 / 59 (33.90%)
Cardiac disorders			
Hypotension			
subjects affected / exposed	22 / 59 (37.29%)	22 / 60 (36.67%)	20 / 59 (33.90%)
occurrences (all)	1	1	1
Gastrointestinal disorders			
Nausea/Vomiting			
subjects affected / exposed	5 / 59 (8.47%)	5 / 60 (8.33%)	7 / 59 (11.86%)
occurrences (all)	1	1	1
Skin and subcutaneous tissue disorders			

Pruritus subjects affected / exposed occurrences (all)	21 / 59 (35.59%) 1	18 / 60 (30.00%) 1	13 / 59 (22.03%) 1

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/27137756