



Clinical trial results: Intrauterine resuscitation during term labor by maternal hyperoxygenation.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2015-001654-15 |
| Trial protocol | NL |
| Global end of trial date | 12 April 2018 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 09 March 2022 |
| First version publication date | 09 March 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | NL53018.015.15 |
|-----------------------|----------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Máxima Medisch Centrum |
| Sponsor organisation address | De Run 4600, Veldhoven, Netherlands, 5504 DB |
| Public contact | Principal investigator - Professor Guid Oei, Máxima Medisch Centrum, 0031 624225377, guidoei@outlook.com |
| Scientific contact | Principal investigator - Professor Guid Oei, Máxima Medisch Centrum, 0031 624225377, laurenbullens@gmail.com |

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 | 07 June 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 12 April 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 12 April 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Primary Objective: the primary objective is to investigate the effect of maternal hyperoxygenation with 100% oxygen on fetal heart rate pattern. We will describe the difference in FHR deceleration depth, duration and frequency, baseline and variability 10 minutes before and after maternal oxygen administration.

Protection of trial subjects:

The non-rebreathing mask used to deliver oxygen fits tight to the nose and mouth, which may cause some discomfort. Patients are allowed to withdraw from the study anytime.

Background therapy:

Co-interventions may be initiated after 10 minutes of oxygen administration without a satisfactory effect on FHR. Co-interventions are 'conventional care', including lateral positioning of the parturient, stop oxytocin infusion, intermittent pushing, intravenous administration of a tocolytic drug or termination of labor by vaginal assisted delivery or caesarean section. In the control group 10 minutes after inclusion in the study 'conventional care' can be applied.

Evidence for comparator:

The control group will receive conventional care (no additional oxygen). The only difference in treatment between the intervention and control group is the use of additional oxygen. Therefore, it is likely that any difference in outcome will be caused by the use of additional oxygen.

| | |
|---|-------------------|
| Actual start date of recruitment | 01 September 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 | Netherlands: 117 |
| Worldwide total number of subjects | 117 |
| EEA total number of subjects | 117 |

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) | 117 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patient recruitment started on March 1st 2016, and was fulfilled on April 30th 2018. Recruitment took place in The Netherlands.

Pre-assignment

Screening details:

All patients eligible to be included in this study were asked to participate when they visited the outpatient's clinic, or when they were admitted to the delivery ward. The total number of women eligible to be included in this study is not clear.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

The patient and attending physician/midwife was not blinded to the allocation. Also the attending pediatrician providing Apgar score was not blinded. The investigator analyzing FHR patterns and fECG was blinded. Laboratory results are not influenced by the knowledge of the allocation and therefore laboratory staff did not need to be blinded.

Arms

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

Arm description:

Maternal hyperoxygenation with 100% oxygen at 10 L/min delivered by a non-rebreathing mask (fraction of inspired oxygen 0.80)

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Oxygen |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Inhalation vapour |
| Routes of administration | Inhalation use |

Dosage and administration details:

100% oxygen via non-rebreathing mask from the onset of fetal heart rate abnormalities, until delivery.

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

Arm description:

The control group will receive conventional care (no additional oxygen).

| | |
|---|-----------------|
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 1 | Intervention group | Control group |
|--------------------------------|--------------------|---------------|
| Started | 57 | 60 |
| Completed | 57 | 60 |

Baseline characteristics

Reporting groups

| | |
|---|--------------------|
| Reporting group title | Intervention group |
| Reporting group description: Maternal hyperoxygenation with 100% oxygen at 10 L/min delivered by a non-rebreathing mask (fraction of inspired oxygen 0.80) | |
| Reporting group title | Control group |
| Reporting group description: The control group will receive conventional care (no additional oxygen). | |

| Reporting group values | Intervention group | Control group | Total |
|--|--------------------|---------------|-------|
| Number of subjects | 57 | 60 | 117 |
| 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) | 57 | 60 | 117 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous | | | |
| Maternal age | | | |
| Units: years | | | |
| median | 31.8 | 30.7 | |
| standard deviation | ± 4.2 | ± 3.4 | - |
| Gender categorical | | | |
| Female | | | |
| Units: Subjects | | | |
| Female | 27 | 34 | 61 |
| Male | 30 | 26 | 56 |
| Parity | | | |
| Primiparous versus multiparous women | | | |
| Units: Subjects | | | |
| primiparous women | 35 | 33 | 68 |
| multiparous women | 22 | 27 | 49 |
| Fetal sex | | | |
| Units: Subjects | | | |
| Male | 30 | 26 | 56 |
| Female | 27 | 34 | 61 |
| Gestational age | | | |
| Gestational age | | | |
| Units: days | | | |
| median | 279 | 280 | |
| standard deviation | ± 9.0 | ± 8.8 | - |

| | | | |
|--------------------------------|---------|---------|---|
| Birthweight | | | |
| Units: gram(s) | | | |
| median | 3510 | 3541.4 | |
| standard deviation | ± 471.7 | ± 560.2 | - |
| Body mass index | | | |
| Maternal body mass index | | | |
| Units: kilogram(s)/cubic meter | | | |
| median | 25 | 24 | |
| standard deviation | ± 4.7 | ± 5.0 | - |

End points

End points reporting groups

| | |
|---|--------------------|
| Reporting group title | Intervention group |
| Reporting group description: Maternal hyperoxygenation with 100% oxygen at 10 L/min delivered by a non-rebreathing mask (fraction of inspired oxygen 0.80) | |
| Reporting group title | Control group |
| Reporting group description: The control group will receive conventional care (no additional oxygen). | |

Primary: Change in fetal heart rate pattern before and after start of the study protocol

| | |
|---|---|
| End point title | Change in fetal heart rate pattern before and after start of the study protocol |
| End point description: | |
| End point type | Primary |
| End point timeframe: 10 minutes before the start of the study protocol compared to 5-15 minutes after the start of the study protocol. | |

| End point values | Intervention group | Control group | | |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 36 | 35 | | |
| Units: Improvement of FHR | | | | |
| Deterioration FHR | 3 | 12 | | |
| Equal FHR | 28 | 22 | | |
| Improvement FHR | 5 | 1 | | |

Statistical analyses

| | |
|---|------------------------------------|
| Statistical analysis title | Changes in FHR Odds ratio |
| Comparison groups | Control group v Intervention group |
| Number of subjects included in analysis | 71 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 5.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.7 |
| upper limit | 19.1 |

Secondary: 1-minute Apgar score

| | |
|-----------------|----------------------|
| End point title | 1-minute Apgar score |
|-----------------|----------------------|

End point description:

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

End point timeframe:

1 minute after birth

| End point values | Intervention group | Control group | | |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 | 60 | | |
| Units: number | | | | |
| 1 minute AS <5 | 4 | 4 | | |
| 1 minute AS > 5 | 53 | 56 | | |

Statistical analyses

| | |
|----------------------------|--------------------------------------|
| Statistical analysis title | 1-minute Apgar score chi-square test |
|----------------------------|--------------------------------------|

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

| | |
|---|-----|
| Number of subjects included in analysis | 117 |
|---|-----|

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

| | |
|---------------|-------------|
| Analysis type | equivalence |
|---------------|-------------|

| | |
|---------|-----|
| P-value | = 1 |
|---------|-----|

| | |
|--------|-------------|
| Method | Chi-squared |
|--------|-------------|

Secondary: 5-minute Apgar score

| | |
|-----------------|----------------------|
| End point title | 5-minute Apgar score |
|-----------------|----------------------|

End point description:

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

End point timeframe:

5 minutes after birth

| End point values | Intervention group | Control group | | |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 | 60 | | |
| Units: Number | | | | |
| 5-minute AS <7 | 1 | 3 | | |
| 5-minute AS >7 | 56 | 57 | | |

Statistical analyses

| | |
|---|-------------------------------------|
| Statistical analysis title | 5-minute Apgar score Fisher's exact |
| Comparison groups | Intervention group v Control group |
| Number of subjects included in analysis | 117 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.62 |
| Method | Fisher exact |

Secondary: Median arterial umbilical cord pH

| | |
|--|-----------------------------------|
| End point title | Median arterial umbilical cord pH |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Generally umbilical cord pH is estimated <15 minutes after birth | |

| End point values | Intervention group | Control group | | |
|---------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 53 | | |
| Units: pH | | | | |
| median (inter-quartile range (Q1-Q3)) | 7.22 (7.19 to 7.26) | 7.20 (7.16 to 7.27) | | |

Statistical analyses

| | |
|----------------------------|------------------------------------|
| Statistical analysis title | Medium arterial pH Mann-Whitney |
| Comparison groups | Intervention group v Control group |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 98 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.35 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Median venous umbilical cord pH

| | |
|---|---------------------------------|
| End point title | Median venous umbilical cord pH |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Generally umbilical cord pH is estimated < 15 minutes after birth | |

| End point values | Intervention group | Control group | | |
|---------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 | 60 | | |
| Units: pH | | | | |
| median (inter-quartile range (Q1-Q3)) | 7.30 (7.26 to 7.34) | 7.30 (7.26 to 7.35) | | |

Statistical analyses

| | |
|---|------------------------------------|
| Statistical analysis title | Median venous pH Mann-Whitney |
| Comparison groups | Intervention group v Control group |
| Number of subjects included in analysis | 117 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.94 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Arterial base excess

| | |
|---|----------------------|
| End point title | Arterial base excess |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Umbilical cord blood values are generally estimated < 15 minutes after birth. | |

| End point values | Intervention group | Control group | | |
|---------------------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 51 | | |
| Units: mmol/l | | | | |
| median (inter-quartile range (Q1-Q3)) | -6 (-8 to -3) | -6 (-8 to -4) | | |

Statistical analyses

| | |
|---|------------------------------------|
| Statistical analysis title | Arterial base excess Mann-Whitney |
| Comparison groups | Intervention group v Control group |
| Number of subjects included in analysis | 96 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.69 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Arterial pCO2 umbilical cord blood

| | |
|---|------------------------------------|
| End point title | Arterial pCO2 umbilical cord blood |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Umbilical cord blood values are generally estimated < 15 minutes after birth. | |

| End point values | Intervention group | Control group | | |
|---------------------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 52 | | |
| Units: mmHg | | | | |
| median (inter-quartile range (Q1-Q3)) | 56 (51.5 to 59.5) | 57 (52 to 62) | | |

Statistical analyses

| | |
|----------------------------|------------------------------------|
| Statistical analysis title | Arterial pCO2 Mann-Whitney |
| Comparison groups | Intervention group v Control group |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 97 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.54 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Arterial malondialdehyde

| | |
|---|--------------------------|
| End point title | Arterial malondialdehyde |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Umbilical cord blood values are generally estimated < 15 minutes after birth. | |

| End point values | Intervention group | Control group | | |
|---------------------------------------|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 41 | 48 | | |
| Units: umol/l | | | | |
| median (inter-quartile range (Q1-Q3)) | 4.45 (3.68 to 5.35) | 4.15 (3.40 to 4.75) | | |

Statistical analyses

| | |
|---|---------------------------------------|
| Statistical analysis title | Arterial malondialdehyde Mann-Whitney |
| Comparison groups | Intervention group v Control group |
| Number of subjects included in analysis | 89 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.15 |
| Method | Wilcoxon (Mann-Whitney) |

Secondary: Venous malondialdehyde

| | |
|---|------------------------|
| End point title | Venous malondialdehyde |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Umbilical cord blood values are generally estimated < 15 minutes after birth. | |

| End point values | Intervention group | Control group | | |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 45 | 54 | | |
| Units: umol/l | | | | |
| arithmetic mean (standard deviation) | 4.67 (\pm 1.27) | 4.38 (\pm 1.15) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Venous malondialdehyde independent T-test |
| Comparison groups | Intervention group v Control group |
| Number of subjects included in analysis | 99 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.21 |
| Method | t-test, 2-sided |

Secondary: NICU admission

| | |
|--|----------------|
| End point title | NICU admission |
| End point description: | |
| Neonatal Intensive Care Unit admission | |
| End point type | Secondary |
| End point timeframe: | |
| Directly after birth | |

| End point values | Intervention group | Control group | | |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 | 60 | | |
| Units: number | 1 | 2 | | |

Statistical analyses

| | |
|----------------------------|------------------------------------|
| Statistical analysis title | NICU admission s Fisher's exact |
| Comparison groups | Intervention group v Control group |

| | |
|---|---------------|
| Number of subjects included in analysis | 117 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 1 |
| Method | Fisher exact |

Secondary: Episiotomy for all indications

| | |
|------------------------|--------------------------------|
| End point title | Episiotomy for all indications |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Second stage of labor | |

| End point values | Intervention group | Control group | | |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 | 60 | | |
| Units: number | 30 | 33 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Episiotomy all indications Chi-squared |
| Comparison groups | Intervention group v Control group |
| Number of subjects included in analysis | 117 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.8 |
| Method | Chi-squared |

Secondary: Episiotomy for fetal indication

| | |
|------------------------|---------------------------------|
| End point title | Episiotomy for fetal indication |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Second stage of labor | |

| End point values | Intervention group | Control group | | |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 | 60 | | |
| Units: number | 17 | 27 | | |

Statistical analyses

| Statistical analysis title | Episiotomy for fetal indication Chi-squared |
|---|---|
| Comparison groups | Intervention group v Control group |
| Number of subjects included in analysis | 117 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.09 |
| Method | Chi-squared |

Secondary: Assisted delivery for all indications

| | |
|------------------------|---------------------------------------|
| End point title | Assisted delivery for all indications |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Second stage of labor | |

| End point values | Intervention group | Control group | | |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 | 60 | | |
| Units: number | 7 | 9 | | |

Statistical analyses

| Statistical analysis title | Assisted delivery all indications Chi-squared |
|---|---|
| Comparison groups | Intervention group v Control group |
| Number of subjects included in analysis | 117 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.67 |
| Method | Chi-squared |

Secondary: Assisted delivery for fetal indication

| | |
|-----------------|--|
| End point title | Assisted delivery for fetal indication |
|-----------------|--|

End point description:

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

End point timeframe:

Second stage of labor.

| End point values | Intervention group | Control group | | |
|-----------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 | 60 | | |
| Units: Number | 4 | 6 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Assisted delivery fetal indication Fisher's exact |
|----------------------------|---|

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

| | |
|---|-----|
| Number of subjects included in analysis | 117 |
|---|-----|

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

| | |
|---------------|-------------|
| Analysis type | equivalence |
|---------------|-------------|

| | |
|---------|--------|
| P-value | = 0.74 |
|---------|--------|

| | |
|--------|--------------|
| Method | Fisher exact |
|--------|--------------|

Secondary: Active second stage of labor

| | |
|-----------------|------------------------------|
| End point title | Active second stage of labor |
|-----------------|------------------------------|

End point description:

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

End point timeframe:

Second stage of labor.

| End point values | Intervention group | Control group | | |
|---------------------------------------|--------------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 57 | 60 | | |
| Units: minutes | | | | |
| median (inter-quartile range (Q1-Q3)) | 35 (20 to 64) | 25 (14 to 58) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Active second stage of labor Mann-Whitney |
| Comparison groups | Intervention group v Control group |
| Number of subjects included in analysis | 117 |
| Analysis specification | Pre-specified |
| Analysis type | equivalence |
| P-value | = 0.32 |
| Method | Wilcoxon (Mann-Whitney) |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Within 15 days after the sponsor has first knowledge of the serious adverse events. SAEs that result in death or are life threatening not later than 7 days after the responsible investigator has first knowledge of the adverse event.

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

Dictionary used

| | |
|--------------------|----------------|
| Dictionary name | ToetsingOnline |
| Dictionary version | NA |

Reporting groups

| | |
|--------------------------------|--------------------|
| Reporting group title | Control group |
| Reporting group description: - | |
| Reporting group title | Intervention group |
| Reporting group description: - | |

| Serious adverse events | Control group | Intervention group | |
|---|---|--------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 60 (3.33%) | 1 / 44 (2.27%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory disorder neonatal | Additional description: NICU-admissions | | |
| subjects affected / exposed | 2 / 60 (3.33%) | 1 / 44 (2.27%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Control group | Intervention group | |
|---|---|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 30 / 60 (50.00%) | 25 / 44 (56.82%) | |
| Surgical and medical procedures | | | |
| Caesarean section | Additional description: Prolonged hospital stay due to secondary cesarean section | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 1 / 44 (2.27%) | |
| occurrences (all) | 1 | 1 | |
| Cardiac disorders | | | |

