



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 remifentanyl was increased. Hypotension (systolic blood pressure \leq 80 mm Hg) was treated by decreasing the Ce remifentanyl (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 standard deviation | 1.6 ± 0.02 | 1.7 ± 0.05 | - |
| Maintenance Fa CO2 Units: mm Hg arithmetic mean standard deviation | 35 ± 3 | 38 ± 2 | - |
| Emergence Fa CO2 Units: mm Hg arithmetic mean standard deviation | 37 ± 2 | 39 ± 1 | - |
| duration anesthetic agent administration Units: minute arithmetic mean standard deviation | 128 ± 84 | 150 ± 63 | - |
| duration anesthesia Units: minute arithmetic mean standard deviation | 133 ± 88 | 157 ± 60 | - |
| duration remifentanil infusion Units: minute arithmetic mean standard deviation | 125 ± 85 | 153 ± 64 | - |
| minute ventilation during maintenance Units: litre/minute arithmetic mean standard deviation | 4.2 ± 0.5 | 5.3 ± 1.4 | - |
| minute ventilation during emergence Units: litre/minute arithmetic mean standard deviation | 4.2 ± 0.6 | 10.7 ± 2.7 | - |
| tidal volume Units: millilitre(s) arithmetic mean standard deviation | 429 ± 43 | 478 ± 73 | - |
| respiratory rate maintenance Units: 1/minute arithmetic mean standard deviation | 10 ± 1 | 10 ± 2 | - |
| respiratory rate emergence Units: 1/minute arithmetic mean standard deviation | 10 ± 1 | 20 ± 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 (\pm 2.9) | 7.6 (\pm 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 (\pm 0.15) | 0.12 (\pm 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 (\pm 0.10) | 0.11 (\pm 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