Clinical trial results:
Does isocapnic hyperventilation hasten early recovery with sevoflurane and desflurane in O2/air?

Summary

EudraCT number	2014-000678-20
Trial protocol	BE
Global end of trial date	06 August 2024

Results information

Result version number	v1 (current)
This version publication date	04 May 2025
First version publication date	04 May 2025
Summary attachment (see zip file)	article study (Acta Anaesthesiol Scand - 2018 - De Baerdemaeker - The effect of isocapnic hyperventilation on early recovery after.pdf)

Trial information

Trial identification

Sponsor protocol code	SEVODESHV

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	UZ Brussel
Sponsor organisation address	Laarbeeklaan 101, 1090, Belgium,
Public contact	Datanurse, UZ Brussel, +32 24763134, veerle.vanmossevelde@uzbrussel.be
Scientific contact	Datanurse, UZ Brussel, +32 24763134, veerle.vanmossevelde@uzbrussel.be

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	17 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 April 2018
Global end of trial reached?	Yes
Global end of trial date	06 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The goal of the study is to examine the effect of hyperventilation on early recovery parameters when sevoflurane or desflurane is used. CO2 will be added to the inspired gas to avoid hypocapnia ("isocapnic hyperventilation")

Protection of trial subjects:

Trial subjects were closely monitored through the whole study conduct as from signing the informed consent.
If heart rate or blood pressure increased 20% above baseline (immediate preinduction values) or systolic blood pressure increased above 140 mm Hg, Ce remifentanil was increased. Hypotension (systolic blood pressure ≤80 mm Hg) was treated by decreasing the Ce remifentanil (with a 1.5 ng/mL lower limit), additional fluid administration, and by intravenous phenylephrine or ephedrine, depending on the prevailing heart rate.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 February 2014
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	Belgium: 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: -	

Pre-assignment	
Screening details: -	

Pre-assignment period milestones	
Number of subjects started	34
Number of subjects completed	25

Pre-assignment subject non-completion reasons	
Reason: Number of subjects	no data captured: 9

Period 1	
Period 1 title	study conduct (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms	
Are arms mutually exclusive?	Yes
Arm title	Normoventilation group
Arm description: -	
Arm type	SOC Group
No investigational medicinal product assigned in this arm	
Arm title	Isocapnic hyperventilation group
Arm description: -	
Arm type	test group
Investigational medicinal product name	Respiratory rate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Unknown use

Dosage and administration details:

respiratory rate was doubled for this group after anesthesia was stopped.

Number of subjects in period 1[1]	Normoventilation group	Isocapnic hyperventilation group
Started	13	12
Completed	13	12

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 34 patients were enrolled (ICF signed) in the study. However 9 patients were lost due to failed data retrieval during surgery/anesthesia.

Baseline characteristics

Reporting groups	
Reporting group title	Normoventilation group
Reporting group description: -	
Reporting group title	Isocapnic hyperventilation group
Reporting group description: -	

Reporting group values	Normoventilation group	Isocapnic hyperventilation group	Total
Number of subjects	13	12	25
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	56	47	
standard deviation	± 18	± 21	-
Gender categorical Units: Subjects			
Female	6	6	12
Male	7	6	13
Height Units: centimetre			
arithmetic mean	166	170	
standard deviation	± 10	± 8	-
weight Units: kilogram(s)			
arithmetic mean	73	74	
standard deviation	± 13	± 14	-
Lean body mass Units: kilogram(s)			
arithmetic mean	51	52	
standard deviation	± 8	± 7	-
BMI Units: kilogram(s)/square metre			
arithmetic mean	26	26	
standard deviation	± 4	± 5	-
maintenance partial pressure sevoflurane			

Units: percent			
arithmetic mean	1.6	1.7	
standard deviation	± 0.02	± 0.05	-
Maintenance Fa CO2			
Units: mm Hg			
arithmetic mean	35	38	
standard deviation	± 3	± 2	-
Emergence Fa CO2			
Units: mm Hg			
arithmetic mean	37	39	
standard deviation	± 2	± 1	-
duration anesthetic agent administration			
Units: minute			
arithmetic mean	128	150	
standard deviation	± 84	± 63	-
duration anesthesia			
Units: minute			
arithmetic mean	133	157	
standard deviation	± 88	± 60	-
duration remifentanil infusion			
Units: minute			
arithmetic mean	125	153	
standard deviation	± 85	± 64	-
minute ventilation during maintenance			
Units: litre/minute			
arithmetic mean	4.2	5.3	
standard deviation	± 0.5	± 1.4	-
minute ventilation during emergence			
Units: litre/minute			
arithmetic mean	4.2	10.7	
standard deviation	± 0.6	± 2.7	-
tidal volume			
Units: millilitre(s)			
arithmetic mean	429	478	
standard deviation	± 43	± 73	-
respiratory rate maintenance			
Units: 1/minute			
arithmetic mean	10	10	
standard deviation	± 1	± 2	-
respiratory rate emergence			
Units: 1/minute			
arithmetic mean	10	20	
standard deviation	± 1	± 4	-

End points

End points reporting groups	
Reporting group title	Normoventilation group
Reporting group description: -	
Reporting group title	Isocapnic hyperventilation group
Reporting group description: -	

Primary: time to proper response to verbal command	
End point title	time to proper response to verbal command
End point description:	
End point type	Primary
End point timeframe:	
Time from the beginning of emergence to proper response to verbal command.	