| | | | |
|--|--|-----------------|--|
| Hypertension subjects affected / exposed occurrences (all) | Additional description: Hypertension or pre-eclampsia | | |
| | 2 / 60 (3.33%) | 0 / 44 (0.00%) | |
| | 2 | 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Meconium stain subjects affected / exposed occurrences (all) | Additional description: Prolonged observation neonate because of Apgar Score 4/7/9 and meconium-stained amniotic fluid | | |
| | 1 / 60 (1.67%) | 0 / 44 (0.00%) | |
| | 1 | 0 | |
| Moaning neonatal subjects affected / exposed occurrences (all) | Additional description: Observation neonate due to moaning after vacuum-assisted delivery | | |
| | 1 / 60 (1.67%) | 0 / 44 (0.00%) | |
| | 1 | 0 | |
| Streptococcus test positive subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) | 3 / 44 (6.82%) | |
| | 1 | 3 | |
| | | | |
| Apgar score low subjects affected / exposed occurrences (all) | Additional description: Prolonged observation neonate because of Apgar Score 1/6/8 | | |
| | 2 / 60 (3.33%) | 0 / 44 (0.00%) | |
| | 2 | 0 | |
| SSRI use mother subjects affected / exposed occurrences (all) | Additional description: Prolonged observation neonate due to birth >24h after rupture of membranes and due to use of medication mother (Selective serotonin reuptake inhibitors) | | |
| | 1 / 60 (1.67%) | 1 / 44 (2.27%) | |
| | 1 | 1 | |
| Premature baby subjects affected / exposed occurrences (all) | Additional description: Prolonged observation neonate due to premature delivery with glucose checks neonate because of small for gestational age | | |
| | 2 / 60 (3.33%) | 0 / 44 (0.00%) | |
| | 2 | 0 | |
| Small for dates baby subjects affected / exposed occurrences (all) | Additional description: Prolonged observation neonate with glucose checks neonate because of small for gestational age. | | |
| | 3 / 60 (5.00%) | 6 / 44 (13.64%) | |
| | 3 | 6 | |
| Infection susceptibility increased subjects affected / exposed occurrences (all) | Additional description: Prolonged observation neonate due to birth >24h after rupture of membranes of maternal fever during labor | | |
| | 12 / 60 (20.00%) | 6 / 44 (13.64%) | |
| | 12 | 6 | |
| Macrosomia subjects affected / exposed occurrences (all) | Additional description: Prolonged observation neonate with glucose checks neonate because of large for gestational age. | | |
| | 8 / 60 (13.33%) | 8 / 44 (18.18%) | |
| | 8 | 8 | |
| Puerperal infection | | | |

| | | | |
|--|--|---------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 60 (1.67%) 1 | 1 / 44 (2.27%) 1 | |
| Nervous system disorders Postspinal headache subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 44 (2.27%) 1 | |
| Blood and lymphatic system disorders Post partum hemorrhage | Additional description: Prolonged hospital stay because of postpartum hemorrhage of 2.4 liter due to vaginal tear and uterine atony. Hemoglobin postpartum 3.6 mmol/l for which the patient received 3 packed cells | | |
| subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 44 (2.27%) 1 | |
| neonatal anemia subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 44 (2.27%) 1 | |
| Renal and urinary disorders Bladder dysfunction | Additional description: Prolonged hospital stay due to urine retention of the mother | | |
| subjects affected / exposed occurrences (all) | 2 / 60 (3.33%) 2 | 2 / 44 (4.55%) 2 | |
| Metabolism and nutrition disorders Hyperbilirubinaemia neonatal subjects affected / exposed occurrences (all) | 0 / 60 (0.00%) 0 | 1 / 44 (2.27%) 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 15 October 2015 | Inclusion criteria changed to including small for gestational age fetuses (estimated fetal weight < p10) |
| 15 March 2016 | Implementation of a modified method to monitor fECG. |
| 23 March 2017 | Asking patients enrolled in the study to fulfill a short questionnaire about how they feel about their labor. |

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.

13 women in the intervention group did not receive oxygen administration for >5 minutes.

20 women were included while having exclusion criteria.

Healthcare providers were not blinded for the allocation to the intervention or control group.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/33345953>

<http://www.ncbi.nlm.nih.gov/pubmed/33049730>