Clinical trial results:
Comparison of continuous paravertebral blockade (PVB) and continuous thoracic epidural analgesia (TEA) for analgesia following open renal surgery

Summary

EudraCT number	2008-004998-17
Trial protocol	IE
Global end of trial date	22 November 2010

Results information

Result version number	v1 (current)
This version publication date	22 October 2022
First version publication date	22 October 2022
Summary attachment (see zip file)	Comparison of the analgesic efficacy and side effect profile of continuous epidural analgesia and paravertebral blockade with patient controlled analgesia in patients undergoing Open Renal Surgery (Finnerty et.al.doc) Postoperative Morphine consumption (Figure 1 Postoperative Morphine consumption.jpg) Postoperative Pain scores (Figure 2 Postoperative Pain Scores.jpg) Postoperative heart rate and mean arterial pressure (Figure 3 Postoperative heart rate and mean arterial pressure.jpg) Intraoperative heart rate and mean arterial pressure (Figure 4 Intraoperative heart rate and mean arterial pressure.jpg) Distributon of sensory block postoperatively (Figure 5 Sensory distribution of blocks postoperatively.jpg)

Trial information

Trial identification

Sponsor protocol code	0none

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Dept Anaesthesia, UCHG
Sponsor organisation address	Newcastle Rd, Galway, Ireland, H91YR71
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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	20 June 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 November 2010
Global end of trial reached?	Yes
Global end of trial date	22 November 2010
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

We aim to compare the analgesic efficacy of paravertebral and epidural blockage, for post operative pain in the first 24 post operative hours, following open renal surgery.

1. Severity of Postoperative Pain, [VAS and Categorical pain Scales]
2. Total opiate usage in the first 48 hours after surgery

Protection of trial subjects:

The trial subjects were reassured they could discontinue involvement in the study at any time.
The main trial researcher OF was available by telephone or in person to assist concerns about analgesia, data collection or privacy etc.

Background therapy:

Intravenous paracetamol was given to both study groups.

Evidence for comparator:

A multimodal postoperative pain treatment regimen that provides high quality analgesia with minimal side effects is ideal. Epidural analgesia is the gold standard for laparotomy [2,3] and hence open renal procedures, but may not be available either due to the patient’s characteristics or due to staff or equipment shortages. Where epidural analgesia is not available or contra-indicated, high amounts of opioid analgesia, is usually required. However the heavy use of opioids can result in significant adverse effects, including sedation, nausea and vomiting [4]. These, coupled with the reactive pleural effusion on the side of surgery, contribute significantly to respiratory morbidity [5]. Epidural analgesia may result in vasodilatation, leading to increased postoperative haemodynamic instability, motor block and increased nursing workload [6]. Alternative approaches, which reduce the requirement for strong opioids postoperatively, are needed.

Paravertebral analgesia has been used successfully for many procedures from cholecystectomy to abdominal vascular surgery [7-9]. Recent reviews conclude that PVB analgesia may be superior to epidural analgesia in maintaining respiratory function following thoracotomy [10-12]. These findings prompted us to commence a trial comparing epidural and PVB analgesia for open renal surgery.

1. Wall PD, Melzack R (chapter title) Wall PD, Melzack R editors. Textbook of Pain. 4th ed. Edinburgh: Churchill Livingstone, 1999:401-28.
2. Werawatganon T, Charuluxananan S. Patient controlled intravenous opioid analgesia versus continuous epidural analgesia for pain after intra-abdominal surgery. Cochrane Database of Systematic Reviews 2005, Issue 1. Art. No.: CD004088. DOI: 10.1002/14651858.CD004088.pub2.
3. Block BM, Liu SS, Rowlingson AJ, Cowen AR, Cowan JA Jr, Wu CL. Efficacy of postoperative epidural analgesia; a meta-analysis. Journal of the American Medical Association 2003; 290: 2455-63.
4. Benyamin R, Trescot AM, Datta S, Buenaventur

Actual start date of recruitment	22 September 2008
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	Ireland: 51
Worldwide total number of subjects	51
EEA total number of subjects	51

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)	38
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients were invited to participate in the study as soon as they were scheduled for renal surgery through outpatients at University College Hospital Galway between early September 2008 and November 2010.

Pre-assignment

Screening details:

ASA physical status I-III, between 18 and 80 years of age, They were scheduled for open renal surgery. Exclusion criteria: contraindication to neuraxial blockade, local infection at the site of block insertion, relevant drug allergy, concurrent use of MAOIs or use within 2 weeks prior to surgery, sepsis, severe kyphoscoliosis, previous thoracic ve

Period 1

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

Blinding implementation details:

The patients were randomized in batches of ten, to receive either epidural analgesia (Group E, n = 25) or PVB analgesia with patient controlled intravenous morphine (Group P, n = 26). The allocation sequence was generated by a random number table, and group allocation was concealed in sealed, opaque envelopes, which were not opened until patient consent had been obtained.

Arms

Are arms mutually exclusive?	Yes
Arm title	Paravertebral

Arm description:

This group had PVB analgesia

Arm type	Active comparator
Investigational medicinal product name	Chirocaine
Investigational medicinal product code	PL00037/0300
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Perineural use

Dosage and administration details:

0.25% Levobupivacaine. Local anaesthetic for epidural injection.

Arm title	Epidural

Arm description:

This group received epidural analgesia.

Arm type	Active comparator
Investigational medicinal product name	Chirocaine
Investigational medicinal product code	PL00037/0300
Other name	Levobupivacaine
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

Levobupivacaine 0.25%. Local anaesthetic solution for epidural and perineural use.

Number of subjects in period 1	Paravertebral	Epidural
Started	26	25
Completed	26	25

Baseline characteristics

Reporting groups	
Reporting group title	Paravertebral
Reporting group description:	
This group had PVB analgesia	
Reporting group title	Epidural
Reporting group description:	
This group received epidural analgesia.	

Reporting group values	Paravertebral	Epidural	Total
Number of subjects	26	25	51
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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
arithmetic mean	55.7	62.2	
standard deviation	± 17.7	± 14.9	-
Gender categorical			
Units: Subjects			
Female	15	11	26
Male	11	14	25

End points

End points reporting groups

Reporting group title	Paravertebral
Reporting group description: This group had PVB analgesia	
Reporting group title	Epidural
Reporting group description: This group received epidural analgesia.	

Primary: Interim analysis

End point title	Interim analysis
End point description: The study would be terminated in the event that the analysis of 24-hour morphine consumption demonstrated that morphine consumption was 20% higher in the PVB group, with a p value < 0.01. The interim analysis demonstrated that morphine consumption was significantly (P < 0.01) greater in the group that received PVB analgesia, disproving the primary hypothesis. The study was terminated at this point and the analysis of the data completed.	
End point type	Primary
End point timeframe: This interim analysis was carried out following recruitment of the 51st patient.	

End point values	Paravertebral	Epidural		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	25		
Units: mg Morphine				
arithmetic mean (standard deviation)	83.2 (± 51.8)	21.3 (± 39.7)		

Attachments (see zip file)	Figure 1 Postoperative Morphine consumption.jpg

Statistical analyses

Statistical analysis title	Satistical analysis
Statistical analysis description: All statistical analyses were performed using a standard statistical program (Sigmastat 3.5, Systat Software, San Jose, CA, USA). Demographic data were analyzed using Student's t or Fisher's exact tests as appropriate. The data were tested for normality using the Kolmogorov-Smirnov normality test. Repeated measurements (pain scores, nausea scores) were analyzed by repeated measures ANOVA where normally distributed, with further paired comparisons at each time interval performed using the t test.	
Comparison groups	Epidural v Paravertebral

Number of subjects included in analysis	51
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	< 0.01 [2]
Method	t-test, 1-sided

Notes:

[1] - For the purposes of sample size calculation, we assumed that, for PVB blockade to be deemed to provide equivalent analgesia, the 24-hour postoperative morphine requirement could not be greater than 20% higher compared to patients receiving epidural blockade. Based on initial pilot studies we projected a mean 24-hour morphine requirement of 10mg with a standard deviation of 5mg in the epidural group.

[2] - The study would be terminated in the event that the analysis of 24-hour morphine consumption demonstrated that morphine consumption was 20% higher in the PVB group, with a p value < 0.01.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Any adverse events were recorded from the start of anaesthesia of any patient up to 72hours postoperatively or at the end of data collection

Assessment type	Non-systematic

Dictionary used

Dictionary name	Self reporting
Dictionary version	0

Reporting groups

Reporting group title	Paravertebral

Reporting group description:

This group had PVB analgesia

Reporting group title	Epidural

Reporting group description: -

Serious adverse events	Paravertebral	Epidural	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	0 / 25 (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	Paravertebral	Epidural	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	
Nervous system disorders			
Pain	Additional description: One epidural was not effective despite boluses and other measures.		
subjects affected / exposed	0 / 26 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Respiratory depression	Additional description: One patient had a respiratory rate of 8 breaths/min at one time interval.		
subjects affected / exposed	1 / 26 (3.85%)	1 / 25 (4.00%)	
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? Yes

Date	Interruption	Restart date
03 July 2009	The trial recruitment was paused for three months from July to September 2009 inclusive due to serious illness and bereavement of a family member of a core investigator.	28 September 2009

Notes:

Limitations and caveats

None reported