



Clinical trial results:

Erector spinae plane block for minimal invasive direct coronary artery bypass surgery. A double blind, prospective randomized placebo-controlled trial.

Summary

EudraCT number	2019-000596-16
Trial protocol	BE
Global end of trial date	14 August 2021

Results information

Result version number	v1 (current)
This version publication date	03 July 2022
First version publication date	03 July 2022

Trial information

Trial identification

Sponsor protocol code	DH112018
-----------------------	----------

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	UZ Leuven
Sponsor organisation address	Herestraat 49, 3000, Belgium,
Public contact	Anesthesiology Research, University Hospitals Leuven, 32 16344270, christel.huygens@uzleuven.be
Scientific contact	Anesthesiology Research, University Hospitals Leuven, 32 16344270, christel.huygens@uzleuven.be

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	08 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 August 2021
Global end of trial reached?	Yes
Global end of trial date	14 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The goal of our study was to investigate if, in robot-assisted minimally invasive direct coronary artery bypass surgery with multimodal analgesia, intermittent ESP block with ropivacaine (intervention group) compared to normal saline 0.9% (control group) is effective in reducing postoperative pain.

Protection of trial subjects:

Patients received acetaminophen (15 mg kg⁻¹) every 6 hours and morphine patient-controlled intravenous analgesia (PCIA) up to 24 hours post-extubation. Rescue analgesia consisted of a bolus of morphine, ketorolac, acetylsalicylic acid and/or removal or infiltration of chest tubes according to a standardized flowchart (supplementary figure S1). Twenty-four hours post-extubation, morphine PCIA was stopped and further analgesic treatment consisted of acetaminophen combined with tramadol or morphine.

Background therapy:

Irrespective of group allocation, every patient received a bolus of IV morphine (0.1 mg kg⁻¹) and acetaminophen IV (1g) at thorax closure. After having received the interventional treatment, patients were transferred intubated to the PACU under analgosedation with dexmedetomidine and remifentanyl. Following extubation (T0), patients received PCIA pump with morphine (on-demand-only mode with a morphine bolus of 1.5 mg up to every 7 minutes).

Evidence for comparator:

While in numerous case reports the ESP block has been described to adequately provide perioperative analgesia after adult cardiac surgery, the evidence from randomized controlled trials (RCT) is scarce. In the four RCTs that investigated the ESP block in adult cardiac surgery, bilateral ESP blocks were used for cardiac surgery cases requiring a sternotomy. In addition, double-blinding of allocation was limited to only 1 trial.

Actual start date of recruitment	15 April 2019
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	Belgium: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	31
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

102 patients between May 14th 2019 and July 12th 2021 were screened of whom 64 were eligible for participation.

Pre-assignment

Screening details:

All consecutive adult patients scheduled for either RAMIDCAB surgery using the left internal mammary artery (LIMA) or MIMVS were evaluated for enrollment according to the inclusion criteria. They were included if 18-75 years of age, BMI <35, EuroSCORE <3, admitted to the PACU with our epilepsy, chronic opioid use or OSAS without treatment.

Period 1

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

Blinding implementation details:

All patients were randomized through a computer-generated permuted block randomisation sequence (variable block-size with 1:1 allocation). Enclosing assignments in opaque, sequentially numbered, sealed envelopes ensured allocation concealment. Following uneventful surgery and confirmation of post-anesthesia care unit (PACU) admittance, the envelope was opened by research personnel and the trial medication was prepared. Syringes were then labelled with the mark "trial medication".

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:

After completion of the surgery, an ESP block (with placement of a catheter) was performed with 30mL of trial medication. There after,, 20mL trial medication through the ESP-catheter at the PACU was given every 6 hours after the first dose (B0 +6h, B0 +12h, and B0 +18h), three times in total.

Arm type	Experimental
Investigational medicinal product name	Ropivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Injection

Dosage and administration details:

Initial dose of 30mL followed after 6, 12 and 18 hours with a dose of 20mL.

Arm title	Control
------------------	---------

Arm description:

After completion of the surgery, an ESP block (with placement of a catheter) was performed with 30mL of trial medication. There after,, 20mL trial medication through the ESP-catheter at the PACU was given every 6 hours after the first dose (B0 +6h, B0 +12h, and B0 +18h), three times in total.

Arm type	Placebo
Investigational medicinal product name	Normal saline 0.9%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Injection

Dosage and administration details:

Initial dose of 30mL followed after 6, 12 and 18 hours with a dose of 20mL.

Number of subjects in period 1	Intervention	Control
Started	32	32
Completed	32	32

Baseline characteristics

Reporting groups

Reporting group title	Intervention
-----------------------	--------------

Reporting group description:

After completion of the surgery, an ESP block (with placement of a catheter) was performed with 30mL of trial medication. There after,, 20mL trial medication through the ESP-catheter at the PACU was given every 6 hours after the first dose (B0 +6h, B0 +12h, and B0 +18h), three times in total.

Reporting group title	Control
-----------------------	---------

Reporting group description:

After completion of the surgery, an ESP block (with placement of a catheter) was performed with 30mL of trial medication. There after,, 20mL trial medication through the ESP-catheter at the PACU was given every 6 hours after the first dose (B0 +6h, B0 +12h, and B0 +18h), three times in total.

Reporting group values	Intervention	Control	Total
Number of subjects	32	32	64
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	15	16	31
From 65-84 years	17	16	33
85 years and over	0	0	0
Age continuous Units: years			
geometric mean	64	63	
standard deviation	± 9.0	± 7.2	-
Gender categorical Units: Subjects			
Female	7	2	9
Male	25	30	55

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description: After completion of the surgery, an ESP block (with placement of a catheter) was performed with 30mL of trial medication. There after,, 20mL trial medication through the ESP-catheter at the PACU was given every 6 hours after the first dose (B0 +6h, B0 +12h, and B0 +18h), three times in total.	
Reporting group title	Control
Reporting group description: After completion of the surgery, an ESP block (with placement of a catheter) was performed with 30mL of trial medication. There after,, 20mL trial medication through the ESP-catheter at the PACU was given every 6 hours after the first dose (B0 +6h, B0 +12h, and B0 +18h), three times in total.	

Primary: Morphine consumption 24 hours

End point title	Morphine consumption 24 hours
End point description:	
End point type	Primary
End point timeframe: Assessed 24 hours after extubation	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	30 ^[1]		
Units: mg				
geometric mean (standard deviation)	61 (± 30)	70 (± 27)		

Notes:

[1] - 2 early withdrawals (1 due to surgical revision and 1 due to ESP device malfunction)

Statistical analyses

Statistical analysis title	Primary outcome
Comparison groups	Control v Intervention
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other ^[2]
P-value	≤ 0.05
Method	t-test, 2-sided

Notes:

[2] - Mann-Whitney U test

Secondary: Numerical rating score for pain

End point title	Numerical rating score for pain
-----------------	---------------------------------

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

Pain scores assessed 2 hours after extubation

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	31 ^[3]		
Units: NRS scale				
median (inter-quartile range (Q1-Q3))	3 (2 to 4)	3 (1 to 3)		

Notes:

[3] - 1 early withdrawal due to surgical revision

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From enrollment until 24 hours after extubation.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	25
--------------------	----

Reporting groups

Reporting group title	Intervention
-----------------------	--------------

Reporting group description:

After completion of the surgery, an ESP block (with placement of a catheter) was performed with 30mL of trial medication. There after,, 20mL trial medication through the ESP-catheter at the PACU was given every 6 hours after the first dose (B0 +6h, B0 +12h, and B0 +18h), three times in total.

Reporting group title	Control
-----------------------	---------

Reporting group description:

After completion of the surgery, an ESP block (with placement of a catheter) was performed with 30mL of trial medication. There after,, 20mL trial medication through the ESP-catheter at the PACU was given every 6 hours after the first dose (B0 +6h, B0 +12h, and B0 +18h), three times in total.

Serious adverse events	Intervention	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	2 / 32 (6.25%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Surgery	Additional description: Surgical revision due to bleeding.		
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device defectives	Additional description: Defect of ESP delivery system		
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Intervention	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 32 (65.63%)	19 / 32 (59.38%)	
Cardiac disorders			
Atrial fibrillation	Additional description: New onset atrial fibrillation		
subjects affected / exposed	0 / 32 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
Pericarditis			
subjects affected / exposed	8 / 32 (25.00%)	11 / 32 (34.38%)	
occurrences (all)	8	11	
Gastrointestinal disorders			
Nausea	Additional description: Postoperative nausea and vomiting		
subjects affected / exposed	14 / 32 (43.75%)	10 / 32 (31.25%)	
occurrences (all)	14	10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 October 2020	Extension of recruitment period due to COVID-19 pandemic

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported