Doxapram in preterm newborns

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24880

Source
Nationaal Trial Register

Brief title
DOXA Trial

Health condition

Apnea of prematurity, respiratory insufficiency

Sponsors and support

Primary sponsor: Erasmus University Medical Center Rotterdam
Source(s) of monetary or material Support: ZonMw, Goed Gebruik Geneesmiddelen

Intervention

Outcome measures

Primary outcome

Death or severe disability at the age of 2 years corrected age.

Disability will be defined as 1 or more of the following:
- cognitive delay
- cerebral palsy
- severe hearing loss
- bilateral blindness

Secondary outcome

- BPD at 36 weeks post menstrual age
- Death at the age of 36 weeks post menstrual age and at hospital discharge
- Short term neonatal co-morbidity : Incidence of endotracheal intubations after start study medication; number of days on invasive ventilation; number of days on ventilatory support; number of days with supplemental oxygen; length of stay on the intensive care; cumulative number of apnea , number of incidents associated with bradycardia; incidence of late onset sepsis; solitary intestinal perforation; necrotizing enterocolitis > stage 2 according to Bell; IVH; PVL; Growth, length, head circumference at 36 weeks PMA; retinopathy of prematurity
- Additional long term outcome at 2 years corrected age; readmissions since first discharge home; weight, length and head circumference at 24 months; behavioral problems
- Parent reported outcome with the PARCA-R questionnaire
- Long term follow-up until the age of 5.5 and 8 years to determine long term effects on neurodevelopment , health, quality of life.
- Adverse-effects and potential adverse drug reactions will be monitored and analyzed.

Study description

Background summary

Preterm infants often suffer from apnea of prematurity (AOP; a cessation of breathing) due to immaturity of the respiratory system. AOP can lead to oxygen shortage and a low heart rate which might harm the development of the newborn, especially the central nervous system. In order to prevent oxygen shortage, infants are treated with non-invasive respiratory support and caffeine. Despite these treatments, many preterm newborns still suffer from AOP and may need invasive mechanical ventilation. Although this will result in complete resolution of AOP, invasive mechanical ventilation has the disadvantage of being a major risk of chronic lung disease and impaired neurodevelopmental outcome. Restrictive invasive ventilation is therefore advocated nowadays in preterm infants.
Doxapram is a respiratory stimulant that has been administered off-label to treat AOP. Doxapram, as add-on treatment, seems to be effective in treating AOP and to prevent invasive mechanical ventilation. It is unclear if a preterm infant benefit from doxapram treatment on the longer term. This study compares doxapram to placebo and hypothesizes that doxapram will protect preterm infants from both invasive ventilation (and related lung disease) and AOP related oxygen shortage (and related impaired brain development).

The main objective of the trial is to investigate if doxapram is safe and effective in reducing the composite outcome of death and neurodevelopmental impairment/severe disability at 2 years corrected age as compared to placebo. This multicenter double blinded randomized placebo-controlled superiority trial will be conducted in neonatal intensive care units in the Netherlands and Belgium, including 8 years follow-up. After written informed-consent the patients will be randomized into the doxapram treatment group or the placebo treatment group. Randomization will be stratified based on center and gestational age < or >= 26

weeks.

Study objective

This study hypothesizes that doxapram will protect preterm infants from both invasive ventilation (and related lung disease) and apnea of prematurity related hypoxia (and related impaired brain development).

Study design

Baseline, 36 weeks of postmenstrual age, hospital discharge, and follow-up at 2, 5.5 and 8 years.

Intervention

Blinded continuous doxapram or placebo (glucose 5%) infusion as long as needed. Therapy is down titrated or stopped based on the patients' condition. If endotracheal intubation is needed study drug is stopped. After extubation study drug may be restarted. Switch to gastro-enteral administration is allowed if no iv-access is needed for other reasons.

Contacts

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Eligibility criteria

Inclusion criteria

- Admitted to the NICU of one of the participating centres
- Written informed consent of both parents or legal representatives
- Gestational age at birth < 29 weeks
- Caffeine therapy, adequately dosed

- Optimal non-invasively supported according to the local treatment policy (with nasal CPAP or ventilation ((S)NIPPV, NIV-NAVA, BIPAP/Duopap, SIPAP)
- Apnea that require a medical intervention as judged by the attending physician

Exclusion criteria

- previous use of open label doxapram
- use of theophylline (to replace doxapram)
- chromosomal defects (e.g. trisomy 13, 18, or 21)
- major congenital malformations that: compromise lung function (e.g. surfactant protein deficiencies, congenital diaphragmatic hernia); result in chronic ventilation (e.g. Pierre Robin sequence); increase the risk of death or adverse neurodevelopmental outcome (congenital cerebral malformations, chromosomal abnormalities); palliative care or treatment limitations because of high risk of impaired outcome

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2020
Enrollment:	398
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Yes

Plan description
https://dmponline.dcc.ac.uk/plans/31885/export.pdf

Ethics review

Positive opinion

Date:	15-01-2020
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8288
Other	METC Erasmus MC : MEC2020xxx

Study results