



Clinical trial results: Effect of Perineural Dexamethasone on the Duration of Single Injection Saphenous Nerve Block for Analgesia After Major Ankle Surgery

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2014-004207-78 |
| Trial protocol | DK |
| Global end of trial date | 16 December 2015 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 |
| This version publication date | 16 July 2017 |
| First version publication date | 16 July 2017 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | ProtokolSB1 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02346110 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Aarhus University Hospital |
| Sponsor organisation address | Nørrebrogade 44, Aarhus C, Denmark, 8000 |
| Public contact | Department of Anesthesia and Intensive Care, Aarhus University Hospital, +45 51542997, tfb@dadlnet.dk |
| Scientific contact | Department of Anesthesia and Intensive Care , Aarhus University Hospital, +45 51542997, tfb@dadlnet.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 | 29 March 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 16 December 2015 |
| Global end of trial reached? | Yes |
| Global end of trial date | 16 December 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective is to investigate whether addition of the adjuvant dexamethasone to bupivacaine-adrenaline can prolong the analgesic effect of the saphenous block compared to plain bupivacaine-adrenaline in patients after major ankle and hind foot surgery.

Protection of trial subjects:

Patients received a PCA pump with morphine to provide instant pain relief at bolus request. Patients were visited at regular intervals during the observation period with extra focus on their pain management.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 27 April 2015 |
| 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 | Denmark: 39 |
| Worldwide total number of subjects | 39 |
| EEA total number of subjects | 39 |

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) | 25 |
| From 65 to 84 years | 14 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

Patients were enrolled from 27/Apr/2015 - 14/Dec/2015.

Pre-assignment

Screening details:

62 patients were screened.

Reasons for primary exclusion:

Operation type not included (n = 5)

Logistical reasons (n = 6)

Operation cancelled/rescheduled (n = 4)

Daily intake of strong opioids (n = 2)

Allergy to opioids (n = 1)

Communication problems (n = 1)

BMI > 35 (n = 2)

Neuropathy (n = 1)

Period 1

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

Blinding implementation details:

The hospital pharmacy performed the randomization in blocks of 10 and a 1:1 ratio, and prepared 40 consecutively numbered black nontransparent plastic bags containing 1 mL of saline or 1 mL of dexamethasone according to the randomization list. Isotonic saline and dexamethasone are both transparent liquids, all containers and bags were identical.

One patient was excluded due to incorrect inclusion (communication problems) this patient is not included in any data analysis.

Arms

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

Arm description:

Saphenous block with 10 mL Marcain-adrenalin + 1 ml (4 mg) Dexamethasone.

| | |
|--|--------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Dexamethason |
| Investigational medicinal product code | |
| Other name | Dexagalen |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Perineural use |

Dosage and administration details:

4 mg

| | |
|--|------------------------|
| Investigational medicinal product name | Marcain-adrenalin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Perineural use |

Dosage and administration details:

10 mL Marcain-adrenalin containing:

BUPIVACAINE HYDROCHLORIDE 5 mg/ml milligram

EPINEPHRINE 5 µg/ml

| | |
|------------------|---------------|
| Arm title | Control group |
|------------------|---------------|

Arm description:

Saphenous block with 10 mL Marcain-adrenalin + 1 mL saline

| | |
|--|------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Marcain-adrenalin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Perineural use |

Dosage and administration details:

10 mL Marcain-adrenalin containing:

BUPIVACAINE HYDROCHLORIDE 5 mg/ml

EPINEPHRINE 5 µg/ml

| Number of subjects in period 1 | Intervention | Control group |
|---------------------------------------|--------------|---------------|
| Started | 19 | 20 |
| Completed | 19 | 20 |

