



Clinical trial results:

Comparison of the efficacy of ephedrine versus norepinephrine in the treatment of hypotension occurring after induction of general anesthesia in patients with chronic renal failure: randomized double-blind pilot study

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2022-002892-12 |
| Trial protocol | BE |
| Global end of trial date | 27 July 2023 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 21 July 2024 |
| First version publication date | 21 July 2024 |

Trial information

Trial identification

| | |
|-----------------------|---------------|
| Sponsor protocol code | CHUB-VASO-IRC |
|-----------------------|---------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | CHU Brugmann |
| Sponsor organisation address | 4 Place Arthur Van Gehuchten , Brussels, Belgium, 1020 |
| Public contact | Anesthesiology Department, CHU Brugmann, 32 24775676, zakaria.cheffi@chu-brugmann.be |
| Scientific contact | Anesthesiology Department, CHU Brugmann, 32 24775676, zakaria.cheffi@chu-brugmann.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 | 27 July 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 27 July 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 July 2023 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The main aim of this study is to compare the efficacy of ephedrine versus norepinephrine in the treatment of hypotension occurring after induction of general anesthesia in patients with chronic renal failure during elective surgery.

Protection of trial subjects:

The risk to which the patient is exposed is the risk linked to general anesthesia. This risk is in practice controlled by the means implemented daily for patients undergoing general anesthesia within the hospital.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 13 September 2022 |
| 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: 24 |
| Worldwide total number of subjects | 24 |
| EEA total number of subjects | 24 |

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) | 11 |
| From 65 to 84 years | 13 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This is a monocentric study held within the CHU Brugmann Hospital. Recruitment started on 13 september 2022. The study did not reach its recruitment goal (early termination on 27 July 2023).

Pre-assignment

Screening details:

The study was offered to all patients of the CHU Brugmann Hospital with chronic renal failure either during the anesthesia consultation or during the pre-anesthetic visit in the room.

Period 1

| | |
|------------------------------|-------------------------------|
| Period 1 title | Entire trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|--|---------------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Noradrenalin |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Noradrenaline tartate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous bolus use |

Dosage and administration details:

The patient receives a bolus of 2ml of noradrenalin 3µg/ml every 3 minutes if he/she is hypotensive, until the blood pressure is above the set thresholds (mean arterial pressure (MAP) >65 mmHg).

| | |
|--|--|
| Arm title | Ephedrin |
| Arm description: - | |
| Arm type | Active comparator |
| Investigational medicinal product name | Ephedrine hydrochloride |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Intravenous bolus use |

Dosage and administration details:

The patient receives a bolus of 2 ml of ephedrine 3 mg/ml every 3 minutes if he/she is hypotensive, until the blood pressure is above the set thresholds (mean arterial pressure (MAP) >65 mmHg).

| Number of subjects in period 1 | Noradrenalin | Ephedrin |
|---------------------------------------|--------------|----------|
| Started | 12 | 12 |
| Completed | 8 | 9 |
| Not completed | 4 | 3 |
| Adverse event, serious fatal | 1 | - |
| Consent withdrawn by subject | 2 | - |
| Not randomized | - | 1 |
| Lost to follow-up | - | 1 |
| Protocol deviation | 1 | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Noradrenalin |
|-----------------------|--------------|

| |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| | |
|-----------------------|----------|
| Reporting group title | Ephedrin |
|-----------------------|----------|

| |
|--------------------------------|
| Reporting group description: - |
|--------------------------------|

| Reporting group values | Noradrenalin | Ephedrin | Total |
|--|--------------|----------|-------|
| Number of subjects | 12 | 12 | 24 |
| 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) | 5 | 6 | 11 |
| From 65-84 years | 7 | 6 | 13 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 4 | 2 | 6 |
| Male | 8 | 10 | 18 |

End points

End points reporting groups

| | |
|--------------------------------|--------------|
| Reporting group title | Noradrenalin |
| Reporting group description: - | |
| Reporting group title | Ephedrin |
| Reporting group description: - | |

Primary: Amount of boluses to maintain a mean arterial pressure >65mmHg

| | |
|-----------------|---|
| End point title | Amount of boluses to maintain a mean arterial pressure >65mmHg ^[1] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the start of the surgical procedure until the first parameter measurement in the post-intervention monitoring room.

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: The trial ended prematurely without reaching its recruitment goal. It makes no sense to perform statistics on such a small patient sample.

| End point values | Noradrenalin | Ephedrin | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 9 | | |
| Units: N/A | | | | |
| median (inter-quartile range (Q1-Q3)) | 0.5 (0 to 4.25) | 0 (0 to 3) | | |

Statistical analyses

No statistical analyses for this end point

Primary: Mean arterial pressure (MAP) during intervention

| | |
|-----------------|---|
| End point title | Mean arterial pressure (MAP) during intervention ^[2] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the start of the surgical procedure until the first parameter measurement in the post-intervention monitoring room.

Notes:

[2] - 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: The trial ended prematurely without reaching its recruitment goal. It makes no sense to perform statistics on such a small patient sample.

| | | | | |
|---------------------------------------|---------------------|-----------------|--|--|
| End point values | Noradrenalin | Ephedrin | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 8 | 9 | | |
| Units: mmHg | | | | |
| median (inter-quartile range (Q1-Q3)) | 88 (79.75 to 99.25) | 87 (73 to 92) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Entire trial

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Noradrenalin |
|-----------------------|--------------|

Reporting group description: -

| | |
|-----------------------|----------|
| Reporting group title | Ephedrin |
|-----------------------|----------|

Reporting group description: -

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: The study team confirmed no non-serious AE occurred.

| Serious adverse events | Noradrenalin | Ephedrin | |
|---|----------------|---------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 9 (0.00%) | |
| number of deaths (all causes) | 1 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Infections and infestations | | | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 9 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Noradrenalin | Ephedrin | |
|---|---------------|---------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 9 (0.00%) | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 04 November 2022 | - Modifications in inclusion/exclusion criteria (age extended to 75 years, BMI limit 35) - Modifications in the 'standard of care' procedure for anesthesia (details on the hypnotic and curarizing agents) - Change in co-investigators |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|--------------|------------------------|--------------|
| 27 July 2023 | Premature end of trial | - |

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Methodological issue: in order to have significant results, 360 patients (180 per group) would be needed (instead of the 60 foreseen by the protocol). This is not feasible in our hospital setting.

Notes: