Clinical trial results:
A study to Investigate the Effect of Intraperitoneal Levobupivacaine on Post Operative Laparoscopic Pain

Summary

EudraCT number	2009-011207-23
Trial protocol	GB
Global end of trial date	27 July 2015

Results information

Result version number	v1 (current)
This version publication date	11 August 2019
First version publication date	11 August 2019

Trial information

Trial identification

Sponsor protocol code	R0831

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Hull and East Yorkshire Hospitals NHS Trust
Sponsor organisation address	Anlaby Road , Hull, United Kingdom, HU3 2JZ
Public contact	Research & Development Department , Hull and East Yorkshire Hospitals NHS Trust, 044 01482461903, research.development@hey.nhs.uk
Scientific contact	Women and Children's Hospital , Hull and East Yorkshire Hospitals NHS Trust, 044 01482461271, research.development@hey.nhs.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	19 May 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principle research question is whether leaving a local anaesthetic solution in the abdomen after keyhole surgery improves pain relief.

Protection of trial subjects:

Nothing specific to this trial, all participants received general anaesthesia as per normal surgical practice.

Background therapy:

General anaesthetic as per Trust standard induction process.

Evidence for comparator:

The comparator in this study was sodium chloride. This was the choice of comparator due to the minimal risk of any adverse reactions or complications.

Actual start date of recruitment	09 June 2011
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: 109
Worldwide total number of subjects	109
EEA total number of subjects	109

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)	103
From 65 to 84 years	6

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All patients were recruited between 09.06.11 and 27.07.15. All patients were recruited from surgical/gynaecological clinics within the Hull and East Yorkshire Hospitals NHS Trust.

Pre-assignment

Screening details:

Patients attended for minor laparoscopic gynaecological procedure. They had a BMI of less than 35 who weighed more than 50kg with an ASA less than or equal to 2. Any patient no fulfilling these criteria were excluded from the study.

Period 1

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

Blinding implementation details:

IMP and comparator dispensed in identical packaging from pharmacy directly to the anaesthetist who administered this.

Arms

Are arms mutually exclusive?	Yes
Arm title	Levobupvicaine

Arm description:

Patients received 40mls of 0.25% levobupivacaine instilled into the peritoneal cavity at the end of the procedure and left in situ.

Arm type	Experimental
Investigational medicinal product name	Levobupivicaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for injection
Routes of administration	Intraperitoneal use

Dosage and administration details:

Levobupivicaine 0.25% 40mls

Investigational medicinal product name	Sodium Chloride
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intraperitoneal use

Dosage and administration details:

Sodium Chloride 0.9% 40mls

Arm title	Comparator

Arm description:

0.9% normal saline

Arm type	Placebo
Investigational medicinal product name	Saline 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intraperitoneal use

Dosage and administration details:
40 mls administered viaintraperitoneal route

Number of subjects in period 1	Levobupvicaine	Comparator
Started	54	55
Completed	50	51
Not completed	4	4
Consent withdrawn by subject	-	1
Patient underwent spinal surgery	-	2
Underwent spinal surgery	3	-
Surgery cancelled	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall study

Reporting group description: -

Reporting group values	Overall study	Total	
Number of subjects	109	109	
Age categorical			
Subjects were all female aged between 18- 80 years of age.			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	103	103	
85 years and over	6	6	
Gender categorical			
All patients were female			
Units: Subjects			
Female	109	109	
Male	0	0	

End points

End points reporting groups

Reporting group title	Levobupvicaine
Reporting group description:	
Patients received 40mls of 0.25% levobupivacaine instilled into the peritoneal cavity at the end of the procedure and left in situ.	
Reporting group title	Comparator
Reporting group description:	
0.9% normal saline	

Primary: Pain

End point title	Pain
End point description:	
Each subject was asked to record a score for pain at the wound sites, pelvis and shoulder tip at each of the time points. A record was kept of anaesthesia administered and of analgesia administered postoperatively whilst still in hospital and analgesia taken after discharge until the completion of their four-day numerical scale completion.	
End point type	Primary
End point timeframe:	
Assessment of post-operative pain at 3 hours, 8 hours, 24 hours and 96 hours.	

End point values	Levobupvicaine	Comparator		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	52		
Units: 1 to 10				
number (not applicable)	50	52		

Statistical analyses

Statistical analysis title	Should tip pain 3 hours post surgery
Statistical analysis description:	
A correlation will be sought between the two groups - pain scores (at the various sites and time points)	

Comparison groups	Levobupvicaine v Comparator
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036 [1]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - Shoulder tip pain 3 hour post surgery

Statistical analysis title	Wound pain 8 hour post surgery
Comparison groups	Comparator v Levobupvicaine
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.045
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Wound pain 4 day post surgery
Comparison groups	Levobupvicaine v Comparator
Number of subjects included in analysis	102
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.042
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From time of consent to 30 days post intervention.	
Adverse event reporting additional description: Pain scores and diary completion.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups	
Reporting group title	Comparator
Reporting group description: Patients who received 0.9% saline	
Reporting group title	Levobuvicaine
Reporting group description: Received IMP	

Serious adverse events	Comparator	Levobuvicaine	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 52 (3.85%)	0 / 50 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
Irritable bowel syndrome	Additional description: Event was not related to the study treatment.		
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Aspiration	Additional description: Event occurred during surgery but before IMP was administrated.		
subjects affected / exposed	1 / 52 (1.92%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Comparator	Levobuvicaine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
Skin and subcutaneous tissue disorders			
Redness and itching	Additional description: Redness and itching at the cannula site post morphine administration prior to IMP administration.		
subjects affected / exposed	0 / 52 (0.00%)	1 / 50 (2.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 September 2009	Details unknown, the amendment was pre-approval.
01 March 2011	Text regarding the target patient number was inserted. Clarification of the solution to be used. Clarification of the randomisation and dispensing method.
22 January 2013	No documents changed. Temporary halt while replacement PI found.
30 July 2013	Change of PI from Professor Killick to Mr Phillips.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
22 January 2013	PI left Trust	30 July 2013

Notes:

Limitations and caveats

None reported