Clinical trial results:
Muscle relaxation during open upper abdominal surgery -can the surgical conditions be optimized?

(The laparotomy study)

Influence of deep neuromuscular blockade on the surgeons´ assessment of surgical conditions during laparotomy: a randomized controlled double blinded trial with rocuronium and sugammadex

Summary

EudraCT number	2014-001155-22
Trial protocol	DK
Global end of trial date	04 August 2016

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	Lap2014NMB

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02140593
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Herlev Hospital
Sponsor organisation address	Herlev Ringvej, Herlev, Denmark,
Public contact	Department of Anesthesiology, Mona Ring Gätke, mona.gatke@regionh.dk
Scientific contact	Department of Anesthesiology, Mona Ring Gätke, 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	01 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2016
Global end of trial reached?	Yes
Global end of trial date	04 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the study is to investigate if intense NMB improves surgical conditions during operation in patients scheduled for elective open upper abdominal surgery. Hypothesis: Intense NMB (PTC 0-1) compared to standard NMB improves average of surgical condition scores evaluated on a subjective rating scale.

Protection of trial subjects:

An epidural catheter was placed preoperatively, and a test dose of 3 ml of lidocaine 20 mg ml-1 with adrenalin was installed. No further medicine was given in the epidural catheter until after closure of the abdominal wall. Anaesthesia was induced with propofol 2 mg kg-1 and remifentanil 1.0 µg kg-1 min-1. Anaesthesia was maintained with propofol 0.5 mg kg-1 hour-1 and remifentanil 0.25-0.5 µg kg-1 min-1, and adjusted according to depth of anaesthesia under guidance of arterial blood pressure and entropy 30-50 (Entropy Sensor, GE Healthcare, Hillerød, Denmark). The protocol allowed change to sevoflurane anaesthesia during surgery if the attending anaesthesiologist deemed this necessary.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 May 2014
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: 128
Worldwide total number of subjects	128
EEA total number of subjects	128

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	56
From 65 to 84 years	71
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients aged > 18 years scheduled for elective open upper abdominal surgery (Whipple, gastrectomy, splenectomy, gastric resection, liver resection and laparotomies due to bile obstruction, i.e. hepaticojejunostomy (not cholecystectomy)) were eligible.

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:

Intervention medicine was prepared in the operating room before surgery under double control by a nurse anaesthetist and by the investigator who also performed the randomization. The TOF-Watch and the arm with the neuromuscular equipment were covered and the readings from the TOF-Watch were only seen on the connected computer by the nurse anaesthetist and the investigator. The surgeon and any surgical personnel were blinded to the patients' group allocation.

Arms

Are arms mutually exclusive?	Yes
Arm title	Deep NMB

Arm description:

Deep neuromuscular blockade

Arm type	Experimental
Investigational medicinal product name	rocuronium
Investigational medicinal product code	25246
Other name	
Pharmaceutical forms	Injection
Routes of administration	Injection

Dosage and administration details:

Endotracheal intubation was performed two minutes after administration of rocuronium 0.6 mg kg-1. In group DEEP after tracheal intubation patients received rocuronium infusion (2 mg ml-1) with a target level of PTC 0-1. Just before skin incision, 1 ml of saline (placebo) was administered.

Arm title	Standard NMB

Arm description:

Standard neuromuscular blockade

Arm type	standard treatment

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Deep NMB	Standard NMB
Started	65	63
Completed	65	63

Baseline characteristics

Reporting groups	
Reporting group title	Deep NMB
Reporting group description: Deep neuromuscular blockade	
Reporting group title	Standard NMB
Reporting group description: Standard neuromuscular blockade	

Reporting group values	Deep NMB	Standard NMB	Total
Number of subjects	65	63	128
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	63	65	
full range (min-max)	31 to 78	35 to 85	-
Gender categorical Units: Subjects			
Female	26	30	56
Male	39	33	72

End points

End points reporting groups	
Reporting group title	Deep NMB
Reporting group description: Deep neuromuscular blockade	
Reporting group title	Standard NMB
Reporting group description: Standard neuromuscular blockade	

Primary: surgical rating scale	
End point title	surgical rating scale
End point description:	
End point type	Primary
End point timeframe: During surgery	

End point values	Deep NMB	Standard NMB		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	63		
Units: score				
median (standard deviation)				
surgical rating score	4.75 (± 0.54)	4 (± 0.91)		

Statistical analyses

Statistical analysis title	Mann-Whitney
Statistical analysis description: the Mann-Whitney test was used to compare ordinal or continuous variables that were not normally distributed	
Comparison groups	Deep NMB v Standard NMB
Number of subjects included in analysis	128
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: September 2014 and May 2016	
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 Danish Medicines Agency and monitored by the GCP unit.

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/29040455