Clinical trial results:
Double blind randomised multicentre study to assess the effect of local anaesthesia during vaginal hysterectomy

Summary

EudraCT number	2013-004124-11
Trial protocol	GB
Global end of trial date	13 December 2018

Results information

Result version number	v1 (current)
This version publication date	27 May 2020
First version publication date	27 May 2020

Trial information

Trial identification

Sponsor protocol code	POPPOP

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	King's College Hospital NHS Foundation Trust
Sponsor organisation address	Denmark Hill, London, United Kingdom, SE5 9RS
Public contact	Prof Linda Cardozo, KCH NHS Foundation Trust, 0044 2032993000, linda.cardozo@nhs.net
Scientific contact	Prof Linda Cardozo, KCH NHS Foundation Trust, 0044 2032993000, linda.cardozo@nhs.net

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	13 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 December 2018
Global end of trial reached?	Yes
Global end of trial date	13 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Does the injection of local anaesthetic and adrenaline solution into the superficial tissue around the uterine cervix during vaginal hysterectomy reduce post-operative pain?

Protection of trial subjects:

Participants will be invited from those who have decided to under vaginal hysterectomy with or without concomitant pelvic floor surgery.

Both local anaesthetic and adrenaline have been used safely for many years and pose minimal risk to patients.

All patients must be able to provide written informed consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 June 2014
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: 153
Worldwide total number of subjects	153
EEA total number of subjects	153

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)	105
From 65 to 84 years	46

85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Recruitment took place in 5 UK centres between 18 Feb 2015 and 13 Dec 2018
All women booking for a vaginal hysterectomy will be given information about the study at the booking clinic itself. Participation will be discussed when attending the pre-operative clinic.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	153
Number of subjects completed	153

Period 1

Period 1 title	Overall Trial Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

For safety reasons, the anaesthetist will not be blinded at any point.

Arms

Are arms mutually exclusive?	Yes
Arm title	Bupivacaine with adrenaline

Arm description:

Bupivacaine (2.5mg/ml (0.25%) with adrenaline 1 in 200 000 (5 micrograms per ml) (5micrograms per ml).

Arm type	Experimental
Investigational medicinal product name	Bupivicaine and Adrenaline Injection
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intracervical use

Dosage and administration details:

Maximum 100 mg total by infiltration.

Arm title	Placebo

Arm description:

Normal saline

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Infiltration, Intracervical use, Vaginal use

Dosage and administration details:

40 mls of normal saline was used as the placebo.

Number of subjects in period 1	Bupivacaine with adrenaline	Placebo
Started	78	75
Completed	74	70
Not completed	4	5
Consent withdrawn by subject	3	4
Lost to follow-up	1	-
Protocol deviation	-	1

Baseline characteristics

End points

End points reporting groups

Reporting group title	Bupivacaine with adrenaline
Reporting group description: Bupivacaine (2.5mg/ml (0.25%) with adrenaline 1 in 200 000 (5 micrograms per ml) (5micrograms per ml).	
Reporting group title	Placebo
Reporting group description: Normal saline	

Primary: Post Operative Pain Same Day

End point title	Post Operative Pain Same Day
End point description:	
End point type	Primary
End point timeframe: Patient pain score 3-5 hours post operation	

End point values	Bupivacaine with adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	75		
Units: McGill Pain Score	78	75		

Attachments (see zip file)	Independent Samples Test/POPPOP Independent Samples Test. Stats Report/POPPOP Stats Report.pdf

Statistical analyses

Statistical analysis title	All continuous variables
Comparison groups	Bupivacaine with adrenaline v Placebo
Number of subjects included in analysis	153
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - Null Hypothesis

Primary: Post Operative Pain Next Day

End point title	Post Operative Pain Next Day

End point description:

End point type	Primary

End point timeframe:

24 hours post operation

End point values	Bupivacaine with adrenaline	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	75		
Units: McGill Pain Score	78	75		

Statistical analyses

Statistical analysis title	All continuous variables
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Analysis specification	Pre-specified
Analysis type	other
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Adverse events

Adverse events information	
Timeframe for reporting adverse events: From consent to 30 days after IMP dose.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1
Reporting groups	
Reporting group title	Bupivacaine with adrenaline
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Bupivacaine with adrenaline	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 78 (0.00%)	0 / 75 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Bupivacaine with adrenaline	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 78 (8.97%)	8 / 75 (10.67%)	
Injury, poisoning and procedural complications			
Post operative ileus			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Vaginal bleeding			
subjects affected / exposed	0 / 78 (0.00%)	2 / 75 (2.67%)	
occurrences (all)	0	2	
Vaginal discharge			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
cystotomy unintentional			

subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Urinary retention			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
vaginal soreness			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Vault haematoma			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Went home with catheter			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Generally unwell			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Rectoenterocele recurrent			
subjects affected / exposed	0 / 78 (0.00%)	1 / 75 (1.33%)	
occurrences (all)	0	1	
Infections and infestations			
Low temperature	Additional description: Possible UTI		
subjects affected / exposed	1 / 78 (1.28%)	0 / 75 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 78 (1.28%)	1 / 75 (1.33%)	
occurrences (all)	1	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