Clinical trial results:
The effect of saphenous nerve and obturator nerve block combined with systemic high dose glucocorticoid versus local infiltration analgesia combined with a systemic high dose glucocorticoid on opioid consumption and pain after total knee arthroplasty.

Summary

EudraCT number	2014-003343-35
Trial protocol	DK
Global end of trial date	16 November 2015

Results information

Result version number	v1 (current)
This version publication date	25 January 2021
First version publication date	25 January 2021

Trial information

Trial identification

Sponsor protocol code	CR-TFB-2014/502

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 99, Aarhus, Denmark, 8200
Public contact	Centre of Elective Surgery, Hospital of Silkeborg, 0045 25883172, charlotte.runge@aarhus.rm.dk
Scientific contact	Centre of Elective Surgery, Hospital of Silkeborg, 0045 25883172, charlotte.runge@aarhus.rm.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	20 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 November 2015
Global end of trial reached?	Yes
Global end of trial date	16 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim is to investigate the effect of combined saphenous nerve and obturator nerve block with a mixture of local analgesics; ropivacaine and adrenaline, compared with combined local infiltration analgesia in the tissue around the knee joint both methods combined with systemic high dose glucocorticoid on opioid consumption after total knee arthroplasty.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki and approved by the Danish Medicines Agency, the Central Denmark Region Committees on Health Research Ethics, and the Danish Danish Protection Agency. The trial was prospectively registered in the EudraCT data base and was monitored by the Good Clinical Practice Unit at Aalborg and Aarhus University Hospitals. Prior to inclusion, written informed consent was obtained from all subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 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: 82
Worldwide total number of subjects	82
EEA total number of subjects	82

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)	12
From 65 to 84 years	70

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

INCLUSION:> 50 years, ASA I–III, scheduled for cemented, unilateral, primary TKA, and spinal anesthesia.
EXCLUSION: Inability to cooperate, non-Danish speakers, immunosuppressive therapy, diabetes, lower-limb neuropathy, daily glucocorticoids/opioids, allergy to drugs used in the study, alcohol or drug abuse, and intolerance to NSAID.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Combined active ONB+FTB group

Arm description:

Combined active ONB+FTB group: Active ONB + active FTB + active intravenous ketorolac (1 mL 30 mg) + sham LIA.
All patients received intravenous dexamethasone 16 mg prior to the spinal anesthesia

ONB = obturator nerve block; FTB = femoral triangle block; LIA = local infiltration analgesia

Arm type	Experimental
Investigational medicinal product name	Ropivacaine 0.75% w. epinephrine 5 micrograms/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Perineural use

Dosage and administration details:

Ropivacaine 10 mL for each active ONB and FTB.

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

Dosage and administration details:

150 mL for sham LIA.

Investigational medicinal product name	Ketorolac 3%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

30 mg (1 mL) intravenously.

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

All patients received intravenous dexamethasone 16 mg

Arm title	Active LIA

Arm description:

Active LIA: Active LIA + sham ONB + sham FTB + sham intravenous ketorolac (1 mL saline).
All patients received intravenous dexamethasone 16 mg prior to spinal anesthesia.

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

Dosage and administration details:

10 mL for each sham ONB and FTB.

Investigational medicinal product name	Ropivacaine 0.2% w. epinephrine 5 micrograms/mL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Infiltration

Dosage and administration details:

150 mL for active LIA.

Investigational medicinal product name	Ketorolac 3%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Infiltration

Dosage and administration details:

45 mg for active LIA

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

All patients received intravenous dexamethasone 16 mg

Number of subjects in period 1	Combined active ONB+FTB group	Active LIA
Started	41	41
Completed	35	39
Not completed	6	2
Failed spinal anesthesia	-	1
Adverse event, non-fatal	1	-

Preoperative opioid use	1	1
Competitive hip pain	1	-
Not able to cooperate	1	-
Perioperative angina	1	-
NSAID intolerance	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Combined active ONB+FTB group

Reporting group description:

Combined active ONB+FTB group: Active ONB + active FTB + active intravenous ketorolac (1 mL 30 mg) + sham LIA.
All patients received intravenous dexamethasone 16 mg prior to the spinal anesthesia

ONB = obturator nerve block; FTB = femoral triangle block; LIA = local infiltration analgesia

Reporting group title	Active LIA

Reporting group description:

Active LIA: Active LIA + sham ONB + sham FTB + sham intravenous ketorolac (1 mL saline).
All patients received intravenous dexamethasone 16 mg prior to spinal anesthesia.

Reporting group values	Combined active ONB+FTB group	Active LIA	Total
Number of subjects	41	41	82
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	69	68	
standard deviation	± 6.5	± 9.2	-
Gender categorical			
Units: Subjects			
Female	24	19	43
Male	17	22	39
BMI			
Body Mass Index			
Units: kilogram(s)/square meter			
arithmetic mean	28.8	29.1	
standard deviation	± 4.5	± 4.5	-
Duration of surgery			
Units: minute			
arithmetic mean	66	69	
standard deviation	± 14	± 15	-

End points

End points reporting groups

Reporting group title	Combined active ONB+FTB group

Reporting group description:

Combined active ONB+FTB group: Active ONB + active FTB + active intravenous ketorolac (1 mL 30 mg) + sham LIA.
All patients received intravenous dexamethasone 16 mg prior to the spinal anesthesia

ONB = obturator nerve block; FTB = femoral triangle block; LIA = local infiltration analgesia

Reporting group title	Active LIA

Reporting group description:

Active LIA: Active LIA + sham ONB + sham FTB + sham intravenous ketorolac (1 mL saline).
All patients received intravenous dexamethasone 16 mg prior to spinal anesthesia.

Primary: Opioid consumption

End point title	Opioid consumption

End point description:

The primary outcome was cumulated consumption of intravenous morphine equivalents during the first 20 hours after surgery, which was selected to ensure that all nerve blocks would remain fully effective during the entire time interval

End point type	Primary

End point timeframe:

20 hours after surgery

End point values	Combined active ONB+FTB group	Active LIA		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35[1]	39[2]		
Units: milligram(s)				
median (inter-quartile range (Q1-Q3))	6 (2 to 18)	20 (12 to 28)		

Notes:

[1] - 6 patients were excluded before data was collected ana analyzed

[2] - 2 patients were excluded before data was collected ana analyzed

Statistical analyses

Statistical analysis title	Opioid consumption

Statistical analysis description:

Continuous variables with skewed distribution are presented as median (inter- quartile range [IQR]. For nonparametric data, Mann-Whitney U test was used.

Comparison groups	Active LIA v Combined active ONB+FTB group

Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
From block/LIA procedure and until surgery	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0

Reporting groups	
Reporting group title	Combined active ONB+FTB group
Reporting group description:	
Combined active ONB+FTB group: Active ONB + active FTB + active intravenous ketorolac (1 mL 30 mg) + sham LIA. ONB = obturator nerve block; FTB = femoral triangle block; LIA = local infiltration analgesia	
Reporting group title	Active LIA
Reporting group description:	
Active LIA: Active LIA + sham ONB + sham FTB + sham intravenous ketorolac (1 mL saline)	

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: 2 serious adverse events were reported. No non-serious adverse events were reported from block/LIA procedure and until surgery.
After surgery dizziness was reported:
Group active ONB + FTB: 2 patients after 6 hrs; 5 patients after 20 hrs; 9 patients after 24 hrs.
Group active LIA: 5 patients after 6 hrs; 18 patients after 20 hrs; 18 patients after 24 hrs.

Serious adverse events	Combined active ONB+FTB group	Active LIA	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 41 (4.88%)	0 / 41 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Vasovagal event			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Combined active ONB+FTB group	Active LIA	
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	

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