Clinical trial results:
Surgical anesthesia for elective hip surgery - hemodynamic effect of lumbosacral plexus blockade compared to continuous spinal anesthesia

Summary

EudraCT number	2015-003498-13
Trial protocol	DK
Global end of trial date	24 February 2017

Results information

Result version number	v1 (current)
This version publication date	09 May 2018
First version publication date	09 May 2018

Trial information

Trial identification

Sponsor protocol code	HIP/FUSION#1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02544269
WHO universal trial number (UTN)	-
Other trial identifiers	Local health research ethics committee no.: 51392, Danish data protection agency no.: 2015-57-0002

Notes:

Sponsors

Sponsor organisation name	Institut for Klinisk Medicin
Sponsor organisation address	Noerrebrogade 44, building 22, 1st floor, Aarhus C, Denmark, 8000
Public contact	Niels Dalsgaard Nielsen, Institut for Klinisk Medicin, Aarhus Universitet, +45 2283 8334, nielsdn@dadlnet.dk
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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	05 April 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 February 2017
Global end of trial reached?	Yes
Global end of trial date	24 February 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Comparison of the hemodynamic effect of lumbosacral plexus blockade versus continuous spinal anesthesia.

Protection of trial subjects:

Continuous hemodynamic monitoring (electrocardiogram, pulseoxymetri, invasive arterial and central venous blood pressures, heart rate, cardiac output, cardiac stroke volume, systemic vascular resistance and central venous oxygen saturation) allowed for early detection of hemodynamic adverse events.
All skin punktures were preceded by subdermal infiltration with local anaesthetics (lidocaine 10 mg/mL).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 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: 8
Worldwide total number of subjects	8
EEA total number of subjects	8

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)	4
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screened 24 patients.

Period 1

Period 1 title	Pilot study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Subjects not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Lumbosacral plexus block

Arm description:

Surgical anaesthesia with lumbosacral plexus block by a combination of the following:
Lumbar plexus block (Shamrock-block as described by A. Sauter)
Sacral plexus block (Parasacral parallel shift-block as described by TF. Bendtsen)
Iliohypogastric block (Fascia transversalis plane block as described by P. Hubbard)

Arm type	Experimental
Investigational medicinal product name	Ropivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Perineural use

Dosage and administration details:

Lumbar plexus block: 20 mL ropivacain 7,5 mg/mL perineural, single injection
Sacral plexus block: 10 mL ropivacain 7,5 mg/mL perineural, single injection
Iliohypogastric block: 10 mL ropivacain 7,5 mg/mL perineural, single injection

Arm title	Continuous spinal anesthesia

Arm description:

Surgical anaesthesia with repeated intrathecal doses of bupivacain through a spinal catheter.

Arm type	Active comparator
Investigational medicinal product name	Bupivacaine, CSA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intrathecal use

Dosage and administration details:

Repeated intrathecal doses of 0,5 mL bupivacaine 5 mg/mL. Dose repeated after 10 min and subsequent doses after 5 min if spinal anesthesia had not reached a level of the iliac crest. Max cumulated dose was 3 mL/15 mg.

Arm title	Single-dose spinal anesthesia

Arm description:

Surgical anesthesia with a single intrathecal injection of bupivacaine

Arm type	Active comparator

Investigational medicinal product name	Bupivacaine, SDSA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intrathecal use

Dosage and administration details:

Single intrathecal injection of 2 mL bupivacaine 5 mg/mL through a spinal catheter.

Number of subjects in period 1	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia
Started	3	3	2
Completed	3	2	1
Not completed	0	1	1
Protocol deviation	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Pilot study

Reporting group description: -

Reporting group values	Pilot study	Total	
Number of subjects	8	8	
Age categorical 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)	4	4	
From 65-84 years	4	4	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	67		
standard deviation	± 7.928	-	
Gender categorical Units: Subjects			
Female	4	4	
Male	4	4	
ASA-score			
American Society of Anesthesiologists physical status classification system			
Units: Subjects			
ASA I	0	0	
ASA II	8	8	
ASA III	0	0	
Height Units: Centimeters			
arithmetic mean	175		
standard deviation	± 11.13	-	
Weight Units: Kilograms			
arithmetic mean	81.1		
standard deviation	± 18.23	-	
Charlson Comorbidity Index Units: Index			
median	0		
full range (min-max)	0 to 1	-	