End point values	Normoventilation group	Isocapnic hyperventilation group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: minute				
arithmetic mean (standard deviation)	9.9 (± 2.9)	7.6 (± 2.2)		

Statistical analyses

Statistical analysis title	ANOVA + t-test
Comparison groups	Normoventilation group v Isocapnic hyperventilation group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANOVA

Primary: time to ETT removal	
End point title	time to ETT removal
End point description:	
End point type	Primary
End point timeframe:	
Time from the beginning of emergence to ETT removal	

End point values	Normoventilation group	Isocapnic hyperventilation group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: minute				
arithmetic mean (standard deviation)	11.0 (± 2.4)	7.6 (± 2.6)		

Statistical analyses

Statistical analysis title	ANOVA + t-test
Comparison groups	Normoventilation group v Isocapnic hyperventilation group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANOVA

Primary: Time to stating name

End point title	Time to stating name

End point description:

End point type	Primary

End point timeframe:

Time from the beginning of emergence to state name

End point values	Normoventilation group	Isocapnic hyperventilation group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: minute				
arithmetic mean (standard deviation)	12.5 (± 2.6)	8.9 (± 2.8)		

Statistical analyses

Statistical analysis title	ANOVA + t-test
Comparison groups	Normoventilation group v Isocapnic hyperventilation group

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANOVA

Primary: Fa sevoflurane at T(eye)

End point title	Fa sevoflurane at T(eye)

End point description:

End point type	Primary

End point timeframe:

partial pressure of sevoflurane at time to proper respond to verbal command.

End point values	Normoventilation group	Isocapnic hyperventilation group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: percent				
arithmetic mean (standard deviation)	0.25 (± 0.16)	0.12 (± 0.12)		

Statistical analyses

Statistical analysis title	ANOVA + t-test
Comparison groups	Normoventilation group v Isocapnic hyperventilation group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANOVA

Primary: Fa sevo at T(ETT)

End point title	Fa sevo at T(ETT)

End point description:

End point type	Primary

End point timeframe:

partial pressure of sevoflurane at time to ETT removal.

End point values	Normoventilation group	Isocapnic hyperventilation group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: percent				
arithmetic mean (standard deviation)	0.23 (± 0.15)	0.12 (± 0.12)		

Statistical analyses

Statistical analysis title	ANOVA + t-test
Comparison groups	Normoventilation group v Isocapnic hyperventilation group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANOVA

Primary: Fa sevo T(name)

End point title	Fa sevo T(name)

End point description:

End point type	Primary

End point timeframe:

partial pressure of sevoflurane at time to stating name

End point values	Normoventilation group	Isocapnic hyperventilation group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: percent				
arithmetic mean (standard deviation)	0.19 (± 0.10)	0.11 (± 0.11)		

Statistical analyses

Statistical analysis title	ANOVA + t-test
Comparison groups	Normoventilation group v Isocapnic hyperventilation group

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANOVA

Primary: Fa CO2 at T(eye)

End point title	Fa CO2 at T(eye)

End point description:

End point type	Primary

End point timeframe:

partial pressure of CO2 at time to proper respond to verbal command.

End point values	Normoventilation group	Isocapnic hyperventilation group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: mm Hg				
arithmetic mean (standard deviation)	38 (± 2)	39 (± 2)		

Statistical analyses

Statistical analysis title	ANOVA + t-test
Comparison groups	Normoventilation group v Isocapnic hyperventilation group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANOVA

Primary: Fa CO2 at T(ETT)

End point title	Fa CO2 at T(ETT)

End point description:

End point type	Primary

End point timeframe:

partial pressure of CO2 at time to ETT removal

End point values	Normoventilation group	Isocapnic hyperventilation group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: mm Hg				
arithmetic mean (standard deviation)	39 (± 4)	39 (± 2)		

Statistical analyses

Statistical analysis title	ANOVA + t-test
Comparison groups	Normoventilation group v Isocapnic hyperventilation group
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANOVA

Primary: Fa CO2 at T(name)

End point title	Fa CO2 at T(name)

End point description:

End point type	Primary

End point timeframe:

partial pressure of CO2 at time to state name

End point values	Normoventilation group	Isocapnic hyperventilation group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: mm Hg				
arithmetic mean (standard deviation)	38 (± 3)	39 (± 3)		

Statistical analyses

Statistical analysis title	ANOVA + t-test
Comparison groups	Normoventilation group v Isocapnic hyperventilation group

Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	ANOVA

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

adverse events were to be reported as from signing the ICF till the time after surgery the patient could state their name. At that time point, the end of study was reached for every patient.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22

Reporting groups

Reporting group title	study conduct

Reporting group description: -

Serious adverse events	study conduct		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (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	study conduct		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 33 (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: No adverse events were reported because the study ended for the patient after they could state their name after surgery. On average this was 11-12 minutes after emergence.

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