Clinical trial results:
Effect of Perineural Dexamethasone on the Duration of Single Injection Saphenous Nerve Block for Analgesia After Major Ankle Surgery

Summary

EudraCT number	2014-004207-78
Trial protocol	DK
Global end of trial date	16 December 2015
Results information	
Result version number	v2 (current)
This version publication date	25 January 2021
First version publication date	16 July 2017
Version creation reason	• Correction of full data set Correction of p-value

Trial information

Trial identification	
Sponsor protocol code	ProtokolSB1
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02346110
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Nørrebrogade 44, Aarhus C, Denmark, 8000
Public contact	Department of Anesthesia and Intensive Care, Aarhus University Hospital, +45 51542997, tfb@dadlnet.dk
Scientific contact	Department of Anesthesia and Intensive Care , Aarhus University Hospital, +45 51542997, tfb@dadlnet.dk

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	29 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 December 2015
Global end of trial reached?	Yes
Global end of trial date	16 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to investigate whether addition of the adjuvant dexamethasone to bupivacaine-adrenaline can prolong the analgesic effect of the saphenous block compared to plain bupivacaine-adrenaline in patients after major ankle and hind foot surgery.

Protection of trial subjects:

Patients received a PCA pump with morphine to provide instant pain relief at bolus request. Patients were visited at regular intervals during the observation period with extra focus on their pain management.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 April 2015
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	Denmark: 39
Worldwide total number of subjects	39
EEA total number of subjects	39

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)	25
From 65 to 84 years	14

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were enrolled from 27/Apr/2015 - 14/Dec/2015.

Pre-assignment

Screening details:

62 patients were screened.
Reasons for primary exclusion:
Operation type not included (n = 5)
Logistical reasons (n = 6)
Operation cancelled/rescheduled (n = 4)
Daily intake of strong opioids (n = 2)
Allergy to opioids (n = 1)
Communication problems (n = 1)
BMI > 35 (n = 2)
Neuropathy (n = 1)

Period 1

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

Blinding implementation details:

The hospital pharmacy performed the randomization in blocks of 10 and a 1:1 ratio, and prepared 40 consecutively numbered black nontransparent plastic bags containing 1 mL of saline or 1 mL of dexamethasone according to the randomization list. Isotonic saline and dexamethasone are both transparent liquids, all containers and bags were identical.

One patient was excluded due to incorrect inclusion (communication problems) this patient is not included in any data analysis.

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:

Saphenous block with 10 mL Marcain-adrenalin + 1 ml (4 mg) Dexamethasone.

Arm type	Experimental
Investigational medicinal product name	Dexamethason
Investigational medicinal product code	
Other name	Dexagalen
Pharmaceutical forms	Suspension for injection
Routes of administration	Perineural use

Dosage and administration details:

4 mg

Investigational medicinal product name	Marcain-adrenalin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

10 mL Marcain-adrenalin containing:
BUPIVACAINE HYDROCHLORIDE 5 mg/ml milligram
EPINEPHRINE 5 µg/ml

Arm title	Control group

Arm description:

Saphenous block with 10 mL Marcain-adrenalin + 1 mL saline

Arm type	Active comparator
Investigational medicinal product name	Marcain-adrenalin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

10 mL Marcain-adrenalin containing:
BUPIVACAINE HYDROCHLORIDE 5 mg/ml
EOINEOHRINE 5 µg/ml

Number of subjects in period 1	Intervention	Control group
Started	19	20
Completed	19	20

Baseline characteristics

Reporting groups	
Reporting group title	Intervention
Reporting group description:	
Saphenous block with 10 mL Marcain-adrenalin + 1 ml (4 mg) Dexamethasone.	
Reporting group title	Control group
Reporting group description:	
Saphenous block with 10 mL Marcain-adrenalin + 1 mL saline	

Reporting group values	Intervention	Control group	Total
Number of subjects	19	20	39
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	57.2	59.8	
standard deviation	± 12.6	± 13.5	-
Gender categorical Units: Subjects			
Female	9	9	18
Male	10	11	21
ASA physical status			
ASA = American Society of Anesthesiologists			
Units: Subjects			
ASA I	9	7	16
ASA II	10	13	23
Surgical procedures Units: Subjects			
Total ankle replacement	10	11	21
Ankle arthrodesis	2	3	5
Subtalar arthrodesis	5	2	7
Triple arthrodesis	2	4	6
BMI			
Body mass index			
Units: kg/m^2			
arithmetic mean	28.6	26.1	
standard deviation	± 4.07	± 4.13	-

Height			
Units: meter			
arithmetic mean	1.76	1.73	
standard deviation	± 0.11	± 0.1	-
Weight			
Units: kilogram(s)			
arithmetic mean	88.2	78.1	
standard deviation	± 13.3	± 14	-
Preoperative pain at rest, NRS			
NRS = numerical rating scale			
Units: Not applicable			
median	0	0	
inter-quartile range (Q1-Q3)	0 to 0	0 to 0.5	-

End points

End points reporting groups	
Reporting group title	Intervention
Reporting group description: Saphenous block with 10 mL Marcain-adrenalin + 1 ml (4 mg) Dexamethasone.	
Reporting group title	Control group
Reporting group description: Saphenous block with 10 mL Marcain-adrenalin + 1 mL saline	

Primary: Time until first opioid request	
End point title	Time until first opioid request
End point description:	
End point type	Primary
End point timeframe: 0-48 hrs Time zero = end of saphenous block performance	

End point values	Intervention	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: hour				
arithmetic mean (standard deviation)	29.4 (± 8.4)	23.2 (± 10.3)		

Statistical analyses

Statistical analysis title	Time until first opioid request
Comparison groups	Control group v Intervention
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.048
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	12.3

Secondary: Time until first pain

End point title	Time until first pain

End point description:

End point type	Secondary

End point timeframe:

0-48 hrs
Time zero = End of saphenous block performance

End point values	Intervention	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: hour				
arithmetic mean (standard deviation)	28.3 (± 7.9)	21.5 (± 10.2)		

Statistical analyses

Statistical analysis title	Time until first pain

Statistical analysis description:

T-test
Normally distributed data

Comparison groups	Intervention v Control group
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	12.7

Secondary: Opioid consumption 0-24 hrs

End point title	Opioid consumption 0-24 hrs

End point description:

The opioid consumption was not normally distributed

End point type	Secondary

End point timeframe:
0-24 hours

End point values	Intervention	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	1.5 (0 to 14.2)		

Statistical analyses

Statistical analysis title	Opioid consumption 0-24 hrs
Comparison groups	Intervention v Control group
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.046
Method	Wilcoxon (Mann-Whitney)

Notes:
[1] - Opioid consumption was not normally distributed.

Secondary: Opioid consumption 24-48 hrs

End point title	Opioid consumption 24-48 hrs

End point description:
The opioid consumption was not normally distributed

End point type	Secondary

End point timeframe:
24-48 hrs

End point values	Intervention	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	20		
Units: hour				
median (inter-quartile range (Q1-Q3))	15 (10 to 21)	15 (5 to 32.5)		

Statistical analyses

Statistical analysis title	Opioid consumption 24-48 hrs
Comparison groups	Intervention v Control group

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.989
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were reported from inclusion of the first patient 27/Apr/2015 and until the last patient completed the study observation period 16/Dec/2015.	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0
Reporting groups	
Reporting group title	Intervention
Reporting group description:	
Saphenous block with 10 mL Marcain-adrenalin + 1 ml (4 mg) Dexamethasone.	
Reporting group title	Control group
Reporting group description:	
Saphenous block with 10 mL Marcain-adrenalin + 1 mL saline	

Serious adverse events	Intervention	Control group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (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	Intervention	Control group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 20 (25.00%)	8 / 20 (40.00%)	
General disorders and administration site conditions			
Headache			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	5	8	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	5	8	
Nausea			

subjects affected / exposed	5 / 20 (25.00%)	5 / 20 (25.00%)	
occurrences (all)	5	8	
Vomiting			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	5	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 April 2015	Changes: Sensory testing at the 42 hour test time is deleted Pain score at 42 the hour test time is deleted Sensory testing and pain score at 42 hours are deleted because this time point consistently is in the middle of the night, and it is difficult to wake up the patients and get valid test results. Furthermore, as most of the patients will be sleeping we find it more ethical to let the patients sleep through the night. Ankle arthrodesis performed as an arthroscopy is removed as an exclusion criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Five patients did not require opioids at all. These patients contribute to the primary outcome with the time until a shift in sensory thermanalgesia in the infrapatellar area. This was chosen as the best proxy marker for the end of block duration.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28033159