End points

End points reporting groups

Reporting group title	Lumbosacral plexus block
Reporting group description:	
Surgical anaesthesia with lumbosacral plexus block by a combination of the following: Lumbar plexus block (Shamrock-block as described by A. Sauter) Sacral plexus block (Parasacral parallel shift-block as described by TF. Bendtsen) Iliohypogastric block (Fascia transversalis plane block as described by P. Hubbard)	
Reporting group title	Continuous spinal anesthesia
Reporting group description:	
Surgical anaesthesia with repeated intrathecal doses of bupivacain through a spinal catheter.	
Reporting group title	Single-dose spinal anesthesia
Reporting group description:	
Surgical anesthesia with a single intrathecal injection of bupivacaine	

Primary: Change of cardiac output

End point title	Change of cardiac output[1]
End point description:	
Change of cardiac output (mL/min) from baseline (before nerve block performance) to 30 minutes after nerve block.	
End point type	Primary
End point timeframe:	
30 minutes after nerve block performance	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the trial was haltet after the pilot study only data from 6 patients in 3 groups was collected. It was not deemed meaningful to analyse on these sparse numbers.

End point values	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	1	
Units: percent				
arithmetic mean (full range (min-max))	1.8 (-15.8 to 30.2)	0.8 (0 to 1.6)	-13.2 (-13.2 to -13.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time for nerve blockade performance

End point title	Time for nerve blockade performance[2]
End point description:	
Duration of lumbar plexus block (LPB) and sacral plexus block (SPB) performance from beginning of ultrasound scan (after applying sterile dressing) before LPB to withdrawal of nerve block needle after SPB.	

End point type	Secondary

End point timeframe:

After nerve block performance

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As the trial was haltet after the pilot study only data from 6 patients in 3 groups was collected. It was not deemed meaningful to analyse on these sparse numbers.

End point values	Lumbosacral plexus block			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: minute				
arithmetic mean (full range (min-max))	24 (22 to 26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Success rate of surgical anesthesia

End point title	Success rate of surgical anesthesia

End point description:

Rate (0-1) of success of surgical anesthesia.

End point type	Secondary

End point timeframe:

At time of positioning of patient on operating table

End point values	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	1	
Units: Success rate	0	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulated peroperative dose of propofol

End point title	Cumulated peroperative dose of propofol

End point description:

Cummulated dose of intravenous propofol administered during surgery

End point type	Secondary

End point timeframe:

As patient leaves the operating room

End point values	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	1	
Units: milligram(s)				
arithmetic mean (full range (min-max))	183 (153 to 204)	151 (131 to 170)	96 (96 to 96)	

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulated peroperative dose of opioids

End point title	Cumulated peroperative dose of opioids

End point description:

Cumulated dose of intravenous opioids administered during surgery. Converted to peroral morphine equivalents.

End point type	Secondary

End point timeframe:

As patient leaves the operating room

End point values	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	1	
Units: milligram(s)				
arithmetic mean (full range (min-max))	13 (0 to 40)	0 (0 to 0)	23 (23 to 23)	

Statistical analyses

No statistical analyses for this end point

Secondary: Cumulated postoperative does of opioids

End point title	Cumulated postoperative does of opioids

End point description:

Cumulated dose of opioid administered during the first 24 hours after surgery. Converted to peroral morphine equivalents.

End point type	Secondary

End point timeframe:

24 hours after surgery

End point values	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	1	
Units: milligram(s)				
arithmetic mean (full range (min-max))	81 (46 to 148)	63 (0 to 118)	70 (70 to 70)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first opioid dose

End point title	Time to first opioid dose

End point description:

Time from end of surgery to first request for opioids.

End point type	Secondary

End point timeframe:

24 hours after surgery.

End point values	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	1	1	
Units: minute				
arithmetic mean (full range (min-max))	529 (286 to 768)	67 (67 to 67)	170 (170 to 170)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of cardiac stroke volume

End point title	Change of cardiac stroke volume

End point description:

Change of cardiac stroke volume (mL) from baseline (before nerve block performance) to 30 minutes after nerve block.

End point type	Secondary

End point timeframe:

30 minutes after nerve block performance

End point values	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	1	
Units: percent				
arithmetic mean (full range (min-max))	6.4 (-15.6 to 30.2)	-1.7 (-7.2 to 3.8)	-12.3 (-12.3 to -12.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of systemic vascular resistance

End point title	Change of systemic vascular resistance

End point description:

Change of systemic vascular resistance (dyne-s/cm^5) from baseline (before nerve block performance) to 30 minutes after nerve block.

End point type	Secondary

End point timeframe:

30 minutes after nerve block performance

End point values	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	1	
Units: percent				
arithmetic mean (full range (min-max))	0.9 (-33.7 to 23.9)	1.3 (-1.2 to 3.8)	-29.4 (-29.4 to -29.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of mean arterial pressure

End point title	Change of mean arterial pressure

End point description:

Change of mean arterial blood pressure (mm Hg) from baseline (before nerve block performance) to 30 minutes after nerve block.

End point type	Secondary

End point timeframe:

30 minutes after nerve block performance

End point values	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	1	
Units: percent				
arithmetic mean (full range (min-max))	-4.1 (-15 to 6.7)	1 (1 to 1.1)	-40.4 (-40.4 to -40.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change of central venous oxygen saturation

End point title	Change of central venous oxygen saturation

End point description:

Change of central venous oxygen saturation (%) from baseline (before nerve block performance) to 30 minutes after nerve block.

End point type	Secondary

End point timeframe:

30 minutes after nerve block performance

End point values	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	1	
Units: percent				
arithmetic mean (full range (min-max))	3 (-8.2 to 8.7)	3.2 (2.4 to 4.1)	8.2 (8.2 to 8.2)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Pilot study	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups	
Reporting group title	Lumbosacral plexus block
Reporting group description:	
Surgical anaesthesia with lumbosacral plexus block by a combination of the following: Lumbar plexus block (Shamrock-block as described by A. Sauter) Sacral plexus block (Parasacral parallel shift-block as described by TF. Bendtsen) Iliohypogastric block (Fascia transversalis plane block as described by P. Hubbard)	
Reporting group title	Continuous spinal anesthesia
Reporting group description:	
Surgical anaesthesia with repeated intrathecal doses of bupivacain through a spinal catheter.	
Reporting group title	Single-dose spinal anesthesia
Reporting group description:	
Surgical anesthesia with a single intrathecal injection of bupivacaine	

Serious adverse events	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 2 (0.00%)	0 / 2 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Lumbosacral plexus block	Continuous spinal anesthesia	Single-dose spinal anesthesia
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	1 / 2 (50.00%)	1 / 2 (50.00%)
Injury, poisoning and procedural complications			
Hemorrhage and anaemia	Additional description: Per- and postoperative bleeding with resulting anaemia		
subjects affected / exposed[1]	1 / 3 (33.33%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			

Arterial hypotension	Additional description: Arterial hypotension defined as mean arterial blood pressure below 60 mm Hg or below 35 % of baseline (whichever is the highest value).		
subjects affected / exposed[2]	0 / 3 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1
Cardiac disorders			
Atrial fibrillation	Additional description: Occurrence of atrial fibrillation in patients with no prior history of atrial fibrillation.		
subjects affected / exposed[3]	1 / 3 (33.33%)	0 / 2 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Paresthesia			
subjects affected / exposed[4]	0 / 3 (0.00%)	0 / 2 (0.00%)	1 / 1 (100.00%)
occurrences (all)	0	0	1

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: No it's not. 3 subjects was exposed in the lumbosacral plexus block-group, 2 subjects was exposed in the continuous spinal anesthesia-group and 1 subject was exposed in the single-dose spinal anesthesia-group.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: No it's not. 3 subjects was exposed in the lumbosacral plexus block-group, 2 subjects was exposed in the continuous spinal anesthesia-group and 1 subject was exposed in the single-dose spinal anesthesia-group.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: No it's not. 3 subjects was exposed in the lumbosacral plexus block-group, 2 subjects was exposed in the continuous spinal anesthesia-group and 1 subject was exposed in the single-dose spinal anesthesia-group.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: No it's not. 3 subjects was exposed in the lumbosacral plexus block-group, 2 subjects was exposed in the continuous spinal anesthesia-group and 1 subject was exposed in the single-dose spinal anesthesia-group.

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
24 February 2017	In an interim analysis of data from the first 6 patients, who completed the pilot study, no difference in the primary end point (change of cardiac output) was found between the two primary groups (lumbosacral plexus block and continuous spinal anesthesia). This led to doubts about the validity of the study hypothesis, which assumed a subjective difference in change of cardiac output between the two groups. It was considered to change the hypothesis according to the pilot data and thus perform a non-inferiority study. This path was abandoned, however, due to a revised sample-size estimate of 25 patients per group. It was deemed impossible both for practical and economic reasons to include a total of 50 patients. As a consequence, it was decided to terminate the trial.	-

Notes:

Limitations and caveats

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

Results are from a non-randomised non-blinded pilot study.

Notes: