



Clinical trial results:

THE PROGRAMMED INTERMITTENT EPIDURAL BOLUS ADRENALINE STUDY

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2015-004397-14 |
| Trial protocol | NO |
| Global end of trial date | 07 September 2020 |

Results information

| | |
|-----------------------------------|--|
| Result version number | v1 (current) |
| This version publication date | 25 April 2022 |
| First version publication date | 25 April 2022 |
| Summary attachment (see zip file) | programmed intermittend epidural bolus (Haidl-2020-Programmed intermittent boluses vs.pdf) |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 2015-2 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03043781 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Akershus University Hospital |
| Sponsor organisation address | Sykehusveien 25, Loerenskog, Norway, 1478 Loerenskog |
| Public contact | Professor, Akershus university hospital, +47 67964679, vegard.dahl@ahus.no |
| Scientific contact | Professor, Akershus university hospital, +47 67964679, vegard.dahl@ahus.no |

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 | 10 December 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 10 December 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 September 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to investigate whether use of intermittent epidural bolus (IEB) + patient controlled epidural bolus (PCEA) results in lower epidural mixture use per time compared to continuous epidural infusion + PCEA in the setting of an adrenaline containing mixture.

Protection of trial subjects:

We recruited women in labor scheduled for epidural analgesia

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 01 March 2017 |
| 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 | Norway: 151 |
| Worldwide total number of subjects | 151 |
| EEA total number of subjects | 151 |

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) | 151 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Women in labor in need of epidural analgesia

Pre-assignment

Screening details:

age > 18, read and signed written informed consent, one fetus at term

Period 1

| | |
|------------------------------|---|
| Period 1 title | baseline (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind ^[1] |
| Roles blinded | Subject, Monitor, Carer, Assessor, Data analyst |

Blinding implementation details:

Participants received either continuous infusion or programmed intermittent boluses of epidural analgesia

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | continuous |

Arm description:

received continuous infusion of analgesia or bolus once hourly

| | |
|--|---|
| Arm type | Active comparator |
| Investigational medicinal product name | bupivacaine/adrenaline/fentanyl |
| Investigational medicinal product code | n.a |
| Other name | standard EDA mixture |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Epidural use |

Dosage and administration details:

5+5 ml bolus, then 5ml/hr

| | |
|------------------|--------------|
| Arm title | intermittent |
|------------------|--------------|

Arm description:

bolus of 5 ml solution once hourly

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | bupivacaine/adrenaline/fentanyl |
| Investigational medicinal product code | n.a |
| Other name | standard EDA mixture |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Epidural use |

Dosage and administration details:

5+5 ml bolus, then 5ml once hourly

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: Investigator had to be aware of type of intervention, however the parturient, midwife and the person assessing the outcome was blinded

| Number of subjects in period 1 | continuous | intermittent |
|---------------------------------------|------------|--------------|
| Started | 76 | 75 |
| Completed | 75 | 75 |
| Not completed | 1 | 0 |
| Lost to follow-up | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | baseline |
|-----------------------|----------|

Reporting group description: -

| Reporting group values | baseline | Total | |
|--|----------|-------|--|
| Number of subjects | 151 | 151 | |
| Age categorical | | | |
| Aged > 18 years and in labor | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 151 | 151 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| adult women | 0 | 0 | |
| Gender categorical | | | |
| women in labor > 18 year of age | | | |
| Units: Subjects | | | |
| Female | 151 | 151 | |
| Male | 0 | 0 | |

End points

End points reporting groups

| | |
|--|--------------|
| Reporting group title | continuous |
| Reporting group description: received continuous infusion of analgesia or bolus once hourly | |
| Reporting group title | intermittent |
| Reporting group description: bolus of 5 ml solution once hourly | |

Primary: total consumption

| | |
|--|-------------------|
| End point title | total consumption |
| End point description: | |
| End point type | Primary |
| End point timeframe: total consumption of solution per hour during the analgetic time frame | |

| End point values | continuous | intermittent | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 75 | 75 | | |
| Units: ml | | | | |
| number (not applicable) | 9.0 | 8.1 | | |

Statistical analyses

| | |
|--|--------------------------------|
| Statistical analysis title | student T-test |
| Statistical analysis description: mean difference in total consumption between groups | |
| Comparison groups | continuous v intermittent |
| Number of subjects included in analysis | 150 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.08 ^[1] |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.1 |
| upper limit | 1.8 |

Notes:

[1] - the actual measured P-value indicates no difference between groups

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

last included participant in the post-delivery ward

Adverse event reporting additional description:

hypotension, total spinal effect etc

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|-------------|
| Dictionary name | no specific |
|-----------------|-------------|

| | |
|--------------------|---|
| Dictionary version | 0 |
|--------------------|---|

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

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: In these participating parturients, there were no adverse events

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

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

| |
|------|
| none |
|------|

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/32812652>