Clinical trial results:
The effect of subsartorial saphenous block on postoperative pain following major ankle and hind foot surgery

Summary

EudraCT number	2016-000608-27
Trial protocol	DK
Global end of trial date	28 February 2017

Results information

Result version number	v1 (current)
This version publication date	23 January 2018
First version publication date	23 January 2018

Trial information

Trial identification

Sponsor protocol code	ProtokolSB2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02697955
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Nørrebrogade 44, Aarhus C, Denmark, 8000
Public contact	Sponsor: Thomas Fichtner Bendtsen, Aarhus University Hospital Department of Anesthesiology and Intensive Care Medicine, +45 51542997, tfb@dadlnet.dk
Scientific contact	Sponsor: Thomas Fichtner Bendtsen, Aarhus University Hospital Department of Anesthesiology and Intensive Care Medicine, +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	25 June 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2017
Global end of trial reached?	Yes
Global end of trial date	28 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to conduct a prospective, randomized, controlled, double-blinded trial to compare saphenous nerve block with bupivacaine-epinephrine vs. placebo to investigate the effect of a saphenous block as a supplement to sciatic nerve block after major ankle surgery. We hypothesized that a saphenous nerve block reduces the proportion of patients experiencing significant clinical pain after major ankle surgery.

Protection of trial subjects:

The study was monitored by the Good Clinical Practice Unit at Aarhus and Aalborg University Hospitals

In this study all patients received a sciatic nerve block according to the standard treatment at the department. The patients were randomized to active or placebo saphenous nerve block, but the observation period ended when the patient reported significant clinical pain (NRS > 3), and the patient immediately received a rescue saphenous nerve block.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 June 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

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)	7
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient was enrolled 21 June 2016, and the last patient was enrolled and completed 28 February 2017.
All patients were enrolled at the foot and ankle surgery section at the Department of Orthopedic Surgery, Aarhus University Hospital, Denmark.

Pre-assignment

Screening details:

44 patients were screened.
Reasons for primary exclusion:
- Operation type not included (n=6)
- Logistical reasons (n=6)
- Daily intake of opioids (n=3)
- Inability to cooperate (n=2)
- Neuropathy/reduced sensation (n=5)
- Charcot-Marie-Tooth disease (n=1)
- Severe co-morbidity (n=3)

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Active

Arm description:

Saphenous nerve block in the femoral triangle with 10 mL 0.5 % bupivacaine with 1:200,000 epinephrine

Arm type	Experimental
Investigational medicinal product name	Bupivacaine-epinephrine
Investigational medicinal product code	
Other name	Marcaine-adrenaline
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

Single-injection saphenous nerve block with 10 ml Marcaine-adrenaline.
1 ml Marcaine-adrenaline contains 5 mg bupivacainehydrochloride and 5 micrograms adrenaline as tartrate.

Arm title	Placebo

Arm description:

Saphenous nerve block in the femoral triangle with 10 mL saline

Arm type	Placebo
Investigational medicinal product name	Sodium chloride 0.9 %
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:
Single-injection saphenous nerve block with 10 ml Sodium chloride 0.9 %

Number of subjects in period 1	Active	Placebo
Started	9	9
Completed	9	9

Baseline characteristics

Reporting groups	
Reporting group title	Active
Reporting group description:	
Saphenous nerve block in the femoral triangle with 10 mL 0.5 % bupivacaine with 1:200,000 epinephrine	
Reporting group title	Placebo
Reporting group description:	
Saphenous nerve block in the femoral triangle with 10 mL saline	

Reporting group values	Active	Placebo	Total
Number of subjects	9	9	18
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)	4	3	7
From 65-84 years	5	6	11
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	64.9	66.7	
standard deviation	± 7.6	± 10.9	-
Gender categorical			
Units: Subjects			
Female	2	5	7
Male	7	4	11
ASA physical status			
ASA = American Society of Anesthesiologists			
Units: Subjects			
ASA I	5	3	8
ASA II	4	6	10
Surgical procedures			
Units: Subjects			
Total ankle arthroplasty	3	6	9
Ankle arthrodesis	1	0	1
Subtalar arthrodesis	0	1	1
Triple arthrodesis	5	2	7
Weight			
Units: kilogram(s)			
arithmetic mean	84.6	83.3	
standard deviation	± 18.2	± 11.7	-
Height			

Units: meter			
arithmetic mean	1.76	1.71	
standard deviation	± 0.11	± 0.08	-
BMI			
BMI = Body Mass Index			
Units: kilogram(s)/square meter			
arithmetic mean	27.0	28.4	
standard deviation	± 3.5	± 3.4	-

End points

End points reporting groups

Reporting group title	Active
Reporting group description:	
Saphenous nerve block in the femoral triangle with 10 mL 0.5 % bupivacaine with 1:200,000 epinephrine	
Reporting group title	Placebo
Reporting group description:	
Saphenous nerve block in the femoral triangle with 10 mL saline	

Primary: Number of patients experiencing significant clinical pain (NRS > 3)

End point title	Number of patients experiencing significant clinical pain (NRS > 3)
End point description:	
Significant clinical pain at rest is defined as NRS > 3 at any time during the observation period	
End point type	Primary
End point timeframe:	
Patients were observed postoperatively until NRS > 3 or up until 120 minutes after the end of surgery. Pain scores were evaluated at: Arrival at PACU and 30, 45, 60, 75, 90, 105 and 120 min after the end of surgery	

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: Subjects				
NRS > 3	1	8		
NRS ≤ 3	8	1		

Statistical analyses

Statistical analysis title	Fischer’s exact test
Comparison groups	Active v Placebo
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Fisher exact

Secondary: The maximal reported pain score (NRS) during the observation period

End point title	The maximal reported pain score (NRS) during the observation period

End point description:

NRS = numerical rating scale 0-10

End point type	Secondary

End point timeframe:

Patients were observed postoperatively until NRS > 3 or up until 120 minutes after the end of surgery. Pain scores (NRS) were evaluated at: Arrival at PACU and 30, 45, 60, 75, 90, 105 and 120 min after the end of surgery.

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: number				
median (inter-quartile range (Q1-Q3))	0 (0 to 0)	5 (4 to 6)		

Statistical analyses

Statistical analysis title	Mann-Whitney test
Comparison groups	Placebo v Active
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Wilcoxon (Mann-Whitney)

Secondary: Sensory testing of the infrapatellar branch

End point title	Sensory testing of the infrapatellar branch

End point description:

The sensory test was performed as a pinprick test with a neuropen applying a standardized pressure of 40 g. The infrapatellar branch of the saphenous nerve was tested at the midpoint of a line connecting the medial femoral condyle and the tibial tuberosity. Sensation to pinprick was graded on a 3 point scale: 0 = no sensation, 1 = reduced sensation and 2 = normal sensation to pinprick compared to the contralateral side.

End point type	Secondary

End point timeframe:

Baseline test and at the time when the patient reported NRS > 3 during the observation period. In case of NRS ≤ 3 during the entire observation period, sensory testing was conducted at t = 120 min

End point values	Active	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	9		
Units: Subjects				
Normal cutaneous sensation (pinprick score 2)	0	9		
Reduced cutaneous sensation (pinprick score 1)	1	0		
No cutaneous sensation (pinprick score 0)	8	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Reporting period: 21 Jun 2016 until 28 Feb 2017.
Each patient was observed for adverse events from study treatment was given (randomized saphenous nerve block) and until the end of the observation period (maximum 120 min after the end of surgery)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups

Reporting group title	Active
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Active	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (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	Active	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No non-serious adverse events were observed in this trial. The study was small with only 18 patients. The trial period was of very short duration, and the study intervention very similar to the normal standard treatment.

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