Clinical trial results:
Optimizing surgical conditions during laparoscopic umbilical, incisional –and linea alba herniotomy with deep neuromuscular blockade (The hernia study)

Summary

EudraCT number	2014-002802-19
Trial protocol	DK
Global end of trial date	25 February 2017

Results information

Result version number	v1 (current)
This version publication date	21 July 2022
First version publication date	21 July 2022

Trial information

Trial identification

Sponsor protocol code	NMBDKHernia2014

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02247466
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Herlev Hospital
Sponsor organisation address	Herlev Ringvej, Herlev, Denmark,
Public contact	Mona Ring Gätke, Department of Anaesthesiology, mona.gatke@regionh.dk
Scientific contact	Mona Ring Gätke, Department of Anaesthesiology, mona.gatke@regionh.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	28 February 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 February 2017
Global end of trial reached?	Yes
Global end of trial date	25 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary outcome:
Improvement of surgical workspace (rated on a 5-point scale) estimated as the difference between the workspace during deep NMB and the workspace without NMB. Ratings are performed in the same patient during stable pneumoperitoneum at 12 mmHg.

Protection of trial subjects:

Postoperative pain treatment comprised paracetamol, NSAID and morphine according to local guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2015
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: 34
Worldwide total number of subjects	34
EEA total number of subjects	34

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)	34
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were enrolled by an investigator before surgery. Eligible patients were more than 18 years of age scheduled for elective laparoscopic ventral hernia repair.

Pre-assignment

Screening details:

exclusion criteria
were known allergy to sugammadex, mivacurium or rocuronium, severe renal disease,
neuromuscular disease, lactating or pregnant women

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

Blinding implementation details:

The patient’s hand, the nerve stimulator and computer were concealed from the surgeon and the surgical staff.
An investigator prepared the intervention medicine in coded syringes before surgery so that the surgical team was blind to the medication. During surgery, the unblinded investigator was responsible for NMB monitoring and administration of the study drugs.

Arms

Are arms mutually exclusive?	Yes
Arm title	Saline Rocuronium

Arm description:

In group A, patients received a bolus of 3ml of saline and 3 min later the surgeon evaluated the surgical view using a five-point subjective rating scale,16 ranging from 5 (optimal) to 1 (worst), refer to Table 1. Next, a bolus of rocuronium 0.6 mgkg1 was administered, and 3 min later when TOF¼0 was reached, the PTC was measured, and the surgeon re-evaluated the surgical view.

Arm type	Active comparator
Investigational medicinal product name	rocuronium
Investigational medicinal product code	25246
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

rocuronium 0.6 mg/kg intravenous

Arm title	rocuronium sugammadex

Arm description:

In Group B, a bolus of rocuronium 0.6mg/kg was administered and 3 min later when TOF 0 was reached, the PTC was measured and the surgeon evaluated the surgical view using the five-point rating scale. Sugammadex was then administered, 4 to 16mg/kg according to depth of NMB, and 3 min later, the surgeon re-evaluated the surgical view throughout the surgery until last suture

boluses of saline (placebo) were administered. During suturing of the hernial defect, surgical conditions were assessed using the five-point rating scale.
At the end of surgery, NMB was reversed in all patients

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

Dosage and administration details:

A bolus of rocuronium 0.6mg/kg was administered and 3 min later when TOF 0 was reached, the PTC was measured and the surgeon evaluated the surgical view using the five-point rating scale. Sugammadex was then administered, 4 to 16 mg/kg.

Number of subjects in period 1	Saline Rocuronium	rocuronium sugammadex
Started	19	15
Completed	19	15

Baseline characteristics

Reporting groups	
Reporting group title	Saline Rocuronium
Reporting group description:	
In group A, patients received a bolus of 3ml of saline and 3 min later the surgeon evaluated the surgical view using a five-point subjective rating scale,16 ranging from 5 (optimal) to 1 (worst), refer to Table 1. Next, a bolus of rocuronium 0.6 mgkg1 was administered, and 3 min later when TOF¼0 was reached, the PTC was measured, and the surgeon re-evaluated the surgical view.	
Reporting group title	rocuronium sugammadex
Reporting group description:	
In Group B, a bolus of rocuronium 0.6mg/kg was administered and 3 min later when TOF 0 was reached, the PTC was measured and the surgeon evaluated the surgical view using the five-point rating scale. Sugammadex was then administered, 4 to 16mg/kg according to depth of NMB, and 3 min later, the surgeon re-evaluated the surgical view throughout the surgery until last suture boluses of saline (placebo) were administered. During suturing of the hernial defect, surgical conditions were assessed using the five-point rating scale. At the end of surgery, NMB was reversed in all patients	

Reporting group values	Saline Rocuronium	rocuronium sugammadex	Total
Number of subjects	19	15	34
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)	19	15	34
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	57	55	
standard deviation	± 17	± 15	-
Gender categorical Units: Subjects			
Female	4	5	9
Male	15	10	25

End points

End points reporting groups

Reporting group title	Saline Rocuronium

Reporting group description:

In group A, patients received a bolus of 3ml of saline and 3 min later the surgeon evaluated the surgical view using a five-point subjective rating scale,16 ranging from 5 (optimal) to 1 (worst), refer to Table 1. Next, a bolus of rocuronium 0.6 mgkg1 was administered, and 3 min later when TOF¼0 was reached, the PTC was measured, and the surgeon re-evaluated the surgical view.

Reporting group title	rocuronium sugammadex

Reporting group description:

In Group B, a bolus of rocuronium 0.6mg/kg was administered and 3 min later when TOF 0 was reached, the PTC was measured and the surgeon evaluated the surgical view using the five-point rating scale. Sugammadex was then administered, 4 to 16mg/kg according to depth of NMB, and 3 min later, the surgeon re-evaluated the surgical view throughout the surgery until last suture boluses of saline (placebo) were administered. During suturing of the hernial defect, surgical conditions were assessed using the five-point rating scale.
At the end of surgery, NMB was reversed in all patients

Primary: difference in the surgical view

End point title	difference in the surgical view[1]

End point description:

End point type	Primary

End point timeframe:

Immediately

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: This was analyzed as a paired design

End point values	Saline Rocuronium	rocuronium sugammadex		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	15		
Units: score				
arithmetic mean (full range (min-max))	0.21 (0 to 2)	-0.06 (-2 to 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: suturing hernia

End point title	suturing hernia

End point description: subjective assessment of suturing the defect using a five point rating scale. 0 worst, 5 optimal.	
End point type	Secondary
End point timeframe: during suture of the defect	

End point values	Saline Rocuronium	rocuronium sugammadex		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	15		
Units: score				
arithmetic mean (standard deviation)	4.8 (± 0.4)	4.0 (± 1.4)		

Statistical analyses

Statistical analysis title	suture hernia defect
Comparison groups	Saline Rocuronium v rocuronium sugammadex
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Secondary: duration of hernia suturing

End point title	duration of hernia suturing
End point description:	
End point type	Secondary
End point timeframe: during suturing of hernia	

End point values	Saline Rocuronium	rocuronium sugammadex		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	15		
Units: minutes				
arithmetic mean (standard deviation)	10 (± 9)	9 (± 7)		

Statistical analyses

Statistical analysis title	suture hernia defect
Comparison groups	rocuronium sugammadex v Saline Rocuronium
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events were reported according to agreement with the Danish Medicines Agency and monitored by the Good Clinical Research Practice Unit at Copenhagen University Hospitals

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10

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

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: Adverse events were monitored according to agreement with the Danish Medicines Agency and monitored by the GCP unit at Copenhagen University Hospital

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

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29878947