Clinical trial results:
The effects of sufentanil or morphine added to hyperbaric bupivacaine in
spinal anaesthesia for elective caesarean section.

Summary

EudraCT number	2017-001430-25
Trial protocol	ES
Global end of trial date	16 April 2020

Results information

Result version number	v1 (current)
This version publication date	26 March 2021
First version publication date	26 March 2021
Summary attachment (see zip file)	Results report (Resumen resultados final FPS-CES-2017-01.pdf)

Trial information

Trial identification

Sponsor protocol code	FPS-CES-2017-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03386630
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundación Pública Andaluza Progreso y Salud
Sponsor organisation address	Parque Científico y Tecnológico Cartuja, Avda. Américo Vespucio, 15 · Edificio S-2 · 41092 Sevilla, Seville, Spain, 41092
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Scientific contact	Marta Reboredo Ares, Fundación Pública Andaluza Progreso y Salud, 0034 955040450, gestionensayosclinicos.fps@juntadeandalucia.es

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	16 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 April 2020
Global end of trial reached?	Yes
Global end of trial date	16 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of the postoperative pain in caesarean section with hyperbaric bupivacaine 0.5% added to sufentanil (5mcg) or morphine (0.1mg).

Protection of trial subjects:

This study has been designed in accordance with the ethical principles for medical research involving human subjects promulgated in the Declaration of Helsinki of the World Medical Association (64th General Assembly, Fortaleza, Brazil, October 2013) and will be conducted in accordance with the applicable health standards, ethical and good practice standards applicable following the recommendations of the Spanish Ministry of Health on clinical trials, being a Low Intervention Level Clinical Trial, in accordance with Royal Decree 1090/2015, of 4 December, which regulates clinical trials with medicinal products, the Ethics Committees for Research with medicinal products and the Spanish register of Clinical Studies.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2018
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	Spain: 57
Worldwide total number of subjects	57
EEA total number of subjects	57

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)	57
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

- Patients at least 18 years of age and 36 weeks gestation.
- Patients scheduled for non-urgent caesarean section.
- Patients classified in the American Society of Anaesthesiologists (ASA) physical status as grade I-II, and without significant foetal pathological conditions.
- Patients who sign the informed consent form.

Pre-assignment

Screening details:

- Patients at least 18 years of age and 36 weeks gestation.
- Patients scheduled for non-urgent caesarean section.
- Patients classified in the American Society of Anaesthesiologists (ASA) physical status as grade I-II, and without significant foetal pathological conditions.
- Patients who sign the informed consent form.

Period 1

Period 1 title	Recruitment and follow-up
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Sufentanil

Arm description: -

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

Dosage and administration details:

5 micrograms/ml

Arm title	Morphine

Arm description: -

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

Dosage and administration details:

0,01 mg

Number of subjects in period 1	Sufentanil	Morphine
Started	29	28
Completed	29	28

Period 2	
Period 2 title	Data analysis
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes
Arm title	Sufentanil
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Sufentanil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Other use
Dosage and administration details: 5 micrograms/ml	
Arm title	Morphine
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Morphine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Other use
Dosage and administration details: 0,01 mg	

Number of subjects in period 2	Sufentanil	Morphine
Started	29	28
Completed	29	28

Baseline characteristics

Reporting groups	
Reporting group title	Sufentanil
Reporting group description: -	
Reporting group title	Morphine
Reporting group description: -	

Reporting group values	Sufentanil	Morphine	Total
Number of subjects	29	28	57
Age categorical Units: Subjects			
Adults (18-64 years)	29	28	57
Age continuous Units: years			
arithmetic mean	32.14	31.39	
standard deviation	± 5.21	± 4.51	-
Gender categorical Units: Subjects			
Female	29	28	57
Male	0	0	0
Level of obesity Units: Subjects			
No obesidad	14	14	28
Obesidad grado I	8	11	19
Obesidad grado II	7	3	10
ASA Units: Subjects			
ASA 1	0	0	0
ASA 2	29	28	57
ASA 3	0	0	0
ASA 4	0	0	0
Height Units: cm			
arithmetic mean	160.83	161.39	
standard deviation	± 5.80	± 4.41	-
Weight Units: kg			
arithmetic mean	80.52	77.18	
standard deviation	± 13.31	± 11.66	-
IMC Units: kg/m2			
arithmetic mean	31.01	29.52	
standard deviation	± 4.54	± 4.04	-
number of gestation weeks Units: weeks			
arithmetic mean	38.48	38.71	
standard deviation	± 0.82	± 0.76	-

End points

End points reporting groups

Reporting group title	Sufentanil
Reporting group description: -	
Reporting group title	Morphine
Reporting group description: -	
Reporting group title	Sufentanil
Reporting group description: -	
Reporting group title	Morphine
Reporting group description: -	

Primary: Time of onset of pain

End point title	Time of onset of pain[1]

End point description:

End point type	Primary

End point timeframe:

During the study

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Not all the information consulted in this section is available. However, the report on the results, which refers to the statistical analysis carried out, is attached.

