Clinical trial results:
Intraoperative clonidine for prevention of postoperative agitation in children anaesthetised with sevoflurane (PREVENT AGITATION): a randomised, placebo-controlled, double-blind trial

Summary

EudraCT number	2014-001466-10
Trial protocol	DK
Global end of trial date	08 December 2015

Results information

Result version number	v1 (current)
This version publication date	24 November 2018
First version publication date	24 November 2018

Trial information

Trial identification

Sponsor protocol code	MY-clonidin-1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02361476
WHO universal trial number (UTN)	-
Other trial identifiers	National Committee on Biomedical Research Ethics: H-2-2014-072, Danish Data Protection Agency: 30-1348

Notes:

Sponsors

Sponsor organisation name	Copenhagen University Hospital, Rigshospitalet, Juliane Marie Centre, Department of Anaesthesiology
Sponsor organisation address	Blegdamsvej 9, Copenhagen, Denmark, 2100
Public contact	Mogens Ydemann, Copenhagen University Hospital, Rigshospitalet, Juliane Marie Centre, Department of Anaesthesiology, mogens@ydemann.dk
Scientific contact	Mogens Ydemann, Copenhagen University Hospital, Rigshospitalet, Juliane Marie Centre, Department of Anaesthesiology, mogens@ydemann.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	08 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 December 2015
Global end of trial reached?	Yes
Global end of trial date	08 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We aimed to assess the effects of intravenous clonidine administered intraoperatively on the incidence of postoperative agitation, pain, and adverse events.

Protection of trial subjects:

All patients received the same protocol-based care.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 379
Worldwide total number of subjects	379
EEA total number of subjects	379

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)	89
Children (2-11 years)	290
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

We recruited children between January and December, 2015, from: Rigshospitalet, Copenhagen University Hospital, Copenhagen; Vejle Hospital, Vejle, and Zealand University Hospital, Køge

Pre-assignment

Screening details:

Children aged 1–5 years, with an American Society of Anesthesiologists physical classification score of 1–2, who were scheduled for anaesthesia with sevoflurane and fentanyl.

Period 1

Period 1 title	inclusion (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

Blinding implementation details:

Vials were identical, we masked the trial to all participants, investigators, other health-care providers, and statisticians. Additionally, we extended the masking to the authors of the abstract for this Article who initially drafted two versions

Arms

Are arms mutually exclusive?	Yes
Arm title	intervention

Arm description:

3 µg/kg of intravenous clonidine - around 20 min before the end of surgery.

Arm type	Experimental
Investigational medicinal product name	clonidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

3 µg/kg of intravenous clonidine

Arm title	placebo

Arm description:

equal quantity of intravenous isotonic saline - around 20 min before completion of surgery

Arm type	Placebo
Investigational medicinal product name	NaCl
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous bolus use

Dosage and administration details:

equal quantity of intravenous isotonic saline

Number of subjects in period 1	intervention	placebo
Started	191	188
Completed	191	188

Baseline characteristics

Reporting groups	
Reporting group title	intervention
Reporting group description: 3 µg/kg of intravenous clonidine - around 20 min before the end of surgery.	
Reporting group title	placebo
Reporting group description: equal quantity of intravenous isotonic saline - around 20 min before completion of surgery	

Reporting group values	intervention	placebo	Total
Number of subjects	191	188	379
Age categorical			
<2 years			
Units: Subjects			
<2 years	46	43	89
≥2 years	145	145	290
Gender categorical Units: Subjects			
Female	37	38	75
Male	154	150	304

End points

End points reporting groups

Reporting group title	intervention
Reporting group description: 3 µg/kg of intravenous clonidine - around 20 min before the end of surgery.	
Reporting group title	placebo
Reporting group description: equal quantity of intravenous isotonic saline - around 20 min before completion of surgery	
Subject analysis set title	Postoperative agitation
Subject analysis set type	Intention-to-treat
Subject analysis set description: Nine were excluded from the primary outcome analysis because of missing data points.	

Primary: Postoperative agitation

End point title	Postoperative agitation
End point description: A Watcha score of more than 2 was considered as postoperative agitation.	
End point type	Primary
End point timeframe: measured every 15 min in the POCU	

End point values	intervention	placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	187	183		
Units: Watcha score				
agitation	46	86		

Statistical analyses

Statistical analysis title	intention-to-treat
Statistical analysis description: The proportion of patients with one or more incidence of agitation measured on the Watcha-Scale (scores 3 or 4).	
Comparison groups	placebo v intervention
Number of subjects included in analysis	370
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	generalised linear models (GLM)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: until discharge	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	intervention
Reporting group description: 3 µg/kg of intravenous clonidine - around 20 min before the end of surgery.	
Reporting group title	placebo
Reporting group description: equal quantity of intravenous isotonic saline - around 20 min before completion of surgery	

Serious adverse events	intervention	placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 191 (1.05%)	2 / 188 (1.06%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
events leading to admission			
subjects affected / exposed	2 / 191 (1.05%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	intervention	placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 191 (0.00%)	5 / 188 (2.66%)	
General disorders and administration site conditions			
div	Additional description: Opioid-related side-effects Laryngeal spasm Prolonged anaesthesia		
subjects affected / exposed	0 / 191 (0.00%)	5 / 188 (2.66%)	
occurrences (all)	0	5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 July 2015	We increased the number of participants from 304 to 380.

Notes:

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/30169192