Clinical trial results:
Randomised, double blind, phase IV study to compare the incidence of ECG changes during elective caesarean section under spinal anaesthesia when using phenylephrine or ephedrine infusion to maintain baseline systolic blood pressure

Summary

EudraCT number	2009-013293-41
Trial protocol	GB
Global end of trial date	11 January 2016

Results information

Result version number	v1 (current)
This version publication date	28 August 2021
First version publication date	28 August 2021

Trial information

Trial identification

Sponsor protocol code	08/0182

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	Gower Street, London, United Kingdom, WC1E 6BT
Public contact	ctimps@ucl.ac.uk, Joint Research Office, UCL, 4th Floor, West 250 Euston Road London NW1 2PG, ctimps@ucl.ac.uk
Scientific contact	ctimps@ucl.ac.uk, Joint Research Office, UCL, 4th Floor, West 250 Euston Road London NW1 2PG, ctimps@ucl.ac.uk

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	11 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 January 2016
Global end of trial reached?	Yes
Global end of trial date	11 January 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

We would like to conduct a study to investigate whether, by maintaining a mother's normal systolic blood pressure with phenylephrine, as opposed to ephedrine after spinal anaesthesia for caesarean section, we can improve the heart muscle oxygen supply and demand ratio, and as a result see a difference in ECG changes between the 2 groups.

Protection of trial subjects:

No specific measures

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 April 2012
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	United Kingdom: 29
Worldwide total number of subjects	29
EEA total number of subjects	29

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)	29
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Trial planned to recruit 220 women having planned caesarean section under spinal anaesthesia, to complete the study in a 1 year duration. All participants to be recruited from a single UK site.
29 participants were recruited (estimated 15 on phenylephrine arm and 14 on ephedrine). The study was terminated early due to change in clinical practice.

Pre-assignment

Screening details:

29 participants were randomised.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Phenylephrine arm

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Phenylephrine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion of phenylephrine.
Infusion dose 50 mcg / minute (60ml/h)
On/off regimen in response to blood pressure readings every minute
Approx 30 minutes treatment duration.
Total dose 50 mcg – 1500 mcg

Arm title	Ephedrine arm

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Ephedrine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

Intravenous infusion of ephedrine.
Infusion dose 4mg / minute (60ml/h)
On/off regimen in response to blood pressure readings every minute
Approx 30 minutes treatment duration.
Total dose 4 mg – 120 mg.

Number of subjects in period 1	Phenylephrine arm	Ephedrine arm
Started	15	14
Completed	15	14

Baseline characteristics

End points

End points reporting groups

Reporting group title	Phenylephrine arm
Reporting group description: -	
Reporting group title	Ephedrine arm
Reporting group description: -	

Primary: The primary aim is to compare the incidence of ECG changes if maternal blood pressure is maintained with phenylephrine or ephedrine

End point title	The primary aim is to compare the incidence of ECG changes if maternal blood pressure is maintained with phenylephrine or ephedrine[1]

End point description:

Women having planned caesarean section under spinal anaesthesia will be studied. Recruited patients will be connected to a Holter monitor (a 3lead ECG) pre-operatively for continuous ECG monitoring. Following a standardised spinal anaesthetic dose, a vasopressor infusion will be commenced to prevent maternal hypotension. The vasopressor will be ephedrine or phenylephrine depending on randomisation and to maintain the same target systolic blood pressures. The patient and anaesthetists will be blinded. Cardiac output will be studied at baseline and every 5 minutes with a non-invasive suprasternal cardiac output monitor for 20 minutes and at 5 minutes post delivery. The Holter monitor will continue for 4 hours post delivery.

End point type	Primary

End point timeframe:

ST changes on Holter ECG monitoring

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: The study was terminated due to change in clinical practice since the start of the trial in 2011 whereby phenylephrine has replaced ephedrine as the vasopressor of choice. Phenylephrine has been associated with superior treatment of hypotension with higher umbilical blood pH values. This development made recruitment difficult for the trial.
The CI for this study has confirmed that unfortunately there is not enough data from the small number of women that was recruited to perform analysis.

End point values	Phenylephrine arm	Ephedrine arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	14		
Units: ECG output				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: Consent to end of study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No serious adverse events were reported.

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