End point values	Sufentanil	Morphine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	28		
Units: Participants				
No pain	1	3		
0-2 hours	0	7		
2-4 hours	4	10		
4-6 hours	13	0		
6-8	5	2		
8-10	3	2		
10-12	3	2		
18-20	0	2		

Statistical analyses

No statistical analyses for this end point

Primary: Time of application for the first bolus PCA

End point title	Time of application for the first bolus PCA[2]

End point description:

End point type	Primary

End point timeframe:

During the study

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Not all the information consulted in this section is available. However, the report on the results, which refers to the statistical analysis carried out, is attached.

End point values	Sufentanil	Morphine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	28		
Units: Participants				
No bolus	2	4		
0-2 hours	0	6		
2-4 hours	4	4		
4-6 hours	9	2		
6-8 hours	7	0		
8-10 hours	3	3		
10-12 hours	3	0		
12-14 hours	1	3		
14-16 hours	0	1		
16-18 hours	0	0		
18-20 hours	0	2		
20-22 hours	0	3		
22-24 hours	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Reason for indication for caesarean section

End point title	Reason for indication for caesarean section

End point description:

End point type	Secondary

End point timeframe:

During the study

End point values	Sufentanil	Morphine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	28		
Units: Participants				
Transverse	2	0		
Podalic	6	7		
Breech	7	9		

Previous caesarean section	18	10		
DPC	0	1		
Placenta praevia	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Surgical time

End point title	Surgical time

End point description:

End point type	Secondary

End point timeframe:

During the study

End point values	Sufentanil	Morphine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	28		
Units: Minutes				
arithmetic mean (standard deviation)	51.90 (± 14.17)	47.86 (± 12.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: EVA Skin incision

End point title	EVA Skin incision

End point description:

End point type	Secondary

End point timeframe:

During the study

End point values	Sufentanil	Morphine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	28		
Units: Participants				
No pain	29	26		
Mild pain	0	2		
Moderate pain	0	0		
Severe pain	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: EVA Uterine incision and tearing

End point title	EVA Uterine incision and tearing

End point description:

End point type	Secondary

End point timeframe:

During the study

End point values	Sufentanil	Morphine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	28		
Units: Participants				
No pain	27	21		
Mild pain	2	7		
Moderate pain	0	0		
Severe pain	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: EVA Utero-peritoneal manipulation

End point title	EVA Utero-peritoneal manipulation

End point description:

End point type	Secondary

End point timeframe:

During the study

End point values	Sufentanil	Morphine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	28		
Units: Participants				
No pain	27	20		
Mild pain	2	7		
Moderate oain	0	1		
Severe pain	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: EVA Abdominal wall and skin closure

End point title	EVA Abdominal wall and skin closure

End point description:

End point type	Secondary

End point timeframe:

During the study

End point values	Sufentanil	Morphine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	28		
Units: Participants				
No pain	27	19		
Mild pain	2	7		
Moderate pain	0	2		
Severe pain	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From the inclusion of the first patient to the last visit of the last patient.	
Assessment type	Systematic

Dictionary used	
Dictionary name	Not Known
Dictionary version	1

Reporting groups	
Reporting group title	Both groups

Reporting group description: -

Serious adverse events	Both groups		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 57 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Both groups		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 57 (43.86%)		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	8 / 57 (14.04%)		
occurrences (all)	8		
Vomiting			
subjects affected / exposed	8 / 57 (14.04%)		
occurrences (all)	8		
Skin and subcutaneous tissue disorders			
Itching			
subjects affected / exposed	9 / 57 (15.79%)		
occurrences (all)	9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 January 2018	Change of trial site due to change of principal investigator's place of work.
18 July 2018	Due to the logistics of the research team during the performance of the caesarean section procedure (at which time certain parameters of the study are assessed), it is impossible to record certain secondary variables during the surgical procedure. Likewise, during the evaluation of recovery, variables were initially described that do not provide valuable information for the purpose of the study in comparison with the cost of recording them. In any case, none of the variables eliminated (PH of the umbilical cord, onset of sitting and the patient's ability to stand upright) are in line with the main objective of the clinical trial, based on the analysis of pain, so they will be eliminated from the protocol and the data collection notebook, thus avoiding non-compliance with the protocol as not all the variables described therein are being collected. As a consequence, the secondary objectives in which these variables were analysed are also eliminated.
16 May 2019	Due to the logistics of the research team during the performance of the caesarean section procedure (at which time certain parameters of the study are assessed), it is impossible to record certain secondary variables during the surgical procedure. Likewise, during the evaluation of recovery, variables were initially described that do not provide valuable information for the purpose of the study in comparison with the cost of recording them. In any case, none of the variables eliminated (PH of the umbilical cord, onset of sitting and the patient's ability to stand upright) are in line with the main objective of the clinical trial, based on the analysis of pain, so they will be eliminated from the protocol and the data collection notebook, thus avoiding non-compliance with the protocol by not recording all the variables described therein.
16 May 2019	The specific dates given will be changed to adapt them to the actual situation, starting from the trial authorisation date, which was also later than planned. The adaptation of the chronology allows us to have a more up-to-date view of the trial and to submit for authorisation the extension of the timeframe for recruitment of trial participants by 5 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported