Clinical trial results:
Ultrasoundguided Transmuscular Quadratus Lumborum(TQL) block for hand assisted laparoscopic nephrectomy - a randomized controlled trial

Summary

EudraCT number	2017-002130-23
Trial protocol	DK
Global end of trial date	31 July 2019

Results information

Result version number	v1 (current)
This version publication date	06 May 2021
First version publication date	06 May 2021

Trial information

Trial identification

Sponsor protocol code	TQLnephrectomi_v_1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ZUH
Sponsor organisation address	Sygehusvej 1, Roskilde, Denmark, 4000
Public contact	Jens Børglum, Dept of Anesth. Zealand university hospital Roskilde, 45 30700112, jedn@regionsjaelland.dk
Scientific contact	Jens Børglum, Dept of Anesth. Zealand university hospital Roskilde, 45 30700112, jedn@regionsjaelland.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 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2019
Global end of trial reached?	Yes
Global end of trial date	31 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate whether a unilateral USG TQL block can reduce opioid consumption with clinical significance in kidney cancer patients operated with hand ass. lap nephrectomy

Protection of trial subjects:

It wasmonitored by the Good Clinical Practice Unit at Copenhagen
University Hospital affiliated to the Danish Health Authority and all data was protected accordingly to the danish data protection agency

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2017
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: 48
Worldwide total number of subjects	48
EEA total number of subjects	48

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)	20
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Seventy-eight subjects were screened for eligibility from June 2018 to July 2019. Twenty patients did not meet inclusion criteria and eight patients declined to participate. After informed consent, 50 patients were enrolled and randomized

Pre-assignment

Screening details:

patients ≥18 years of age,ASA I-III, elective hand-assisted laparoscopic nephrectomy or laparoscopic robot-assisted partial nephrectomy. Exclusion: inability to cooperate, dementia, allergy to LA and opioids, regular daily opioid requirements, abuse of alcohol or medication, local infection at the site of injection, pregnancy

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, Monitor, Data analyst

Blinding implementation details:

After a computer-generated randomization list with five blocks of 10 with a 1:1 ratio, 50 opaque sealed envelopes numbered 1–50 were prepared. Patients were assigned to receive a preoperative bilateral TQL block with either 60 mL 0.375% ropivacaine (intervention) or 60 mL isotonic saline (control).Following inclusion, two research assistants, with no further involvement in the study, prepared the syringes. All other investigators, staff and patients were blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention

Arm description:

Patients received a preoperative bilateral TQL block with 60 mL 0.375% ropivacaine.

Arm type	Active comparator
Investigational medicinal product name	Ropivacaine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Infiltration

Dosage and administration details:

60 mL 0.375% ropivacaine (intervention) or 60 mL isotonic saline (control). The total dosage of ropivacaine was chosen according to the Danish Medicines Agency accepted dosage of ropivacaine for a single-shot block, previous pharmacokinetic studies regarding the dosage of ropivacaine and two former RCTs using the same dosage.

Arm title	Control

Arm description:

Patients were assigned to receive a

preoperative bilateral TQL block with 60 mL isotonic saline (control).

Arm type	Placebo
Investigational medicinal product name	Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infiltration

Dosage and administration details:

60 mL of Saline was injected(30 mL bilaterally)

Number of subjects in period 1	Intervention	Control
Started	24	24
Completed	24	24

Baseline characteristics

Reporting groups	
Reporting group title	Intervention
Reporting group description:	
Patients received a preoperative bilateral TQL block with 60 mL 0.375% ropivacaine.	
Reporting group title	Control
Reporting group description:	
Patients were assigned to receive a preoperative bilateral TQL block with 60 mL isotonic saline (control).	

Reporting group values	Intervention	Control	Total
Number of subjects	24	24	48
Age categorical			
Intervention group Age 68.5 (38–77)			
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)	11	10	21
From 65-84 years	13	14	27
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	68.5	69	
standard deviation	± 8	± 9	-
Gender categorical			
Units: Subjects			
Female	10	8	18
Male	14	16	30

End points

End points reporting groups

Reporting group title	Intervention
Reporting group description:	
Patients received a preoperative bilateral TQL block with 60 mL 0.375% ropivacaine.	
Reporting group title	Control
Reporting group description:	
Patients were assigned to receive a preoperative bilateral TQL block with 60 mL isotonic saline (control).	

Primary: Postoperative opioid 0-12 hours

End point title	Postoperative opioid 0-12 hours
End point description:	
When entering the PACU, a protocol trained nurse connected the intravenous PCA pump to one of the two intravenous lines. If the NRS score was ≥4 despite the use of PCA morphine, additional intravenous morphine could be required, and the administration hereof was recorded in the patient's electronic file. Intravenous morphine was converted to OME in the ratio 1:3.13	
End point type	Primary
End point timeframe:	
0-12 hours postoperatively	

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: 0-500				
arithmetic mean (confidence interval 95%)	50 (28.5 to 71.5)	87.5 (62.7 to 112.3)		

Statistical analyses

Statistical analysis title	Overall Statistical analysis
Statistical analysis description:	
Data were analyzed using SAS V.9.4. Normal distribution was tested using Q-Q plots. We summarized continuous data using mean, CIs, median and IQR and assessed difference between groups using t tests and Mann-Whitney-Wilcoxon test on both raw and transformed data including integrated average scores. Time-to-event data were analyzed using Kaplan-Meier curves and log-rank tests and data were presented as median (IQR). Frequencies were quantitated and analyzed using $\chi 2$tests or Fischer's exact test	
Comparison groups	Intervention v Control

Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05 [1]
Method	Fisher exact
Parameter estimate	Mean difference (final values)
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard error of the mean

Notes:

[1] - level of significance (a)=0.05 (two-sided)
and power 80% (1−β)

Secondary: Postoperative opioid 12-18

End point title	Postoperative opioid 12-18

End point description:

T0 was defined as arrival time in the PACU. Consequently, when entering the PACU, a protocol trained nurse connected the intravenous PCA pump to one of the two intravenous lines. If the NRS score was ≥4 despite the use of PCA morphine, additional intravenous morphine could be required, and the administration hereof was recorded in the patient's electronic file. Intravenous morphine was converted to OME in the ratio 1:3

End point type	Secondary

End point timeframe:

accumulated OME consumption (mg) at 12–18 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: 0-500				
arithmetic mean (confidence interval 95%)	11.3 (4.5 to 18)	23.1 (14.2 to 32.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: NRS at activity

End point title	NRS at activity

End point description:

Pain scores (NRS) at (1) rest and at (2) activity were assessed at predefined time points from T0 to T24 hours.

End point type	Secondary

End point timeframe:

0-24 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: 0-10				
median (inter-quartile range (Q1-Q3))	2.1 (1.2 to 3.2)	2.9 (2.1 to 3.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: NRS at rest

End point title	NRS at rest

End point description:

Pain scores (NRS) at (1) rest and at (2) activity were assessed at predefined time points from T0 to T24 hours.

End point type	Secondary

End point timeframe:

0-24 hours postoperatively

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: 0-10				
median (inter-quartile range (Q1-Q3))	1.9 (1.1 to 2.0)	2.3 (1.7 to 2.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pain related to block procedure

End point title	Pain related to block procedure

End point description:

Pain scores during block procedure

End point type	Secondary

End point timeframe:

preoperatively

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: 0-10				
median (inter-quartile range (Q1-Q3))	1.8 (1 to 3)	1.8 (1 to 2)		

Statistical analyses

Statistical analysis title	Overall Statistical analysis
Comparison groups	Intervention v Control
Number of subjects included in analysis	48
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	Fisher exact

Secondary: Time to ambulate

End point title	Time to ambulate

End point description:

Time to first ambulation was defined as time from T0 until the patient was able to stand on the floor and independently walk.

End point type	Secondary

End point timeframe:

0-24 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: hours				
median (inter-quartile range (Q1-Q3))	12.6 (4 to 20.3)	15.9 (5.5 to 21)		

Statistical analyses

No statistical analyses for this end point

Secondary: LOS

End point title	LOS

End point description:

Based on the hospital’s standard discharge criteria for laparoscopic nephrectomies, the surgeons decided when to discharge

the patients and recorded this in the patient’s electronic file.

End point type	Secondary

End point timeframe:

until discharge

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Hours				
median (inter-quartile range (Q1-Q3))	28 (26 to 35.5)	35 (25.5 to 47)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to first opioid demand

End point title	Time to first opioid demand

End point description:

Time to first
opioid demand was defined as time from T0 until the first PCA bolus.

End point type	Secondary

End point timeframe:

0-24 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: hours				
median (inter-quartile range (Q1-Q3))	4.4 (2.8 to 17.6)	0.3 (0.1 to 1)		

Statistical analyses

No statistical analyses for this end point

Secondary: nausea and vomiting

End point title	nausea and vomiting

End point description:

nausea and vomiting (yes/no),

End point type	Secondary

End point timeframe:
0-24 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: yes and no				
number (not applicable)	3	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Postoperative opioid 18-24

End point title	Postoperative opioid 18-24

End point description:
accumulated OME consumption (mg) at 18–24 hours,

End point type	Secondary

End point timeframe:
18-24 postoperatively

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: mg				
arithmetic mean (confidence interval 95%)	7.5 (1.6 to 13.4)	16.9 (8.9 to 24.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: total OME 24 hours

End point title	total OME 24 hours

End point description:
total accumulated OME consumption (mg) at 0-24 hours

End point type	Secondary

End point timeframe:
0-24 hours

End point values	Intervention	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: mg				
arithmetic mean (confidence interval 95%)	69.4 (43.2 to 95.5)	127 (96.7 to 158.6)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: The entire study period	
Assessment type	Systematic

Dictionary used	
Dictionary name	SUSAR, SAE, AE
Dictionary version	1

Reporting groups	
Reporting group title	Both groups
Reporting group description: -	

Serious adverse events	Both groups		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Both groups		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 48 (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: There were no adverse events recored in the study period

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

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

No evaluation of block succes

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33106280