Baseline characteristics

Reporting groups

| | |
|---|---------------|
| Reporting group title | Intervention |
| Reporting group description: | |
| Saphenous block with 10 mL Marcain-adrenalin + 1 ml (4 mg) Dexamethasone. | |
| Reporting group title | Control group |
| Reporting group description: | |
| Saphenous block with 10 mL Marcain-adrenalin + 1 mL saline | |

| Reporting group values | Intervention | Control group | Total |
|--|--------------|---------------|-------|
| Number of subjects | 19 | 20 | 39 |
| 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 | 57.2 | 59.8 | |
| standard deviation | ± 12.6 | ± 13.5 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 9 | 9 | 18 |
| Male | 10 | 11 | 21 |
| ASA physical status | | | |
| ASA = American Society of Anesthesiologists | | | |
| Units: Subjects | | | |
| ASA I | 9 | 7 | 16 |
| ASA II | 10 | 13 | 23 |
| Surgical procedures | | | |
| Units: Subjects | | | |
| Total ankle replacement | 10 | 11 | 21 |
| Ankle arthrodesis | 2 | 3 | 5 |
| Subtalar arthrodesis | 5 | 2 | 7 |
| Triple arthrodesis | 2 | 4 | 6 |
| BMI | | | |
| Body mass index | | | |
| Units: kg/m ² | | | |
| arithmetic mean | 28.6 | 26.1 | |
| standard deviation | ± 4.07 | ± 4.13 | - |

| | | | |
|--------------------------------|--------|----------|---|
| Height | | | |
| Units: meter | | | |
| arithmetic mean | 1.76 | 1.73 | |
| standard deviation | ± 0.11 | ± 0.1 | - |
| Weight | | | |
| Units: kilogram(s) | | | |
| arithmetic mean | 88.2 | 78.1 | |
| standard deviation | ± 13.3 | ± 14 | - |
| Preoperative pain at rest, NRS | | | |
| NRS = numerical rating scale | | | |
| Units: Not applicable | | | |
| median | 0 | 0 | |
| inter-quartile range (Q1-Q3) | 0 to 0 | 0 to 0.5 | - |

End points

End points reporting groups

| | |
|---|---------------|
| Reporting group title | Intervention |
| Reporting group description: Saphenous block with 10 mL Marcain-adrenalin + 1 ml (4 mg) Dexamethasone. | |
| Reporting group title | Control group |
| Reporting group description: Saphenous block with 10 mL Marcain-adrenalin + 1 mL saline | |

Primary: Time until first opioid request

| | |
|--|---------------------------------|
| End point title | Time until first opioid request |
| End point description: | |
| End point type | Primary |
| End point timeframe: 0-48 hrs Time zero = end of saphenous block performance | |

| End point values | Intervention | Control group | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: hour | | | | |
| arithmetic mean (standard deviation) | 29.4 (± 8.4) | 23.2 (± 10.3) | | |

Statistical analyses

| | |
|---|---------------------------------|
| Statistical analysis title | Time until first opioid request |
| Comparison groups | Intervention v Control group |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.048 |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 6.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.1 |
| upper limit | 12.3 |

Secondary: Time until first pain

| | |
|-----------------|-----------------------|
| End point title | Time until first pain |
|-----------------|-----------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

0-48 hrs

Time zero = End of saphenous block performance

| End point values | Intervention | Control group | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: hour | | | | |
| arithmetic mean (standard deviation) | 28.3 (± 7.9) | 21.5 (± 10.2) | | |

Statistical analyses

| | |
|----------------------------|-----------------------|
| Statistical analysis title | Time until first pain |
|----------------------------|-----------------------|

Statistical analysis description:

T-test

Normally distributed data

| | |
|-------------------|------------------------------|
| Comparison groups | Intervention v Control group |
|-------------------|------------------------------|

| | |
|---|----|
| Number of subjects included in analysis | 39 |
|---|----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|-------------|
| Analysis type | superiority |
|---------------|-------------|

| | |
|---------|---------|
| P-value | = 0.026 |
|---------|---------|

| | |
|--------|-----------------|
| Method | t-test, 2-sided |
|--------|-----------------|

| | |
|--------------------|--------------------------------|
| Parameter estimate | Mean difference (final values) |
|--------------------|--------------------------------|

| | |
|----------------|-----|
| Point estimate | 6.8 |
|----------------|-----|

Confidence interval

| | |
|-------|------|
| level | 95 % |
|-------|------|

| | |
|-------|---------|
| sides | 2-sided |
|-------|---------|

| | |
|-------------|-----|
| lower limit | 0.9 |
|-------------|-----|

| | |
|-------------|------|
| upper limit | 12.7 |
|-------------|------|

Secondary: Opioid consumption 0-24 hrs

| | |
|-----------------|-----------------------------|
| End point title | Opioid consumption 0-24 hrs |
|-----------------|-----------------------------|

End point description:

The opioid consumption was not normally distributed

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

0-24 hours

| End point values | Intervention | Control group | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: milligram(s) | | | | |
| median (inter-quartile range (Q1-Q3)) | 0 (0 to 0) | 1.5 (0 to 14.2) | | |

Statistical analyses

| Statistical analysis title | Opioid consumption 0-24 hrs |
|---|------------------------------|
| Comparison groups | Intervention v Control group |
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[1] |
| P-value | = 0.046 |
| Method | Wilcoxon (Mann-Whitney) |

Notes:

[1] - Opioid consumption was not normally distributed.

Secondary: Opioid consumption 24-48 hrs

| | |
|------------------------|---|
| End point title | Opioid consumption 24-48 hrs |
| End point description: | The opioid consumption was not normally distributed |
| End point type | Secondary |
| End point timeframe: | 24-48 hrs |

| End point values | Intervention | Control group | | |
|---------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 19 | 20 | | |
| Units: hour | | | | |
| median (inter-quartile range (Q1-Q3)) | 15 (10 to 21) | 15 (5 to 32.5) | | |

Statistical analyses

| Statistical analysis title | Opioid consumption 24-48 hrs |
|----------------------------|------------------------------|
| Comparison groups | Intervention v Control group |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 39 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.989 |
| Method | Wilcoxon (Mann-Whitney) |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from inclusion of the first patient 27/Apr/2015 and until the last patient completed the study observation period 16/Dec/2015.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 10.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------|
| Reporting group title | Intervention |
|-----------------------|--------------|

Reporting group description:

Saphenous block with 10 mL Marcain-adrenalin + 1 ml (4 mg) Dexamethasone.

| | |
|-----------------------|---------------|
| Reporting group title | Control group |
|-----------------------|---------------|

Reporting group description:

Saphenous block with 10 mL Marcain-adrenalin + 1 mL saline

| Serious adverse events | Intervention | Control group | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 0 / 20 (0.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |

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

| Non-serious adverse events | Intervention | Control group | |
|---|-----------------|-----------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 5 / 20 (25.00%) | 8 / 20 (40.00%) | |
| General disorders and administration site conditions | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 5 | 8 | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 5 | 8 | |
| Nausea | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 5 / 20 (25.00%) | 5 / 20 (25.00%) | |
| occurrences (all) | 5 | 8 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 20 (0.00%) | 1 / 20 (5.00%) | |
| occurrences (all) | 5 | 8 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 25 April 2015 | <p>Changes:</p> <p>Sensory testing at the 42 hour test time is deleted</p> <p>Pain score at 42 the hour test time is deleted</p> <p>Sensory testing and pain score at 42 hours are deleted because this time point consistently is in the middle of the night, and it is difficult to wake up the patients and get valid test results. Furthermore, as most of the patients will be sleeping we find it more ethical to let the patients sleep through the night.</p> <p>Ankle arthrodesis performed as an arthroscopy is removed as an exclusion criteria.</p> |

Notes:

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.

Five patients did not require opioids at all. These patients contribute to the primary outcome with the time until a shift in sensory thermal analgesia in the infrapatellar area. This was chosen as the best proxy marker for the end of block duration.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/28033159>